EMDEX

Based on WHO Model Formulary

The Complete

DRUG FORMULARY

For Nigeria's Health Professionals

With Guide to Drug Administration

First Published in 1991

PDF

2006 Edition

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Differentiating information from the WHO Model Formulary (WMF).

As with the print edition, most of the drug product monographs have been reproduced from the WMF (WHO Model Formulary) plus the introductory clinical notes containing guidance on selecting the right medicine for a range of conditions. Appendices 1 to 5 are also reproduced directly from the WMF.

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At the end of a drug monograph, the WHO and/or EDL (Essential Drug List for Nigeria) recommended formula is provided accordingly. This is followed by the proprietary preparations of that particular drug which are approved for use in Nigeria.

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Name changes

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The following name changes, based on the Recommended International Non-proprietary Name (rINN) for medicinal substances, are adopted from the BNF. The new names are also in accordance with those used in the WMF (WHO Model Formulary) 2004 edition. The former names have been retained as synonyms in EMDEX 2006 edition.
The list has been restricted to those names covered in the current edition of EMDEX.

Former Name	rINN
•adrenaline	epinephrine
•amethocaine	tetracaine
•amoxycillin	amoxicillin
•amphetamine	amfetamine
•amylobarbitone	amobarbital
•amylobarbitone sodium	amobarbital sodium
•beclomethasone	beclometasone
•Bendrofluazide	bendroflumethiazide
•benzhexol	trihexyphenidyl
•benztropine	benzatropine
•busulphan	busulfan
•butobarbitone	butobarbital
•cephalexin	cefalexin
•cephradine	cefradine
•chlorbutol	chlorobutanol
•chlormethiazole	clomethiazole
•chlorpheniramine	chlorphenamine
•chlorthalidone	chlortalidone
•cholecalciferol	colecalciferol
•cholestyramine	colestyramine
•clomiphene	clomifene
•corticotrophin	corticotropin
•cyclosporin	ciclosporin
•dimethicone(s)	dimeticone
•dimethyl sulphoxide	dimethyl sulfoxide
•doxycycline HCl (hemihydrate hemiethanolate)	doxycycline hyclate
•ethinyloestradiol	ethinylestradiol
•flumethasone	flumetasone
•flupenthixol	flupentixol

Former Name	rINN
•frusemide	furosemide
•guaiphenesin	guaifenesin
•indomethacin	indometacin
•lignocaine	lidocaine
•methylene blue	methylthioninium chloride
•nicoumalone	acenocoumarol
•noradrenaline	epinephrine
•oestradiol	estradiol
•oestriol	estriol
•oestrone	estrone
•phenobarbitone	phenobarbital
•pramoxine	pramocaine
•procaine penicillin	procaine benzylpenicillin
•riboflavine	riboflavin
•salcatonin	calcitonin (salmon)
•sodium calciumedetate	sodium calcium edetate
•sodium cromoglycate	sodium cromoglicate
•stilboestrol	diethylstilbestrol
•sulphacetamide	sulfacetamide
•sulphadiazine	sulfadiazine
•sulphamethoxazole	sulfamethoxazole
•sulphapyridine	sulfapyridine
•sulphasalazine	sulfasalazine
•sulphathiazole	sulfathiazole
•sulphinpyrazone	sulfinpyrazone
•thiabendazole	tiabendazole
•thiopentone	thiopental
•thyroxine sodium	levothyroxine sodium
•urofollitrophin	urofollitropin

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General Advice to Prescribers

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-Rational approach to therapeutics
-Variation in dose response
-Adherence (compliance) with drug treatment
-Adverse effects and interactions
-Prescription writing
-Sample prescription

Rational approach to therapeutics

Drugs should only be prescribed when they are necessary, and in all cases the benefit of administering the medicine should be considered in relation to the risks involved. Bad prescribing habits lead to ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and harm to the patient, and higher cost. The Guide to Good Prescribing. Geneva: WHO; 1994 provides undergraduates with important tools for training in the process of rational prescribing.

The following steps will help to remind prescribers of the rational approach to therapeutics.

1. **Define the patient's problem**
   Whenever possible, making the right diagnosis is based on integrating many pieces of information: the complaint as described by the patient; a detailed history; physical examination; laboratory tests; X-rays and other investigations.
   This will help in rational prescribing, always bearing in mind that diseases are evolutionary processes.
2. **Specify the therapeutic objective**
   Doctors must clearly state their therapeutic objectives based on the pathophysiology underlying the clinical situation. Very often physicians must select more than one therapeutic goal for each patient.
3. **Selecting therapeutic strategies**
   The selected strategy should be agreed with the patient; this agreement on outcome, and how it may be achieved, is termed concordance. The selected treatment can be non-pharmacological and/or pharmacological; it also needs to take into account the total cost of all therapeutic options.

a) **Non-pharmacological treatment**
   It is very important to bear in mind that the patient does not always need a drug for treatment of the condition. Very often, health problems can be resolved by a change in life style or diet, use of physiotherapy or exercise, provision of adequate psychological support, and other non–pharmacological treatments; these have the same importance as a prescription drug, and instructions must be written, explained and monitored in the same way.

b) Pharmacological treatment

- *Selecting the correct group of drugs*
  Knowledge about the pathophysiology involved in the clinical situation of each patient and the pharmacodynamics of the chosen group of drugs, are two of the fundamental principles for rational therapeutics.
- *Selecting the drug from the chosen group*
  The selection process must consider benefit/risk/cost information. This step is based on evidence about maximal clinical benefits of the drug for a given indication (efficacy) with the minimum production of adverse effects (safety).
  It must be remembered that each drug has adverse effects and it is estimated that up to 10% of hospital admissions in industrialized countries are due to adverse effects.
  Not all drug-induced injury can be prevented but much of it is caused by inappropriate selection of drugs.
  In cost comparisons between drugs, the cost of the total treatment and not only the unit cost of the drug must be considered.
- *Verifying the suitability of the chosen pharmaceutical treatment for each patient*
  The prescriber must check whether the active substance chosen, its dosage form, standard dosage

schedule and standard duration of treatment are suitable for each patient. Drug treatment should be individualized to the needs of each patient.

- *Prescription writing*
  The prescription is the link between the prescriber, the pharmacist (or dispenser) and the patient so it is important for the successful management of the presenting medical condition. This item is covered in more detail in the following section.
- *Giving information, instructions and warnings*
  This step is important to ensure patient adherence and is covered in detail in the following section.
- *Monitoring treatment*
  Evaluation of the follow up and the outcome of treatment allows the stopping of it (if the patient's problem is solved) or to reformulate it when necessary. This step gives rise to important information about the effects of drugs contributing to building up the body of knowledge of pharmacovigilance, needed to promote the rational use of drugs.

Variation in dose response

Success in drug treatment depends not only on the correct choice of drug but on the correct dose regimen. Unfortunately drug treatment frequently fails because the dose is too small or produces adverse effects because it is too large. This is because most texts, teachers and other drug information sources continue to recommend standard doses.

The concept of a standard or 'average' adult dose for every medicine is firmly rooted in the mind of most prescribers. After the initial 'dose ranging' studies on new drugs, manufacturers recommend a dosage that appears to produce the desired response in the majority of subjects. These studies are usually done on healthy, young male Caucasian volunteers, rather than on older men and women with illnesses and of different ethnic and environmental backgrounds. The use of standard doses in the marketing literature suggest that standard responses are the rule, but in reality there is considerable variation in drug response. There are many reasons for this variation which include adherence (see below), drug formulation, body weight and age, composition, variation in absorption, distribution, metabolism and excretion, variation in pharmacodynamics, disease variables, genetic and environmental variables.

Drug formulation

Poorly formulated drugs may fail to disintegrate or to dissolve. Enteric-coated drugs are particularly problematic, and have been known to pass through the gastrointestinal tract intact. Some drugs like digoxin or phenytoin have a track record of formulation problems, and dissolution profiles can vary not only from manufacturer to manufacturer but from batch to batch of the same company. The problem is worse if there is a narrow therapeutic to toxic ratio, as changes in absorption can produce sudden changes in drug concentration. For such drugs quality control surveillance should be carried out.

Body weight and age

Although the concept of varying the dose with the body weight or age of children has a long tradition, adult doses have been assumed to be the same irrespective of size or shape. Yet adult weights vary two to threefold, while a large fat mass can store large excesses of highly lipid soluble drugs compared to lean patients of the same weight.

Age changes can also be important. Adolescents may oxidize some drugs relatively more rapidly than adults, while the elderly may have reduced renal function and eliminate some drugs more slowly.

DOSE CALCULATION IN CHILDREN

Children's doses may be calculated from adult doses by using age, body weight, or body surface area, or by a combination of these factors. The most reliable methods are those based on body surface area; these methods are used for calculating the doses of very toxic drugs.

Body weight may be used to calculate doses expressed in mg/kg. Young children may require a higher dose per kilogram than adults because of their proportionately higher metabolic capacity. Other problems need to be considered. For example, calculation by body weight in an obese child may result in much higher doses being administered than necessary; in such cases, dose should be calculated from an ideal weight, related to height and age.

Body surface area (BSA) estimates are more accurate for calculation of paediatric doses than body weight because many physiological phenomena correlate better with body surface area. The average body surface area of a 70-kilogram human is about 1.8 m2 . Thus, to calculate the dose for a child the following formula may be used:

$$\text{Approximate dose for patient} = \frac{\text{surface area of child } (m^2)}{1.8} \times \text{adult dose}$$

Nomograms are available to allow more precise body surface values to be calculated from a child's height and weight.

Where the dose for children is not readily available, prescribers should seek specialist advice before prescribing for a child.

Physiological and pharmacokinetic variables

Drug absorption rates may vary widely between individuals and in the same individual at different times and in different physiological states. Drugs taken after a meal are delivered to the small intestine much more slowly than in the fasting state, leading to much lower drug concentrations. In pregnancy gastric emptying is also delayed, while some drugs may increase or decrease gastric emptying and affect absorption of other drugs.

Drug distribution

Drug distribution varies widely: fat soluble drugs are stored in adipose tissue, water soluble drugs are distributed chiefly in the extracellular space, acidic drugs bind strongly to plasma albumin and basic drugs to muscle cells. Hence variation in plasma albumin levels, fat content or muscle mass may all contribute to dose variation. With very highly albumin bound drugs like warfarin, a small change of albumin concentration can produce a big change in free drug and a dramatic change in drug effect.

Drug metabolism and excretion

Drug metabolic rates are determined both by genetic and environmental factors. Drug acetylation shows genetic polymorphism, whereby individuals fall clearly into either fast or slow acetylator types. Drug oxidation, however, is polygenic, and although a small proportion of the population can be classified as very slow oxidizers of some drugs, for most drugs and most subjects there is a normal distribution of drug metabolizing capacity, and much of the variation is under environmental control.

Many drugs are eliminated by the kidneys without being metabolized. Renal disease or toxicity of other drugs on the kidney can therefore slow excretion of some drugs.

Pharmacodynamic variables

There is significant variation in receptor response to some drugs, especially central nervous system responses, for example pain and sedation. Some of this is genetic, some due to tolerance, some due to interaction with other drugs and some due to addiction, for example, morphine and alcohol.

Disease variables

Both liver disease and kidney disease can have major effects on drug response, chiefly by the effect on metabolism and elimination respectively (increasing toxicity), but also by their effect on plasma albumin (increased free drug also increasing toxicity). Heart failure can also affect metabolism of drugs with rapid hepatic clearance (for example lidocaine, propranolol). Respiratory disease and hypothyroidism can both impair drug oxidation.

Enviromental variables

Many drugs and environmental toxins can induce the hepatic microsomal enzyme oxidizing system (MEOS) or cytochrome P450 oxygenases, leading to more rapid metabolism and elimination and ineffective treatment. Environmental pollutants, anaesthetic drugs and other compounds such as pesticides can also induce metabolism. Diet and nutritional status also impact on pharmacokinetics. For example in infantile malnutrition and in malnourished elderly populations drug oxidation rates are decreased, while high protein diets, charcoal cooked foods and certain other foods act as metabolizing enzyme inducers. Chronic alcohol use induces oxidation of other drugs, but in the presence of high circulating alcohol concentrations drug metabolism may be inhibited.

Adherence (compliance) with drug treatment

It is often assumed that once the appropriate drug is chosen, the prescription correctly written and the medication correctly dispensed, that it will be taken correctly and treatment will be successful. Unfortunately this is very often not the case, and physicians overlook one of

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the most important reasons for treatment failure—poor adherence (compliance) with the treatment plan.

There are sometimes valid reasons for poor adherence—the drug may be poorly tolerated, may cause obvious adverse effects or may be prescribed in a toxic dose. Failure to adhere with such a prescription has been described as 'intelligent non-compliance'. Bad prescribing or a dispensing error may also create a problem, which patients may have neither the insight nor the courage to question. Even with good prescribing, failure to adhere to treatment is common. Factors may be related to the patient, the disease, the doctor, the prescription, the pharmacist or the health system and can often be avoided.

Low-cost strategies for improving adherence increase effectiveness of health interventions and reduce costs. Such strategies must be tailored to the individual patient.

Health care providers should be familiar with techniques for improving adherence and they should employ systems to assess adherence and to determine what influences it.

Patient reasons

In general, women tend to be more adherent than men, younger patients and the very elderly are less adherent, and people living alone are less adherent than those with partners or spouses. Specific education interventions have been shown to improve adherence. Patient disadvantages such as illiteracy, poor eyesight or cultural attitudes (for example preference for traditional or alternative medicines and suspicion of modern medicine) may be very important in some individuals or societies; as may economic factors. Such disabilities or attitudes need to be discussed and taken account of.

Disease reasons

Conditions with a known worse prognosis (for example cancer) or painful conditions (for example rheumatoid arthritis) elicit better adherence rates than asymptomatic 'perceived as benign' conditions such as hypertension. Doctors should be aware that in most settings less than half of patients initiated on antihypertensive drug treatment are still taking it a year later. Similarly, in epilepsy, where events may occur at long intervals, adherence is notoriously unsatisfactory.

Doctor reasons

Doctors may cause poor adherence in many ways—by failing to inspire confidence in the treatment offered, by giving too little or no explanation, by thoughtlessly prescribing too many medicines, by making errors in prescribing, or by their overall attitude to the patient.

The doctor-patient interaction

There is considerable evidence that this is crucial to concordance. 'Satisfaction with the interview' is one of the best predictors of good adherence. Patients are often well informed and expect a greater say in their health care. If they are in doubt or dissatisfied they may turn to alternative options, including 'complementary medicine'. There is no doubt that the drug 'doctor' has a powerful effect to encourage confidence and perhaps contribute directly to the healing process.

Prescription reasons

Many aspects of the prescription may lead to non-adherence (non-compliance). It may be illegible or inaccurate; it may get lost; it may not be refilled as intended or instructed for a chronic disease. Also, the prescription may be too complex; it has been shown that the greater the number of medications the poorer the adherence, while multiple doses also decrease adherence if more than two doses per day are given. Not surprisingly adverse effects like drowsiness, impotence or nausea reduce adherence and patients may not admit to the problem.

Pharmacist reasons

The pharmacist's manner and professionalism, like the doctor's, may have a positive impact, supporting adherence, or a negative one, raising suspicions or concerns. This has been reported in relation to generic drugs when substituted for brand-name drugs. Pharmacist information and advice can be a valuable reinforcement, as long as it agrees with the doctor's advice.

The health care system

The health care system may be the biggest hindrance to adherence. Long waiting times, uncaring staff, uncomfortable environment, exhausted drug supplies and so on, are all common problems in developing countries, and have a major impact on adherence. An important problem is the distance and accessibility of the clinic from the patient. Some studies have confirmed the obvious, that patients furthest from the clinic are least likely to adhere to treatment in the long term.

Recommendations

- Review the prescription to make sure it is correct.
- Spend time explaining the health problem and the reason for the drug.
- Establish good rapport with the patient.
- Explore problems, for example difficulty with reading the label or getting the prescription filled.
- Encourage patients to bring their medication to the clinic, so that tablet counts can be done to monitor compliance.
- Encourage patients to learn the names of their medicines, and review their regimen with them. Write notes for them.
- Keep treatment regimens simple.
- Communicate with other health care professionals, to develop a team approach and to collaborate on helping and advising the patient.
- Involve the partner or another family member.
- Listen to the patient.

Adverse effects and interactions

Adverse drug reactions

An adverse drug reaction (ADR) may be defined as 'any response to a drug which is noxious, unintended and occurs at doses normally used for prophylaxis, diagnosis, or therapy...'. ADRs are therefore unwanted or unintended effects of a medicine, including idiosyncratic effects, which occur during its proper use. They differ from accidental or deliberate excessive dosage or drug maladministration, (see section 4 for the treatment of poisoning).

ADRs may be directly linked to the properties of the drug in use, the so-called 'A' type reactions. An example is hypoglycaemia induced by an antidiabetic drug. ADRs may also be unrelated to the known pharmacology of the drug, the 'B' type reactions including allergic effects, for example anaphylaxis with **penicillins**.

Thalidomide marked the first recognized public health disaster related to the introduction of a new drug. It is now recognized that clinical trials, however thorough, cannot be guaranteed to detect all adverse effects likely to be caused by a drug. Health workers are thus encouraged to record and report to their national pharmacovigilance centre any unexpected adverse effects with any drug to achieve faster recognition of serious related problems. For example, from reports received in one country, a relationship was established between **thioacetazone** and Stevens-Johnson syndrome when the drug was used in HIV infection, leading to the withdrawal of the drug in that country.

Major factors predisposing to adverse effects

It is well known that different patients often respond differently to a given treatment regimen. For example, in a sample of 2422 patients who had been taking combinations of drugs known to interact, only 7 (0.3%) showed any clinical evidence of interactions. In addition to the pharmaceutical properties of the drug therefore, there are characteristics of the patient which predispose to ADRs.

EXTREMES OF AGE

The very old and the very young are more susceptible to ADRs. Drugs which commonly cause problems in the elderly include hypnotics, diuretics, non-steroidal anti-inflammatory drugs, antihypertensives, psychotropics and digoxin.

All children, and particularly neonates, differ from adults in their response to drugs. Some drugs are likely to cause problems in neonates (for example morphine), but are generally tolerated in children. Other drugs (for example valproic acid) are associated with increased risk of ADRs in children of all ages. Other drugs associated with problems in children include chloramphenicol (grey baby syndrome), antiarrhythmics (worsening of arrhythmias), acetylsalicylic acid (Reye syndrome).

INTERCURRENT ILLNESS

If besides the condition being treated the patient suffers from another disease, such as kidney, liver or heart disease, special precautions may be necessary to prevent ADRs. Remember also that, as well as the above factors, the genetic make-up of the individual patient may predispose to ADRs.

DRUG INTERACTIONS

Interactions (see also Appendix 1) may occur between drugs which compete for the same receptor or act on the same physiological system. They may also occur indirectly when a drug-induced disease or a change in fluid or electrolyte balance alters the response to another drug.

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Interactions may occur when one drug alters the absorption, distribution or elimination of another drug, such that the amount which reaches the site of action is increased or decreased.

Drug-drug interactions are some of the commonest causes of adverse effects. When two drugs are administered to a patient, they may either act independently of each other, or interact with each other. Interaction may increase or decrease the effects of the drugs concerned and may cause unexpected toxicity. As newer and more potent drugs become available, the number of serious drug interactions is likely to increase. Remember that interactions which modify the effects of a drug may involve non-prescription drugs, non-medicinal chemical agents, and social drugs such as **alcohol, marijuana, tobacco, and traditional remedies**, as well as certain types of food for example grapefruit juice. The physiological changes in individual patients, caused by such factors as age and gender, also influence the predisposition to ADRs resulting from drug interactions.

The following table lists drugs under the designation of specific cytochrome P450 isoforms. A drug appears in a column if there is published evidence that it is metabolized, at least in part, via that isoform. Alterations in the rate of the metabolic reaction catalyzed by that isoform are likely to have effects on the pharmacokinetics of the drug.

Incompatibilities between drugs and intravenous fluids

Drugs should not be added to blood, amino acid solutions or fat emulsions. Certain drugs, when added to intravenous fluids, may be inactivated by pH changes, by precipitation or by chemical reaction. Benzylpenicillin and ampicillin lose potency after 6–8 hours if added to dextrose solutions, due to the acidity of these solutions. Some drugs bind to plastic containers and tubing, for example diazepam and insulin . Aminoglycosides are incompatible with penicillins and heparin . Hydrocortisone is incompatible with heparin, tetracycline , and chloramphenicol.

Adverse effects caused by traditional medicines

Patients who have been or are taking traditional herbal remedies may develop ADRs. It is not always easy to identify the responsible plant or plant constituent. Refer to the drug and toxicology information service if available and/or to suitable literature.

The effect of food on drug absorption

Food delays gastric emptying and reduces the rate of absorption of many drugs; the total amount of drug absorbed may or may not be reduced. However, some drugs are preferably taken with food, either to increase absorption or to decrease the irritant effect on the stomach.

Prescription writing

A prescription is an instruction from a prescriber to a dispenser. The prescriber is not always a doctor but can also be a paramedical worker, such as a medical assistant, a midwife or a nurse. The dispenser is not always a pharmacist, but can be a pharmacy technician, an assistant or a nurse. Every country has its own standards for the minimum information required for a prescription, and its own laws and regulations to define which drugs require a prescription and who is entitled to write it. Many countries have separate regulations for prescriptions for controlled drugs such as opioid analgesics.

The following guidelines will help to ensure that prescriptions are correctly interpreted and leave no doubt about the intention of the prescriber. The guidelines are relevant for primary care prescribing; they may, however, be adapted for use in hospitals or other specialist units.

Prescription form

The most important requirement is that the prescription be clear. It should be legible and indicate precisely what should be given. The local language is preferred.

The following details should be shown on the form:

- The prescriber's name, address and telephone number. This will allow either the patient or the dispenser to contact the prescriber for any clarification or potential problem with the prescription.
- Date of the prescription. In many countries the validity of a prescription has no time limit, but in some countries pharmacists do not dispense drugs on prescriptions older than 3 to 6 months.
- Name, form and strength of the drug. The International Nonproprietary Name of the drug should always be used. If there is a specific reason to prescribe a special brand, the trade name can be added.

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CYTOCHROME P450 DRUG INTERACTION TABLE

			SUBSTRATES			
CYP1A2	CYP2B6	CYP2C19	CYP2C9	CYP2D6	CYP2E1	CYP3A4, 5, 7
Theophylline	Cyclophosphamide	Amitriptyline	Ibuprofen	Amitriptyline	Alcohol	Chlorphenamine
	Efavirenz	Clomipramine	Phenytoin	Clomipramine	Paracetamol	Ciclosporin
		Cyclophosphamide	Sulfamethoxazole	Codeine		Diazepam
		Diazepam	Tamoxifen	Haloperidol		Erythromycin
		Phenobarbital	Warfarin	Tamoxifen		Haloperidol
		Phenytoin		Timolol		Indinavir
						Nifedipine
						Quinidine
						Quinine
						Ritonavir
						Saquinavir
						Tamoxifen
						Verapamil
						Vincristine
			INHIBITORS			
1A2	2B6	2C19	2C9	2D6	2E1	3A4
Ciprofloxacin			Isoniazid	Chlorphenamine		Erythromycin
				Clomipramine		Grapefruit juice
				Haloperidol		Indinavir
				Quinidine		Nelfinavir
				Ritonavir		Ritonavir
						Saquinavir
						Verapamil
			INDUCERS			
1A2	2B6	2C19	2C9	2D6	2E1	3A4
Tobacco	Phenobarbital		Rifampicin		Alcohol	Carbamazepine
	Rifampicin				Isoniazid	Phenobarbital
						Phenytoin
						Rifampicin

Generic substitution is allowed in some countries. The pharmaceutical form (for example ‘tablet’, ‘oral solution’, ‘eye ointment’) should also be stated.

- The strength of the drug should be stated in standard units using abbreviations that are consistent with the Système Internationale (SI). ‘Microgram’ and ‘nanogram’ should not, however, be abbreviated. Also, ‘units’ should not be abbreviated. Avoid decimals whenever possible. If unavoidable, a zero should be written in front of the decimal point.
- Specific areas for filling in details about the patient including name, address and age.

Directions

Directions specifying the route, dose and frequency should be clear and explicit; use of phrases such as ‘take as directed’ or ‘take as before’ should be **avoided**.

For preparations which are to be taken on an ‘as required’ basis, the minimum dose interval should be stated together with, where relevant, the maximum daily dose. It is good practice to qualify such prescriptions with the purpose of the medication (for example ‘every 6 hours as required for pain’, ‘at night as required to sleep’).

It is good practice to explain the directions to the patient; these directions will then be reinforced by the label on the medicinal product and possibly by appropriate counselling by the dispenser. It may be worthwhile giving a written note for complicated regimens although it must be borne in mind that the patient may lose the separate note.

Quantity to be dispensed

The quantity of the medicinal product to be supplied should be stated such that it is not confused with either the strength of the product or the dosage directions.

Alternatively, the length of the treatment course may be stated (for example ‘for 5 days’).

Wherever possible, the quantity should be adjusted to match the pack sizes available.

For liquid preparations, the quantity should be stated in millilitres (abbreviated as ‘ml’) or litres (preferably not abbreviated since the letter ‘l’ could be confused with the figure ‘1’).

Narcotics and controlled substances

The prescribing of a medicinal product that is liable to abuse requires special attention and may be subject to specific statutory requirements. Practitioners may need to be authorized to prescribe controlled substances; in such cases it might be necessary to indicate details of the authority on the prescription.

Sample prescription

PRESCRIPTION

Dr. C. Emdex
Lagos,
Nigeria
Tel: 480 7654

Date: _____

Name of patient _____ Date of birth_____

Address _____ Sex _____

_____

_____

Rx

For use by dispensary

1. Central nervous system (CNS) drugs

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1.1 Drugs used in anxiety and sleep disorders
1.1.1 Barbiturates
1.1.2 Benzodiazepines
1.1.3 Chloral derivatives
1.1.4 Others
1.2 Drugs used in psychotic disorders
1.3 Antidotes to antipsychotic drugs
1.4 Drugs used in mood disorders
1.4.1 Drugs used in depressive disorders
1.4.2 Drugs used in bipolar disorders
1.5 Obsessive-compulsive disorders and panic attacks
1.6 Antiparkinson drugs
1.6.1 Drugs used in parkinsonism
1.6.2 Drugs used in essential tremor and related disorders
1.7 Anticonvulsants (Antiepileptics)
1.7.1 Control of epilepsy
1.8 Analgesics
1.8.1 Non-opioid analgesics and antipyretics
1.8.2 Opioid analgesics
1.9 Drugs used in the treatment of migraine
1.9.1 Acute migraine attack
1.9.1.1 Analgesics
1.9.1.2 Ergot alkaloid
1.9.1.3 Antiemetic
1.9.2 Migraine prophylaxis
1.10 Drugs used in the treatment of obesity

1.1 Drugs used in anxiety and sleep disorders

1.1.1 Barbiturates
1.1.2 Benzodiazepines
1.1.3 Chloral derivatives
1.1.4 Others

The most widely used anxiolytics and hypnotics are the benzodiazepines. Treatment of anxiety should be limited to the lowest effective Dose for the shortest possible time. The cause of insomnia should be established and appropriate treatment for underlying factors instituted before hypnotics are considered. Hypnotics may be of value for a few days but rarely longer than a week.

Tolerance and dependence (both physical and psychological) and subsequent difficulty in withdrawing the drug may occur after regular use for more than a few weeks. Patients with chronic anxiety, alcohol or drug dependence or those with personality disorders are more likely to become dependent. Anxiolytics and hypnotics should be prescribed in carefully individualized dosage and use should be limited to control of acute conditions such as panic attacks and acute anxiety and severe, incapacitating insomnia. There is usually no justification for prolonging treatment with anxiolytics and hypnotics for more than one to two weeks.

If used for longer periods, withdrawal should be gradual by reduction of the Dose over a period of weeks or months, as abrupt discontinuation may produce confusion, toxic psychosis, convulsions or a condition resembling delirium tremens. The benzodiazepine withdrawal syndrome may develop at any time up to 3 weeks after stopping a long-acting benzodiazepine but may occur within a few hours in the case of a short-acting one. The syndrome is characterized by insomnia, anxiety, loss of appetite and body-weight, tremor, perspiration, tinnitus and

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perceptual disturbances. These symptoms may be similar to the original complaint and encourage further prescribing. Some symptoms may continue for weeks or months after stopping benzodiazepines. Patients should be warned that their ability to drive or operate machinery may be impaired and that the effects of alcohol may be enhanced.

1.1.1 Barbiturates

AMYLOBARBITONE

Therapeutic category: Hypnotic; Barbiturate
Indication: Intractable insomnia
Contra-indications, Precautions, etc: See Phenobarbitone
Advice to patients: See Label 19 in Appendix 6.
Dose: By mouth, Adult, 100-200mg at bedtime.
Child: Not recommended
See lit. for details

POM **Amylobarbitone** *(EDL 25.1)*
Tablet or Capsule, Amylobarbitone (as Sodium Salt) 200mg.
Injection Amylobarbitone (as Sodium Salt) 250mg; powder in vial.

1.1.2 Benzodiazepines

BROMAZEPAM

Indications: Acute tension and anxiety states; difficulties in interpersonal contact, insomnia, anxious depressive reactions; functional disturbances in the cardiovascular, respiratory, GI and genitourinary Systems.
Contra-indications, Precautions, etc: See diazepam.
Advice to patients: See Label 2 in Appendix 6.
Dose: Usually 1.5-3 mg 2-3 times daily; may be increased depending on response and/or severity.

POM **Bromazepam** *(EDL 25.1)*
Tablets, Bromazepam 1.5 mg, 3 mg.

POM **LEXOTAN®** *(Swipha)*
Tablets, Bromazepam 1.5 mg, 3 mg; scored tabs.
1.5 mg - 30; 500.
3 mg - 30; 500.

CHLORDIAZEPOXIDE

Pharmacology: Chlordiazepoxide is rapidly and completely absorbed following oral administration and this leads to a rapid clinical response. In contrast, i.m. administration results in delayed and possibly incomplete absorption of the active metabolites. Thus it is probably wise to avoid using this drug i.m. Elimination is significantly slower in the elderly.
Indications: Acute and chronic anxiety states, obsessive compulsive neurosis and panic states, alcoholic psychosis.
Contra-indications, Precautions, etc: See Diazepam.
Advice to patients: See Label 2 or 19 in Appendix 6.
Nursing considerations: •Give with food or milk to reduce GI upset; may crush tablet if patient has difficulty swallowing.
•Ensure patient swallows medication.
•Raise bed rails; initiate safety measures; aid with ambulation.
•Relieve dry mouth with frequent sips of water, hard candy or sugarless gum.
•Advise patient to make position changes slowly as fainting may occur, especially in elderly; to avoid abrupt discontinuation after prolonged use, may precipitate seizures.
•Inform patient drug is not for everyday stress and should not be used for more than 4 months without doctor's prescription; not to use more than prescribed amount, may be habit forming.
•Warn patient to avoid activities that require mental alertness and physical coordination until the CNS effects of the drug are established; to avoid alcohol and other CNS depressants, unless prescribed.
•Monitor female patient for pregnancy; drug should not be used during pregnancy.
•Monitor patient on long-term medication for signs of dependency or withdrawal symptoms namely headache, nausea, vomiting, muscle pain, weakness.
Dose: 20-40 mg daily in divided Doses; up to 50-100 mg in severe cases.
See lit. for details.

POM **LIBRIUM®** *(Swipha)*
Capsule, Chlordiazepoxide 10 mg; light-green/black caps.
10 mg - 25.

DIAZEPAM

Pharmacology: Has similar properties to Chlordiazepoxide, but is a more potent tranquillizer and a better anticonvulsant. Absorption after oral administration is rapid and complete, peak plasma levels being reached in 30—90 minutes. An earlier peak occurs in children; a delayed and lower one is seen in the elderly. Absorption is faster from the suspension than from tablets. Following rectal administration, plasma levels are only 50% of those obtained with the same Dose by mouth.

Poor and irregular absorption occurs after i.m. administration. Plasma levels are only 60% of those attained with the same oral Dose. Following i.m. administration, drowsiness and slurred speech occur in a few minutes, and there is a short but definite interval between i.v. injection and the appearance of these effects. The drug should be administered very slowly, the rate being titrated against patient's response, to avoid giving an overDose.

Diazepam is highly protein bound and has plasma half–life of 1–2 days.

Diazepam is a drug of choice in the treatment of status epilepticus in a Dose of 5—10 mg I.V., repeated if necessary.

In the treatment of tetanus, the drug may be given in a Dose of 30–40 mg/day in divided Doses by mouth or nasogastric tube, or I.V. in 10 mg Doses as required.

Indications: Short-term treatment of anxiety or insomnia; premedication in anaesthesia (section 3.2); status epilepticus, recurrent seizures; febrile convulsions, adjunct in acute alcohol withdrawal.

Contra-indications: Myasthenia gravis; respiratory depression, acute pulmonary insufficiency, sleep apnoea, severe hepatic impairment, encephalopathy, shock, coma, acute alcohol intoxication, acute narrow-angle glaucoma, psychoses.

Precautions: Respiratory disease, muscle weakness, history of alcohol or drug abuse, marked personality disorder; pregnancy (Appendix 2); breastfeeding (Appendix 3); reduce Dose in elderly or debilitated and in hepatic impairment (avoid if severe, Appendix 5), renal impairment (Appendix 4); avoid prolonged use and abrupt withdrawal; porphyria; **interactions**: Appendix 1

SKILLED TASKS. MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING

Adverse effects: Drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, salivation changes, gastrointestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention; blood disorders and jaundice; skin reactions; raised liver enzymes

Advice to patients: See Label 2 or 19 in Appendix 6.

Nursing considerations: •Give with food or milk to reduce GI upset; may crush tablet if patient has difficulty swallowing - avoid crushing sustained-release medications.
•Ensure patient swallows medication.
•Give I.V. slowly (not more than 5 mg per minute); monitor respirations frequently.
•Observe the I.V. injection site for phlebitis; do not inject into small veins to minimize the risk of extravasation.
•I.M. injection is painful and absorption is variable; I.V. route is more reliable.
•Provide safety measures (i.e., side rails, night light, and call button); supervise ambulation.
•Relieve dry mouth with frequent sips of water, hard candy or sugarless gum.
•Advise patient to make position changes slowly as fainting may occur, especially in elderly; to avoid abrupt discontinuation after prolonged use.
•Inform patient drug is not for everyday stress and should not be used for more than 4 months without doctor's prescription; not to use more than prescribed amount, may be habit forming.
•Warn patient to avoid activities that require mental alertness and physical coordination until the CNS effects of the drug are established; to avoid alcohol and other CNS depressants, unless prescribed.
•Monitor patient on long-term medication for signs of dependency or withdrawal symptoms namely headache, nausea, vomiting, muscle pain, weakness.

Dose: By mouth, *Anxiety*, 2-5 mg 2-3 times daily; Elderly, half the Adult Dose.
Insomnia: 5-10 mg before going to bed.
Child: *night terrors and somnabulism*, 1-5 mg before going to bed.
Premedication in anaesthesia, 10-20 mg on the evening before.
By I.M. or slow I.V injection (not more than 5 mg per min.), *severe anxiety*, 10 mg, repeated if necessary after 4 hours.
Child, *Febrile convulsions*, 2-10 mg depending on age .
See lit. for details.

POM **Diazepam** *(WMF 24.3)*
Tablets, Diazepam 2 mg, 5 mg.

POM **Diazepam** *(EDL 25.1)*
Tablets, Diazepam 2 mg, 5 mg, 10 mg.
Syrup, Diazepam 2 mg per 5 ml
Injection, Diazepam 5 mg per ml; in 2 ml amp.

POM **ASSIVAL®** *(Dizpharm)*
Tablet, Diazepam 5 mg
5 mg – 1000
Injection, Diazepam 5 mg per ml; in 2 ml amp.
Pack - 100.

POM **CALMPOSE®** *(Ranbaxy)*
Injection, Diazepam 10 mg per 2 ml.
Pack - 100 x 2 ml.

POM **Diazepam** *(Emzor)*
Tablets, Diazepam 2 mg, 5 mg, 10 mg; all yellow scored tabs.

POM **Diazepam** *(Juhel)*
Tablet, Diazepam 5 mg.
5 mg - 1000.

POM **VALINEX–5®** *(Vitabiotics)*
Tablet, Diazepam 5 mg; yellow tablet.
5 mg – 1000's.

POM **VALIUM®** *(Swipha)*
Tablets, Diazepam 5 mg, light-yellow scored tab. marked 'ROCHE 5'.
5 mg - 12; 96; 500.
Injection, Diazepam 10 mg per 2 ml.
Pack - 10.

FLUNITRAZEPAM

Pharmacology: It is readily absorbed from the GIT, 77 to 80% protein bound, extensively metabolised in the liver and excreted mainly in urine as metabolites. It has long half–life and hence, a tendency to cause cumulative and residual effects such as excessive drowsiness,
Therapeutic category: Hypnotic.
Indication: Insomnia.
Contra-indications, Precautions, etc: See diazepam.
Advice to patients: See Label 19 in Appendix 6.
Dose: Adult, 1-2 mg at night
Elderly, 0.5-1 mg at night.

POM **Flunitrazepam** *(EDL 25.1)*
Tablet, Flunitrazepam 1mg.

POM **ROHYPNOL®** *(Swipha)*
Tablet, Flunitrazepam 1 mg; scored tab.
1 mg - 30.

LORAZEPAM

Pharmacology: Lorazepam is one of the newer benzodiazepines, which is effective when given orally, i.m. or i.v. Following oral administration, a peak concentration occurs at 2 hours and this corresponds to the time when clinical effects are maximal.
The elimination half–life is 12 hours and conjugation with glucuronide to form an inactive substance is the major mechanism of lorazepam clearance. Time to peak plasma concentration following i.m. administration is about 3 hours while I.V. administration is followed by a "latency of action" of about 5 minutes prior to the onset of clinical effects.
It is probably a useful drug in the elderly and in liver disease, since it is not hydroxylated or demethylated.
Therapeutic category: Antianxiety Agent; Anticonvulsant; Antiemetic; Benzodiazepine; Sedative.
Indications: Anxiety disorders and short-term relief of the symptoms of anxiety or insomnia.
Contra-indications, Precautions, etc.: see Diazepam.
Advice to patients: See Label 2 or 19 in Appendix 6.
Nursing considerations: •Give drug with food or milk to minimize GI symptoms; crush drug if patient is unable to swallow it whole.
•Ensure patient swallows medication.
•Provide safety measures (i.e., side rails, night light, and call button). Assist patient with ambulation since drowsiness and dizziness may occur.
•Give patient sips of water for dry mouth.
•Advise patient to make position changes slowly as fainting may occur, especially in elderly; to avoid abrupt discontinuation after prolonged use, may precipitate seizures. Female patient of child-bearing age should use birth control.
•Inform patient drug is not for everyday stress and should not be used for more than 4 months without doctor's prescription; not to use more than prescribed amount, may be habit forming.
•Warn patient to avoid activities that require mental alertness and physical coordination until the CNS effects of the drug are established; to avoid alcohol and other CNS depressants, unless prescribed.
•Monitor patient on long-term medication for signs of dependency or withdrawal symptoms namely headache, nausea, vomiting, muscle pain, weakness.
Dose: By mouth, *Anxiety*, 2 -3 mg in divided Doses. *Insomnia*, 1-2 mg usually at bedtime.

POM **Lorazepam** *(EDL 25.1)*
Tablets, Lorazepam 1 mg, 2.5 mg.

POM **ATIVAN®** *(Wyeth/Delpitano)*
Tablets, Lorazepam 1 mg (blue oblong scored tab. marked A1); 2.5 mg (yellow oblong scored tab. marked A2.5).
1 mg - 100
2.5 mg - 100.

MIDAZOLAM

See under Section 3.2.
Midazolam is a new benzodiazepine available for i.v. use. It is given as water–soluble drug and does not damage veins on injection. It has an elimination half–life of 2 hours and no active metabolites. In comparison with diazepam, it has greater amnesic properties.

NITRAZEPAM

Pharmacology: It rapidly induces sleep, lasting

6-8 hours, but accumulation of the drug occurs, since its plasma half–life is 20—31 hours. It is nontoxic in overDose and for this reason has become very popular. A drug with a shorter half–life should replace nitrazepam as the hypnotic of first choice.

Indications: Most etiological forms of insomnia, especially:

- Purely psychogenic insomnia caused by irritability, nervous tension, overwork, conflicts, worrying or anxiety;
- Insomnia of neurotic or psychotic origin, possibly in conjunction with specific treatment of any organic condition.

Contra-indications: Myasthenia gravis.

Precautions: Elderly, pregnancy; may potentiate the effects of centrally acting drugs; patient should be advised to avoid alcoholic drinks.

Advice to patients:See Label 19 in Appendix 6.

Dose: Adult, 5-10 mg at night.
Elderly, 2.5-5 mg at night.
Child (under 1 year), up to 2.5 mg; 1- 5 years, 2.5-5 mg; 6-14 years, 5 mg.
To be swallowed whole or dissolved in liquid.

POM **Nitrazepam** *(EDL 25.1)*
Tablet or Capsule, Nitrazepam 5 mg.

POM **SWIDON®** *(Swipha)*
Tablet, Nitrazepam 5 mg; off-white scored tab.
5 mg - 10.

POM **SOMNAPAM®** *(Vitabiotics)*
Tablet, Nitrazepam 5 mg.
5 mg - 20's.

OXAZEPAM

Pharmacology: It is one of the main metabolites of diazepam and is used as an anxiolytic drug. Oxazepam does not undergo hydroxylation or demethylation in the liver, but is conjugated and then excreted. It may be safer therefore, to use in the elderly or in patients with liver disease.

Therapeutic category: Anxiolytic.

Indications: Short-term relief of symptoms of anxiety.

Contra-indications, Precautions, etc: See Diazepam.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: •See under Lorazepam.

Dose: By mouth, *Anxiety*, 10-30 mg 3-4 times daily.
Reduce Dose in the elderly.

POM **SEREPAX®** *(Wyeth/Delpitano)*
Tablet, Oxazepam 15mg; yellow pentagonal tab. marked WYETH/317 and 5/15.
Capsules, Oxazepam 10mg, white/pink cap. coded 10/15; 15mg, white/red cap. coded 15/6; 30mg, white/maroon cap. coded 30/52. All marked SEREPAX and maker's symbol.
10 mg - 100; 500
15 mg - 100; 500
30 mg - 100; 500

1.1.3 Chloral derivatives

Chloral Hydrate

A chlorinated derivative of ethyl alcohol usually given in solution or as a capsule, since it is irritant to the stomach. It is rapidly absorbed from the small intestine and rapidly reduced in the red cells, liver and kidney to trichloroethanol, which is responsible for the hypnotic action—unchanged parent drug cannot be detected in plasma. This is then conjugated with glucuronic acid to an inert form which is excreted by the kidneys. The average plasma half–life in humans is 8 hours. Following ingestion, sleep occurs in about 15 - 30 minutes and lasts from 6 to 8 hours, there then being little hangover.

It should not be co–administered with anticoagulants, as well as with alcohol.

CHLORAL HYDRATE

Therapeutic category: Sedative/hypnotic

Indication: Short-term use in insomnia

Contra-indications: Hepatic or renal impairment; severe cardiac disease; gastritis.

Precautions: Pregnancy, breast-feeding; reduce Dose in elderly and debilitated; respiratory disease; avoid contact with skin and mucous membrane; hangover effect.

Adverse effects: Gastric irritation, light-headedness, ataxia, nightmares, excitement, confusion, allergic reactions.

Advice to patients: See Labels 19 and 27 in Appendix 6

Nursing considerations: •Give at bedtime on empty stomach with full glass of water or juices for best absorption and to decrease corrosion, or after meals to reduce GI discomfort.
•Ensure patient swallows medication.
•Apply safety measures such as side railing or cot sides; assist with ambulation.
•Teach patient to avoid driving or activities requiring alertness; to avoid alcohol and other CNS depressants; and to avoid abrupt discontinuation after prolonged use.
•Monitor patient on long-term medication for signs of dependency namely frequent requests for the drug, tremors, anxiety, pinpoint pupils.

Dose: *Hypnotic*, 0.5-2 g at night. Child:

RETURN

30-50 mg/kg up to a max. single Dose of 1 g. *Sedative*, 250 mg 3 times daily up to a maximum 2 g daily. Child: 8 mg/kg 3 times daily.
To be taken well diluted with water or milk.

POM **Chloral Hydrate** *(EDL 25.1)*
Mixture, Chloral hydrate 500mg per 5ml.
Mixture (Paediatric), Chloral hydrate 200mg per 5ml.

1.1.4 Others

Chlormezanone

Has anxiolytic, hypnotic, muscle relaxant and analgesic properties, but is chemically distinct from other anxiolytics. It may be a useful hypnotic in the elderly being free from hangover. Routine use is undesirable and dependence occurs.

Propranolol

Propranolol and other beta–blockers are effective in alleviating the palpitations, diarrhoea and tremor which accompany anxiety and apprehension. They do not affect psychological symptoms (worry, tension, fear) and non-autonomic symptoms (muscle tension). They are preferably indicated for patients with predominantly somatic symptoms. Beware: this may, in turn, prevent the onset of worry and fear.

CHLORMEZANONE

Therapeutic category: Tranquillizer.
Indications Short-term treatment of mild anxiety and tension states.
Contra-indications:Acute pulmonary insufficiency, respiratory depression, porphyria.
Precautions: Renal or hepatic impairment, pregnancy, breast-feeding, respiratory disease.
Adverse effects: Drowsiness, nausea, dry mouth, drug rash, cholestatic jaundice, inability to void, weakness, excitement, tremor, confusion and headache.
Advice to patients: See Label 2 or 19 in Appendix 6.
Dose: Adult, 400 mg at bedtime; elderly, 200 mg at bedtime.

POM **Chlormezanone** *(EDL 25.1)*
Tablet, Chlormezanone 200 mg.

POM **TRANCOPAL®** *(GSK)*
Tablet, Chlormezanone 200 mg; white tab. 200 mg - 20; 100.

1.2 Drugs used in psychotic disorders

Treatment of psychotic disorders is both pharmacological and psychosocial. Individual and community programmes for relearning old skills and developing new ones and for learning to cope with the illness should be initiated. Classes of antipsychotic drugs include phenothiazines (for example chlorpromazine), butyrophenones (for example haloperidol), thioxanthenes (for example flupentixol) and newer 'atypical' neuroleptics including clozapine and risperidone. The various antipsychotic drugs do not, in general, differ in their antipsychotic activity, but differ in range and quality of adverse effects (see below).

ACUTE PHASE TREATMENT

The administration of **chlorpromazine** or **haloperidol** will relieve symptoms such as thought disorder, hallucinations and delusions and prevent relapse. They are usually less effective in apathetic, withdrawn patients. However, haloperidol may restore an acutely ill schizophrenic, who was previously withdrawn, or even mute and akinetic, to normal activity and social behaviour. In the acute phase chlorpromazine may be administered by intramuscular injection in a Dose of 25–50 mg which can be repeated every 6–8 hours while observing the patient for possible hypotension. In most cases, however, the intramuscular injection is not needed and patients can be treated with an oral Dose. Haloperidol may be administered in the acute phase.

MAINTENANCE THERAPY

Long-term treatment in patients with a definite diagnosis of schizophrenia may be necessary after the first episode to prevent the manifest illness from becoming chronic.

The lowest possible Dose of antipsychotic drug that will prevent major exacerbations of florid symptoms is used for long-term management. Too rapid a Dose reduction should be avoided. Intramuscular depot preparations such as **fluphenazine decanoate** may be used as an alternative to oral maintenance therapy especially when compliance with oral treatment is unreliable. Exacerbations of illness in patients on maintenance drug therapy can be precipitated by stress.

Withdrawal of maintenance drug treatment requires careful surveillance since it is not possible to predict the course of the disease and the patient may suffer a relapse if treatment is withdrawn inappropriately. Further, the need for continuation of treatment may not be evident on withdrawal of treatment because relapse may be delayed for several weeks.

ADVERSE EFFECTS

They are very common with long-term administration of antipsychotic medicines. Hypotension and interference with temperature regulation, neuroleptic malignant syndrome and bone-marrow depression are the most life-threatening. Hypotension and interference with temperature regulation are Dose-related. They can result in dangerous falls and hypothermia in the elderly and this must be considered before prescribing these drugs for patients over 70 years of age.

Extrapyramidal symptoms are the most troublesome and are caused most frequently by the piperazine phenothiazines such as fluphenazine, the butyrophenones such as haloperidol and the depot preparations. Although easily recognized, they are not so easy to predict because they depend in part on the Dose and patient susceptibility as well as the type of drug. However, there is a general tendency for low-potency drugs to have less extrapyramidal adverse effects, while high-potency drugs such as haloperidol have more extrapyramidal effects but less sedation and anticholinergic (more correctly antimuscarinic) effects. Sedation and anticholinergic effects usually diminish with continued use. Extrapyramidal symptoms consist of parkinsonian-type symptoms including tremor which may occur gradually; dystonia (abnormal face and body movements) and dyskinesia, which may appear after only a few Doses; akathisia (restlessness), which may occur after large initial Doses and may resemble an exacerbation of the condition being treated; and tardive dyskinesia (an orofacial dyskinesia), which usually takes longer to develop but may develop on short-term treatment with low Doses; short-lived tardive dyskinesia may occur after withdrawal of the drug. Parkinsonian symptoms are usually reversible on withdrawal of the drug and may be suppressed by anticholinergic (antimuscarinic) drugs but they may unmask or worsen tardive dyskinesia. Tardive dyskinesia is usually associated with long-term treatment and high dosage of an antipsychotic, particularly in elderly patients (see section 1.6.2). There is no established treatment for tardive dyskinesias, which may be irreversible on withdrawing therapy. However, withdrawal at the earliest signs of tardive dyskinesia may halt its full development. Treatment of all patients on antipsychotics must be carefully and regularly reviewed.

Neuroleptic malignant syndrome (hypothermia, fluctuating levels of consciousness, muscular rigidity, and autonomic dysfunction with pallor, tachycardia, labile blood pressure, sweating and urinary incontinence) is a rare adverse effect of haloperidol and chlorpromazine. It is managed by discontinuing the antipsychotic, correcting fluid and electrolyte defects, and giving bromocriptine and sometimes dantrolene.

CHLORPROMAZINE

Chlorpromazine is a representative antipsychotic. Various drugs can serve as alternatives

Warning: Owing to the risk of contact sensitization, pharmacists, nurses, and other health workers should avoid direct contact with chlorpromazine; tablets should not be crushed and solutions should be handled with care

Indications: Schizophrenia and other psychotic disorders, mania, psychomotor agitation and violent behaviour; adjunct in severe anxiety

Contra-indications: Impaired consciousness due to CNS depression; bone-marrow depression; phaeo-chromocytoma

Precautions: Cardiovascular and cerebrovascular disorders, respiratory disease, parkinsonism, epilepsy, acute infections, pregnancy (Appendix 2), breastfeeding (Appendix 3), renal and hepatic impairment (avoid if severe; Appendices 4 and 5), history of jaundice, leukopenia (blood counts if unexplained fever or infection); hypothyroidism, myasthenia gravis, prostatic hypertrophy, angle-closure glaucoma; elderly (particularly in very hot or very cold weather); avoid abrupt withdrawal; patients should remain supine and the blood

pressure monitored for 30 minutes after intramuscular injection; **interactions**: Appendix 1

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING

Adverse effects: Extrapyramidal symptoms and on prolonged administration, occasionally potentially irreversible tardive dyskinesias (see notes above); hypothermia (occasionally pyrexia), drowsiness, apathy, pallor, nightmares, dizziness, excitement, insomnia, headache, confusion, depression; more rarely, agitation, EEG changes, convulsions, nasal congestion; anticholinergic symptoms including dry mouth, constipation, blurred vision, difficulty in micturition; hypotension, tachycardia and arrhythmias; ECG changes; respiratory depression; menstrual disturbances, galactorrhoea, gynaecomastia, impotence, weight gain; sensitivity reactions such as agranulocytosis, leukopenia, leukocytosis, haemolytic anaemia, photosensitization, contact sensitization and rashes, jaundice and alterations in liver function; neuroleptic malignant syndrome; lupus erythematosus-like syndrome; with prolonged high dosage, corneal and lens opacities, and purplish pigmentation of the skin, cornea and retina; intramuscular injection may be painful and cause hypotension and tachycardia (see Precautions) and nodule formation.

Nursing considerations: •Give with full glass of water, milk or with food to reduce GI upset.

•I.M. injection may sting; give deep I.M. only in upper outer quadrant of buttocks and massage slowly to prevent sterile abscess. Avoid SC injection.

•Observe for orthostatic hypotension, especially with parenteral administration; keep patient supine for 1 hour after I.M. injection. Teach patient that orthostatic hypotension is common, therefore, to rise from sitting or lying positions slowly.

•Supervise ambulation, until patient becomes stabilized on medication.

•Relieve dry mouth with chewing gum or sips of water.

•Increase fluid and bulk in diet to prevent constipation; dilute liquid preparations with water, fruit juice or milk before oral administration.

•Avoid contact of oral solution or injection with skin and clothing (contact dermatitis).

•Teach patient not to involve in strenuous exercise or stand still for long periods to avoid fainting.

•Teach patient not to stop taking drug abruptly (may cause EPS) unless informed by the physician; to avoid alcohol and other CNS depressants, may cause increased drowsiness. Antacids can only be taken 2 hours before or after this drug.

•Observe extrapyramidal symptoms of akathisia (inability to sit still and no pattern to movements), tardive dyskinesia (bizarre movement of the jaw, mouth, tongue, and extremities), pseudoparkinsonism (rigidity, tremors, pill rolling and shuffling gait).

•Withhold therapy and notify the physician if patient develops jaundice, symptoms of blood dyscrasias (fever, sore throat, infection, cellulitis, weakness), persistent extrapyramidal reactions, or any such reactions during pregnancy or in children.

•Advise patient to report urine retention or constipation; drug may turn urine pink or red.

•Photosensitivity reactions can be prevented with sun screening agents and protective clothing.

Dose: *Schizophrenia and other psychoses, mania, psychomotor agitation, violent behaviour, and severe anxiety (adjunct),* by mouth, ADULT initially 25 mg 3 times daily (or 75 mg at night) adjusted according to response to usual maintenance Dose of 100–300 mg daily (but up to 1.2 g daily may be required in psychoses);
ELDERLY (or debilitated) third to half adult Dose;
CHILD (*childhood schizophrenia and autism*) 1–5 years 500 micrograms/kg every 4–6 hours (maximum 40 mg daily); 6–12 years, third to half adult Dose (maximum 75 mg daily)
For relief of acute symptoms, by deep intramuscular injection, ADULT 25–50 mg every 6–8 hours; CHILD 500 micrograms/kg every 6–8 hours (1–5 years, maximum 40 mg daily; 6–12 years, maximum 75 mg daily) (see also Precautions and Adverse effects)

POM **Chlorpromazine** *(WMF 24.1)*
Tablets, Chlorpromazine HCl 100 mg.
Syrup, Chlorpromazine HCl 25 mg per 5 ml
Injection (Solution for injection), Chlorpromazine HCl 25 mg per ml; in 2 ml amp.

POM **Chlorpromazine** *(EDL 25.3)*
Tablets, Chlorpromazine HCl 25 mg, 50 mg, 100 mg.
Syrup, Chlorpromazine HCl 25 mg per 5 ml
Injection, Chlorpromazine HCl 25 mg per ml; in 2 ml amp.

POM **LARGACTIL®** *(May & Baker)*
Tablets, Chlorpromazine HCl 25 mg, 50 mg, 100 mg; white f-c tabs. marked with LG and tab. strength.
25 mg—500.

50 mg - 50; 500
100 mg - 50; 500
Injection, Chlorpromazine HCl 25 mg per ml; in 2 ml amp.
2 ml x 10.

CLOPENTHIXOL

Therapeutic category: Thioxanthene antipsychotic
Indications: Psychoses especially Schizophrenia.
Contra-indications, Precautions, etc.: See Chlorpromazine.
Advice to patients: See Label 2 in Appendix 6.
Dose: By mouth, initially 20-30 mg daily in divided Doses; Maintenance, 20-50 mg daily; max. 150 mg daily.
By deep i.m. injection, initially 100 mg as a test Dose, then 200-400 mg 2-4 weekly; adjust according to patients response.
Not recommended for children.

POM **Clopenthixol** *(EDL 25.3)*
Tablets, Clopenthixol HCl 2 mg, 10 mg, 25 mg.
Injection, Clopenthixol (as decanoate) 200 mg per ml; oily.

CLOZAPINE

Pharmacology: A potentially serious adverse reaction caused by Clozapine therapy is granulocytopenia and agranulocytosis. In view of this risk, the use of Clozapine should be limited to schizophrenic patients who are nonresponsive to or intolerant of conventional antipsychotic drug treatment and in whom regular haematological examinations can be performed.
Clozapine is unique in that it produces virtually no major extrapyramidal reactions such as acute dystonia; parkinsonian-like side effects and akathisia are rare, and no case of tardive dyskinesia has been reported. Unlike other neuroleptics, clozapine produces little or no prolactin elevation and hence, does not have adverse effects such as gynaecomastia, amenorrhoea, galactorrhoea, and impotence.
Indications: Schizophrenia in patients who are non-responsive to or intolerant of classical neuroleptic.
Contra-indications: Previous hypersensitivity to clozapine, history of drug–induced granulocytopenia/agranulocytosis; impaired bone marrow function; uncontrolled epilepsy; alcoholic and other toxic psychoses, drug intoxication, comatose conditions; circulatory collapse and/or CNS depression of any causes; severe hepatic, renal, or cardiac failure; pregnancy, breast-feeding.
Precautions: Before starting treatment, a white blood cell (WBC) count and a differential blood must be performed to ensure that only patients with normal leucocyte findings will receive the drug. After starting treatment, WBC count must be monitored weekly for 18 weeks and thereafter at least monthly as long as the patient is on the drug. Withdraw treatment if leucocyte count falls below 3000/mm^3 and/or the absolute neutrophil granulocyte count drops below 1500/mm^3; patients should report any kind of infection or fever; avoid drugs which depress leucopoiesis; patients with history of seizures; cardiovascular, renal or hepatic disorders, reduce Dose (avoid if severe); prostatic enlargement, paralytic ileus and narrow–angle glaucoma (due to its anticholinergic activity); avoid in children; avoid abrupt withdrawal.
Adverse effects: Granulocytopenia and agranulocytosis; fatigue, drowsiness, sedation, headache; extrapyramidal symptoms, EEG changes, reduce seizure threshold; dry mouth, blurred vision, hypersalivation; tachycardia and postural hypotension (with or without syncope); ECG changes rarely cardiac arrhythmias, pericarditis, and myocarditis; respiratory depression or arrest; GI disturbances, urinary incontinence and urinary retention; benign hyperthermia; rarely hyperglycaemia and increases in CPK values.
Advice to patients: See Label 2 in Appendix 6.
Nursing considerations: Ensure patient swallows medication; check for possible hoarding.
•Supervise ambulation until stabilised on medication.
•Increase intake of fluids and bulk in diet to avoid constipation, especially in elderly.
•Offer sips of water or chewing gum for dry mouth.
•Inform patient weekly blood tests is mandatory to monitor for agranulocytosis; to report sore throat, malaise, fever, bleeding, mouth sores or any other signs of infection.
•Advise patient to rise from sitting or lying positions slowly and to avoid standing still for long periods; to avoid driving or other hazardous activities; seizures may occur.
•Benign, self-limiting temperature elevations sometimes occur during the first 3 weeks of treatment.
•Teach patient to avoid OTC preparations (cough or cold remedies), alcohol or CNS depressants; not to stop taking medication abruptly because EPS may occur.
Dose: By mouth, initially, 12.5 mg 1-2 times daily on first day (elderly 12.5 mg once daily); followed by 25-50 mg on the second day; increased slowly as required by 25-50 mg daily (elderly 25 mg) over 2-3 weeks to 300 mg daily in divided

Doses (larger Dose at night; up to 200 mg daily may be given as a single Dose at bedtime).
Therapeutic Dose range for psychotic patients, 300-450 mg daily (max. 900 mg) in divided Doses; maintenance Dose, 150-300 mg daily.

POM **LEPONEX**® *(Novartis)*
Tablets, Clozapine 25 mg, 100 mg.

FLUPENTHIXOL

Therapeutic category: Thioxanthene antipsychotic
Pharmacology: Flupenthixol differs from the phenothiazines in that it has a significant mood–elevating effect. Extrapyramidal symptoms are the commonest adverse effects.
Indications: Psychoses, but not in overactive patients.
Contra-indications, Precautions, etc.: See under Chlorpromazine.
Advice to patients: See Label 2 in Appendix 6.
Dose: By mouth, 3-9 mg 2 times daily; up to a max. 18 mg daily.
By deep i.m. injection, initially 20 mg as a test Dose, then after 5-10 days, 20-40 mg 2-4 weekly; adjust according to the response.

POM **Flupenthixol** *(EDL 25.3)*
Tablets, Flupenthixol HCl 1.5 mg, 3 mg.
Injections, Flupenthixol decanoate 20 mg, 100 mg per ml; oily.

FLUPHENAZINE

Fluphenazine is a representative depot antipsychotic, used if compliance unlikely to be reliable. Various drugs can serve as alternatives.
Indications: Maintenance treatment of schizophrenia and other psychoses
Contra-indications: Children; confusional states; impaired consciousness due to CNS depression; parkinsonism; intolerance to anti-psychotics; depression; bone-marrow depression; phaeochromocytoma
Precautions: Treatment requires careful monitoring for optimum effect; initial small test Dose as adverse effects are prolonged; extrapyramidal symptoms occur frequently; when transferring from oral to depot therapy, dosage by mouth should be reduced gradually; cardiovascular and cerebrovascular disorders, respiratory disease, epilepsy, acute infections, pregnancy (Appendix 2), breastfeeding (Appendix 3), renal and hepatic impairment (avoid if severe; Appendices 4 and 5), history of jaundice, leukopenia (blood counts if unexplained fever or infection); hypothyroidism, myasthenia gravis, prostatic hypertrophy, angle-closure glaucoma; elderly (particularly in very hot or very cold weather); **interactions**: Appendix 1.
SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.
Adverse effects: As for Chlorpromazine HCl (see above), but less sedating and fewer hypotensive and anticholinergic symptoms; higher incidence of extrapyramidal symptoms (most likely to occur a few hours after injection and continue for about 2 days but may be delayed); systemic lupus erythematosus; pain at injection site, occasionally erythema, swelling, nodules.
Nursing considerations: •Give injection into large muscle mass; to minimise postural hypotension, give injection and keep patient recumbent or seated for 30 min.
•Use a dry needle (to avoid solution becoming cloudy) of at least 21G due to the viscosity fluphenazine decanoate or enanthate injection, which is an oily solution.
•Supervise ambulation until patient is stabilised on medication; patient should not stand for long periods at a time; avoid strenuous activities as fainting may occur.
•Increase fluid intake to prevent constipation and give sips of water or chewing gum for dry mouth.
•Avoid contact of oral solution or injection with skin (contact dermatitis).
•Teach patient not to withdraw drug abruptly to avoid EPS; to avoid OTC preparations or alcoholic beverages and to report sore throat, malaise, fever, bleeding, mouth sores.
•Advise patient to report urine retention or constipation. Drug may turn urine pink or red.
•Photosensitivity reactions can be prevented with sunscreening agents and protective clothing.
Dose: *Maintenance in schizophrenia and other psychoses*, by deep IM injection into gluteal muscle, ADULT test Dose of 12.5 mg (6.25 mg in elderly), then after 4–7 days 12.5–100 mg repeated at intervals of 2–5 weeks, adjusted according to response.
CHILD not recommended.
Administration: According to manufacturer's directions.

POM **Fluphenazine** *(WMF 24.1)*
Oily injection (Solution for injection), Fluphenazine decanoate 25 mg per ml; in

1 ml amp.
Oily injection (Solution for injection), Fluphenazine enantate 25 mg per ml; in 1 ml amp.

POM **Fluphenazine** *(EDL 25.3)*
Injection, Fluphenazine (as decanoate or enanthate) 25 mg per ml; in 1 ml amp.

HALOPERIDOL

Haloperidol is a representative antipsychotic. Various drugs can serve as alternatives.

Indication: Schizophrenia and other psychotic disorders, mania, psychomotor agitation and violent behaviour; adjunct in severe anxiety

Contra-indications: Impaired consciousness due to CNS depression; bone-marrow depression; phaeochromocytoma; porphyria; basal ganglia disease.

Precautions: Cardiovascular and cerebrovascular disorders, respiratory disease, parkinsonism, epilepsy, acute infections, pregnancy (Appendix 2), breastfeeding (Appendix 3), renal and hepatic impairment (avoid if severe; Appendices 4 and 5), history of jaundice, leukopenia (blood count required if unexplained fever or infection); hypothyroidism, myasthenia gravis, prostatic hypertrophy, angle-closure glaucoma; also subarachnoid haemorrhage and metabolic disturbances such as hypokalaemia, hypocalcaemia, or hypomagnesaemia; elderly (particularly in very hot or very cold weather); children and adolescents; avoid abrupt withdrawal; patients should remain supine and the blood pressure monitored for 30 minutes after intramuscular injection; **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: As for Chlorpromazine HCl (see above), but less sedating and fewer hypotensive and anticholinergic symptoms; pigmentation and photosensitivity reactions rare; extrapyramidal symptoms are common, particularly acute dystonia and akathisia (especially in thyrotoxic patients); rarely weight loss, hypoglycaemia, inappropriate antidiuretic hormone secretion.

Nursing considerations: •Give PO with food or milk.
•Give IM inj into large muscle mass using 21G, 2-in needle; not more than 3 ml per inj site; keep patient lying down for at least 30 min after inj.
•Do not use injection that is markedly discoloured; slight yellowing of injection is common.
•Supervise ambulation until patient is stabilised on medication; patient should not stand for long periods at a time; avoid strenuous activities as fainting may occur.
•Increase fluid intake to prevent constipation and give sips of water or chewing gum for dry mouth.
•Teach patient not to withdraw drug abruptly to avoid EPS; to avoid OTC preparations or alcoholic beverages and to report impaired vision, jaundice, tremors, muscle twitching.
•Warn patient to avoid hazardous activities that require mental alertness and physical coordination, and to make position changes slowly to avoid orthostatic hypotension.
•Observe closely for extrapyramidal symptoms of akathisia, tardive dyskinesia and pseudoparkinsonism.

Dose: *Schizophrenia and other psychoses, mania, psychomotor agitation, violent behaviour, and severe anxiety (adjunct)*, by mouth, ADULT initially 1.5–3 mg 2–3 times daily or 3–5 mg 2–3 times daily in severely affected or resistant patients (up to 30 mg daily in resistant schizophrenia);
ELDERLY (or debilitated) initially half adult Dose;
CHILD initially 25–50 micrograms/kg daily in 2 divided Doses (maximum 10 mg daily)
Acute psychotic conditions, by IM injection , ADULT initially 2–10 mg, subsequent Doses every 4–8 hours according to response (up to every hour if necessary) to total maximum of 18 mg; severely disturbed patients may require initial Dose of up to 18 mg; elderly (or debilitated) initially half adult Dose.
CHILD not recommended.

POM **Haloperidol** *(WMF 24.1)*
Tablets, Haloperidol 2 mg, 5 mg.
Injections (Solution for injection), Haloperidol 5 mg per ml; in 1-ml ampoule.

POM **Haloperidol** *(EDL 25.3)*
Tablets, Haloperidol 1.5 mg, 5 mg.
Injections, Haloperidol 2 mg, 5 mg per ml.

POM **HALDOL®** *(CHI)*
Tablets, Haloperidol 1.5 mg, 5 mg, 10 mg; white scored tabs.
1.5 mg - 1000
5 mg - 100; 1000.
10 mg - 20; 100

Injection, Haloperidol 5 mg per ml; in 1 ml amp. Pack - 5.

POM **SERENACE®** *(Morison)*
Tablet, Haloperidol 1.5 mg (white tab. coded 41), 5 mg (pink tab. coded 12). All scored and marked 'SEARLE'.
1.5 mg - 50; 1000
5 mg - 50; 1000.

PIMOZIDE

Therapeutic category: Neuroleptic Agent
Pharmacology: Pimozide is a long–acting and potent antipsychotic with more selective dopamine receptor blocker than chlorpromazine and, therefore, is less sedative.
Indications: Suppression of severe motor and phonic tics in patients with Tourette's disorder.
Contra-indications, Precautions, etc: See Chlorpromazine.
Advice to patients: See Label 2 in Appendix 6. Since Pimoxide may cause serious adverse effects, the patient and his family should be thoroughly informed before a decision is taken, to or not to, take the drug.
Nursing considerations: •Supervise ambulation until patient becomes stabilized on medicadtion.
•Give sips of water or chewing gum to relieve dry mouth.
•Advise patient not to involve in strenous exercise to avoid fainting.
•Warn patient to avoid abrupt discontinuation of therapy and not to exceed the prescribed dose.
•ECG examination before and periodically during therapy is recommended; monitor for prolongd Q-T interval.
•Pimozide may lower the seizure threshold; monitor patient on anticonvulsants for increased seizure activity and notify the doctor.
•Pimozide should be reserved for cases where other agents have failed because it may cause serious adverse effects; patient and his family should be well informed before commencement of therapy.
•Observe closely for extrapyramidal symptoms of akathisia, tardive dyskinesia and pseudoparkinsonism.
Dose: Adult and child (above 12 years), by mouth, initially 1-2 mg daily; then increased as needed every other day to 7-16 mg daily.
Max. Dose: 20 mg daily or 0.3 mg/kg b.wt. daily.

POM **Pimozide** *(EDL 25.3)*
Tablets, Pimozide 4 mg, 10 mg.

POM **ORAP®** *(CHI)*
Tablets, Pimozide 4 mg, 10 mg.

RISPERIDONE

Therapeutic category: Antipsychotic Agent
Indications: Acute and chronic schizophrenia, and other psychotic conditions, in which positive and/or negative symptoms are prominent; also alleviates affective symptoms associated with schizophrenia.
Contra-indications: Known hypersensitivity to risperidone; breast-feeding; children below 15 years.
Precautions: Orthostatic hypotension (alpha-blocking effect); cardiovascular disease; hypotension (reduce Dose); high Dose may cause tardive dyskinesia (give a benzodiazepine for more sedation instead of increasing Dose); Parkinson's disease or epilepsy; weight gain; mental alertness may be impaired; hepatic and renal impairment; pregnancy.
Adverse effects: Insomnia, agitation, anxiety, headache; somnolence, fatigue, dizziness, impaired concentration, constipation, dyspepsia, nausea, abdominal pain, blurred vision, erectile dysfunction, ejaculatory dysfunction, orgasmic dysfunction, rhinitis, rash; low incidence and severity of extra pyramidal symptoms (reversible upon Dose reduction and/or administration of antiparkinson drug); rarely neuroleptic malignant syndrome (discontinue all antipsychotic medication); occasionally orthostatic dizziness, orthostatic hypotension and reflex tachycardia (especially with high initial Doses); hyperprolactinaemia (with galactorrhoea, menstrual disturbances, amenorrhoea, gynaecomastia); rarely water intoxication with hyponatraemia and seizures.
Advise to patients: Ability to drive or operate machinery may be impaired.
Nursing considerations: •Supervise ambulation until patient is stabilised on medication; patient should not stand for long periods at a time; avoid strenuous activities as fainting may occur.
•Increase bulk and fluid in diet if constipation or urinary retention occurs; offer sips of water or chewing gum for dry mouth.
•Warn patient to avoid hazardous activities if drowsy or dizzy, and to make position changes slowly to avoid orthostatic hypotension.
•Teach patient not to stop taking drug abruptly, may cause EPS; to avoid alcohol and other CNS depressants which may cause increased drowsiness.
•Monitor and observe for extrapyramidial effects, orthostatic blood pressure changes for 3-5 days after starting or increasing dose.
Dose: By mouth, Adult and child above 15 years, initially 1 mg twice daily; increased to 2 mg twice daily on Day 2 and 3mg twice daily on Day 3.
Maintenance Dose: 2-4 mg twice daily (max.: 8 mg twice daily). Doses above 5 mg twice daily may increase the risk of extrapyramidal symptoms and may

only be used if benefit considered to outweigh risk.
Elderly, Patients with renal and liver disease, initially, 0.5 mg twice daily; individually adjusted with 0.5 mg twice daily increments to 1-2 mg twice daily.
Not recommended in children below 15 years.

POM **RISPERDAL**® (*Janssen-Cilag*)
Tablets, Risperidone 1 mg, white oblong tab.; 2 mg, pale orange oblong tab.; 3 mg, yellow oblong tab.; 4 mg, green oblong tab.
1 mg - 6.
2 mg - 20.
3 mg - 20.

THIORIDAZINE

Therapeutic category: Antipsychotic/ Anxiolytic.
Pharmacology: Thioridazine is used as a sedative especially in the elderly due to its low propensity to cause extrapyramidal side–effects. At medium and high Doses, thioridazine is effective in controlling severe symptoms of psychotic and non–psychotic mental disorder. It has a strong atropine-like action. Retinal damage may occur in high dosage.
Indications: Schizophrenia and related psychoses, tranquillisation and emergency control in behaviour disturbances, agitation in elderly patients, short-term adjunctive treatment of severe anxiety.
Contra-indications: Comatose states or severe depression of the CNS; history of hypersensitivity to other 'phenothiazines' and of blood dyscrasia; severe cardiovascular disease, children below 1 year of age.
Precautions: Narrow-angle glaucoma, prostatic hypertrophy, cardiovascular disease; road users; liver disease; pregnancy, breast-feeding.
Adverse effects: Nausea, sedation; anticholinergic effects such as nasal stuffiness, dry mouth; allergic skin reactions; neuroleptic malignant syndrome such as muscular rigidity - discontinue the drug; jaundice, weight change, hyperthermia.
Advice to patients: See Label 2 in Appendix 6.
Nursing considerations: •Dilute liquid preparations with water or fruit juice just before giving.
•Keep patient lying down for at least 30 min after IM inj.
•Supervise ambulation until patient is stabilised on medication; patient should not stand for long periods at a time; avoid strenuous activities as fainting may occur.
•Increase fluid/bulk intake to prevent constipation; give sips of water or chewing gum for dry mouth.
•Warn patient to avoid hazardous activities if drowsy or dizzy, and to rise from sitting or lying positions slowly to avoid orthostatic hypotension.
•Teach patient not to withdraw drug abruptly to avoid EPS; to avoid OTC preparations or alcoholic beverages and to report sore throat, malaise, fever, bleeding, mouth sores.
•Avoid contact of liquid preparations with skin and clothing to prevent contact dermatitis; wear glove when diluting liquid dosage forms.
•Photosensitivity reactions can be prevented with sunscreening agents and protective clothing.
Dose: Adult, 25-600 mg daily depending on the indication; up to a max. 800 mg daily. Child (1 year and above), 1-4 mg/kg body-wt. daily. See lit. for details.

POM **Thioridazine** *(EDL 25.3)*
Tablets, Thioridazine HCl 25 mg, 50 mg.
Syrup, Thioridazine HCl 25 mg per 5 ml.

POM **APO-THIORIDAZINE**® *(Lahams)*
Tablet, Thioridazine HCl 100 mg; dark green, f-c tab. marked '100'
100 mg - 100

POM **MELLERIL**® *(Novartis)*
Tablets, Thioridazine HCl 25 mg, 50 mg; white f-c tabs. marked 'MEL' and tab strength.
25 mg - 100
50 mg - 100
Syrup, Thioridazine HCl 25 mg per 5 ml.
Pack - 100 ml.

POM **THIORIL**® *(Hovid)*
Tablets, Thioridazine HCl 25 mg, 100 mg; f-c tabs.
25 mg - 1000
100 mg - 1000.

TRIFLUOPERAZINE

Therapeutic category: Anti-psychotic/ Anxiolytic.
Pharmacology: Trifluoperazine is much more potent than chlorpromazine; it is more rapid in onset of action and has a longer duration of effect. It is a powerful antiemetic and tranquillizer. High incidence of extrapyramidal effects, however, limits its use.
Indications: Acute and chronic Schizophrenia, catatonic hebephrenic and paranoid psychosis due to organic brain damage, toxic psychoses and behaviour disorders in mental subnormality.
Contra-indications: Coma caused by CNS depressants, bone-marrow deression, close-angle glaucoma.
Precautions: Elderly, cardiovascular disease,

parkinsonism, pregnancy, breast-feeding, epilepsy.

Adverse effects: Drowsiness, apathy, insomnia, depression, dry-mouth, nasal congestion, constipation, difficulty in micturition and blurred vision.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: •Watch for hypotension when administering I.M. or I.V.; observe for extrapyramidal effects.

•See also under Chlorpromazine.

Dose: By mouth, *Psychoses*, initially 5 mg twice daily or 10 mg daily in slow-release form; increased by 5 mg after 1 week depending on the response.

Severe anxiety, 2-4 mg daily in divided Doses.

By deep I.M. injection (for acute symptoms), 1-3 mg daily in divided Doses; up to a max. 6 mg daily.

POM **Trifluoperazine** *(EDL 25.3)*

Tablet, Trifluoperazine HCl 1 mg, 5 mg.

Syrup, Trifluoperazine HCl 1 mg per 5 ml.

Injection; Trifluoperazine HCl 1 mg per ml.

POM **APO-TRIFLUOPERAZINE**® *(Lahams)*

Tablets, Trifluoperazine 5 mg; deep blue, f-c tab. marked '5'.

5 mg - 1000

POM **STELAZINE**® *(GSK)*

Tablets, Trifluoperazine (as HCl) 1 mg, 5 mg; blue s-c tabs marked SKF.

1 mg - 20; 50; 1000.

5 mg - 20.

Syrup, Trifluoperazine (as HCl) 1 mg per 5 ml.

Injection, Trifluoperazine (as HCl) 1 mg per ml.

Pack - 1 ml x 10.

1.3 Antidotes to antipsychotic drugs

Extrapyramidal symptoms (EPS) are the most important adverse effect in terms of frequency and the reason for patient's non–compliance with neuroleptic therapy. There are three categories of EPS:

(a) Dystonic reactions involve an acute spasm of muscle group. The high-potency neuroleptic drugs, such as fluphenazine and haloperidol, are more likely to cause dystonic reactions than the low–potency drugs such as thioridazine and chlorpromazine. Usually brief and most responsive to treatment.

(b) Pseudoparkinsonism resembles Parkinson's disease and is of two forms, akinesia and tremor. It is more commonly seen in the elderly, is more likely to be caused by the low–potency neuroleptic drugs, and is generally responsive to treatment.

(c) Akathisia is often difficult to distinguish from psychotic agitation; this can result in the neuroleptic Dose being increased, thus worsening the akathisia. It is the most common and troublesome of all EPS, and is caused more by the high potency neuroleptic drugs.

Tardive dyskinesia is a late–appearing effect that looks like an EPS but in aetiology and treatment is opposite to EPS. It typically appears upon neuroleptic Dose reduction or discontinuation, improves when the neuroleptic Dose is increased, worsens with administration of anticholinergic drugs, and may persist for months or years after neuroleptic drugs are discontinued.

Anticholinergic Drugs Used in EPS: **Benzhexol, Benztropine** and **Biperiden** are all anticholinergic drugs used in the treatment of EPS but not tardive dyskinesia (see notes above); benztropine has also antihistaminic properties.

Benzhexol (trihexyphenidyl) and benztropine are two most commonly used drugs. They are equal in efficacy and adverse effects, but three differences should be noted:

(a) Both are available as 2 mg tablets, but benztropine is twice as potent as benzhexol.

(b) The duration of effect of benztropine is longer than benzhexol, allowing benztropine to be Dosed once daily or at most twice daily. Benzhexol must be Dosed at least three times daily. When benztropine is given once daily, it should be given in the morning. Bedtime dosing is of no value since the extrapyramidal tracts shut down during sleep and EPS is not present during the night.

(c) Benzhexol, unlike benztropine, is subject to abuse since it may cause euphoria along with other possible CNS intoxication symptoms including confusion, delirium, and psychosis Biperiden is rarely used, but is virtually identical to benzhexol.

Parenteral anticholinergic drugs such as benztropine or biperiden are used only for acute dystonic reactions and for single"Dose treatments for other EPS to determine if the symptoms are drug responsive. Benztropine 2 mg i.m. will exert its effect within 20 mins, while the effect of i.v. administration will be apparent within a few minutes. A second i.m. Dose after 20-30 mins is appropriate if the dystonic reaction does not respond. For pseudoparkinsonism and akathisia, oral benztropine 1–2 mg twice daily or benzhexol 2 mg three or four times daily represent usual starting Doses, with the maximum Doses usually being 6mg and 15mg respectively. Occasionally, some patients may require up to

8 mg of benztropine or 20 mg of benzhexol daily, but peripheral anticholinergic effects become troublesome at these Doses.

Anticholinergic prophylaxis (as adjunctive treatment to neuroleptic therapy) is justified when the patient has a history of EPS or is given a high–potency neuroleptic. Prophylaxis is not indicated when low–potency neuroleptic drugs are given or when the neuroleptic Dose is very low.

The duration of anticholinergic prophylaxis depends on the Dose and potency of the neuroleptic drug as well as on the patient response. After about 3 months, the anticholinergic drug Dose should be reduced gradually, and if no EPS recur, the drug should be discontinued.

BENZHEXOL

See under Section 1.5

BENZTROPINE

Therapeutic category: Anticholinergic Agent; Anti-Parkinson's Agent.

Indications: Adjunctive treatment of Parkinson's disease; also used in treatment of drug-induced extrapyramidal effects (except tardive dyskinesia) and acute dystonic reactions.

Contra-indications, Precautions, etc: See under Benzhexol in section 1.5.

Advice to patients: See under Benzhexol

Nursing considerations: •Administer with or after meals to minimize GI upset; may crush tablets and mix with food.

•No significant difference in onset of I.M. or I.V. injection, therefore, there is usually no need to use the I.V. route. Improvement is sometimes noticeable a few minutes after injection.

•Increase bulk, fluid, exercise if constipation occurs; relieve dry mouth with cool drinks, chewing gum or ice chips.

•Notify physician if urinary hesitancy or retention persists. Do not discontinue drug abruptly.

•Teach patient not to stop taking drug abruptly, may cause withdrawal symptoms namely EPS, tremors, insomnia, tachycardia, restlessness; to avoid cough and cold remedies with alcohol, antihistamines unless prescribed.

•Advise patient to avoid hazardous tasks that require mental alertness or physical coordination, as the drug may cause drowsiness; and to make position changes slowly to avoid orthostatic hypotension.

•Observe for intermittent conspitation, distension, abdominal pain (may be onset of paralytic ileus).

•May increase susceptibility to heat stroke; advise patient to limit activities during hot weather.

Dose: *Drug-induced extrapyramidal reaction*, by mouth, I.M. or I.V., Adult, 1-4 mg 1-2 times daily;
Child (above 3 years), 0.02-0.05 mg/kg b.wt. 1-2 times daily;
Acute dystonia, by I.M. or I.V., Adult, 1-2 mg.
Parkinsonism, by mouth, Adult, 0.5-6 mg daily in 1-2 divided Doses;
Elderly, initially 0.5 mg 1-2 times daily; increase by 0.5 mg as needed at 5-6 days interval upto a max. 6 mg daily.

Note: Not recommended for children under 3 years of age except in life threatening emergencies.

POM **Benztropine** *(EDL 25.4)*
Tablet, Benztropine mesylate 2mg
Injection, Benztropine mesylate 1mg per ml.

BIPERIDEN

See under Section 1.5

1.4 Drugs used in mood disorders

1.4.1 Drugs used in depressive disorders
1.4.2 Drugs used in bipolar disorders

Mood disorders can be classified as depression (unipolar disorder) and mania; alternating episodes of mania and depression (manic depression) are termed bipolar disorder.

Electroconvulsive therapy (ECT) has been shown to be rapidly effective in the urgent treatment of severe depression. Counselling and psychotherapy have an important role in treating some forms of depression.

1.4.1 Drugs used in depressive disorders

Tricyclic and related antidepressants and the more recently introduced selective serotonin reuptake inhibitors (SSRIs) are the most widely used drugs in the treatment of depressive disorders. The response to antidepressant therapy is usually delayed with a lag-period of up to two weeks and at least six weeks before maximum improvement occurs. It is important to use Doses that are sufficiently high for effective treatment, but not so high as to cause toxic effects. Low Doses should be used for initial treatment in the elderly. The use of more than one antidepressant at a time is not recommended since this does not enhance effectiveness and it may result in enhanced adverse effects or interactions. Patients should be reviewed every 1–2 weeks at the start of treatment. Treatment should be continued for at least 4 weeks

(6 weeks in the elderly) before considering whether to change to another antidepressant due to lack of efficacy. In the case of a partial response, treatment may be continued for a further 2 weeks (elderly patients may take longer to respond). Remission usually occurs after 3–12 months. Treatment at full therapeutic Dose should be continued for at least 4–6 months after resolution of symptoms (about 12 months in the elderly). Treatment should not be withdrawn prematurely otherwise symptoms are likely to recur. Patients with a history of recurrent depression should continue to receive maintenance treatment (for at least 5 years and possibly indefinitely). Lithium may be used as an alternative for maintenance treatment (see section 1.4.2). Reduction in Dose should be gradually carried out over a period of about 4 weeks or longer if withdrawal symptoms emerge (6 months in patients who have been on long-term maintenance treatment).

Tricyclic and related antidepressants can be divided into those with more or less sedative effect. Those with sedative properties include **amitriptyline** and those with less sedative effects include imipramine. These drugs are most effective in the treatment of depression associated with psychomotor and physiological disturbances. Adverse effects include anticholinergic (more correctly amtimuscarinic) symptoms of dry mouth, blurred vision, constipation and urinary retention. Arrhythmias and heart block can occur. Minimal quantities of tricyclic antidepressants should be prescribed at any one time because they are dangerous in overDose.

The SSRIs characteristically cause gastrointestinal disturbances, sleep disturbances and hypersensitivity reactions including rash (may be a sign of an impending serious systemic reaction and discontinuation should be considered) but they are less sedating and have fewer anticholinergic (antimuscarinic) and cardiotoxic effects than tricyclic antidepressants. The SSRIs are less toxic in overDose than the older tricyclic compounds. They may be preferred in patients in whom the risk of suicide is strong, but there is some concern that SSRIs may increase suicidal ideation.

Nursing Considerations:- Antidepressants

•Give with food or milk to reduce GI upset; may increase fluid intake (if urinary retention occurs) or bulk in diet (if constipation occurs), especially in children and elderly.
•Ensure patient swallows PO medication; may crush the medication if patient cannot swallow.
•Relieve dry mouth with gum, hard candy or frequent sips of water.
•Assist with ambulation, raise side rails as safety measures particularly in the elderly as drowsiness, dizziness occur.
•May increase appetite; observe weight changes.
•Monitor all relevant parameters: B/P, blood, liver and mental status.
•Observe for EPS (rigidity, dystonia, akathisia) particularly in the elderly.
•Inform patient that therapeutic effect may take 2-3 weeks.
•Warn patient that drug may cause drowsiness, dizziness, blurred vision; driving or other activities requiring alertness should be avoided. Patient should also avoid alcohol and other CNS depressants.
•Advise patient not to discontinue drug abruptly after long-term use; may cause withdrawal symptoms including nausea, headache, malaise.

AMITRIPTYLINE

Amitriptyline HCl is a representative tricyclic antidepressant. Various drugs can serve as alternatives.

Indications: Moderate to severe depression.

Contra-indications: Recent myocardial infarction, arrhythmias (especially heart block); manic phase in bipolar disorders; severe liver disease; children; porphyria

Precautions: Cardiac disease (see Contraindications above), history of epilepsy; pregnancy (Appendix 2); breastfeeding (Appendix 3); elderly; hepatic impairment (Appendix 5); thyroid disease; phaeochromocytoma; history of mania, psychoses (may aggravate psychotic symptoms); angle-closure glaucoma, history of urinary retention; concurrent electroconvulsive therapy; avoid abrupt withdrawal; anaesthesia (increased risk of arrhythmias and hypotension); **interactions**: Appendix 1SKILLED TASKS. MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Sedation, dry mouth, blurred vision (disturbance of accommodation, increased intra-ocular pressure), constipation, nausea, difficulty in micturition; cardiovascular adverse effects particularly with high dosage including ECG changes, arrhythmias, postural hypotension, tachycardia, syncope; sweating, tremor, rash and

RETURN

hypersensitivity reactions (urticaria, photosensitivity); behavioural disturbances; hypomania or mania, confusion (particularly in elderly), interference with sexual function, blood sugar changes; increased appetite and weight gain (occasional weight loss); endocrine adverse effects such as testicular enlargement, gynaecomastia and galactorrhoea; convulsions, movement disorders and dyskinesias, fever, agranulocytosis, leukopenia, eosinophilia, purpura, thrombocytopenia, hyponatraemia (may be due to inappropriate antidiuretic hormone secretion); abnormal liver function test

In overDose, excitement, restlessness, marked anticholinergic effects; severe symptoms including unconsciousness, convulsions, myoclonus, hyperreflexia, hypotension, acidosis, respiratory and cardiac depression with arrhythmias.

Nursing considerations: •Administer with food or milk to reduce GI upset; ensure that drug is crushed if patient cannot swallow.

•Give increased fluid and bulk in diet if constipation occurs.

•Whenever possible, full dose should be given at bedtime (if daytime sedation is a problem), but warn patient that morning orthostatic hypotension may occur.

•Assist with ambulation as a safety measure.

•Relieve dry mouth by giving sips of water, sugarless gum or hard candy.

•Advise patient not to discontinue drug abruptly after prolonged use as nausea, headache, malaise may occur.

•Caution patients on activities requiring alertness as drug may cause drowsiness, dizziness, blurred vision; and to make position changes slowly to avoid fainting, especially in elderly.

•Effect of drug may take several weeks to appear.

•Instruct patient to avoid alcohol and other CNS depressants; he should consult the pharmacist or physician before taking OTC medications particularly cough and cold remedies.

•May increase appetite and possibly a craving for sweets.

Dose: *Depression*, by mouth , ADULT initially 75 mg (elderly and adolescents 30–75 mg) daily in divided Doses or as a single Dose at bedtime increased gradually as necessary to 150–200 mg daily; CHILD under 16 years not recommended for depression.

POM **Amitriptyline** *(WMF 24.2.1)*
Tablet, Amitriptyline HCl 25 mg.

POM **Amitriptyline** *(EDL 25.2)*
Tablets, Amitriptyline HCl 25 mg, 50 mg.

POM **APO-AMITRIPTYLINE**® *(Lahams)*
Tablets, Amitriptyline HCl 25 mg, yellow f-c tab. marked '25'; 50 mg, beige f-c tab. marked '50'.
25 mg - 1000
50 mg - 1000

CLOMIPRAMINE

Therapeutic category: Tricyclic antidepressant

Indications: Depressive states including that associated with schizophrenia and personality disorders; Obsessive-compulsive syndromes (section 1.5), phobias, panic attacks, cataplexy accompanying narcolepsy, chronic painful conditions, and nocturnal enuresis.

Contra-indications, Precautions, etc: See amitriptyline.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: See under Amitriptyline.

Dose: By mouth, usually 75-150 mg daily according to the patient's needs.
Elderly and children: Initially, 10 mg 3 times daily. See lit. for details.

POM **ANAFRANIL**® *(Novartis)*
Tablet, Clomipramine 25 mg.
25 mg - 30; 100.

POM **ANAFRANIL SR**® *(Novartis)*
Tablet, Clomipramine 75 mg; s–r tab.
75 mg - 20.

IMIPRAMINE

Therapeutic category: Tricyclic antidepressant.

Indications: Depressive states of varying aetiology and symptomatology including masked forms; panic attacks; chronic painful conditions; Pavor nocturnus, nocturnal enuresis.

Contra-indications: Hypersensitivity to tricyclic antidepressants of the dibenzazepine group; acute stage of myocardial infarction; hypersensitivity to sulphites in parenteral admin.

Precautions: CV disturbances, AV block (grades I - III); narrow-angle glaucoma, disturbances of micturition, lowered convulsion threshold, electro-convulsion therapy, severe hepatic or renal damage, tumours of the adrenal medulla, hyperthyroidism or concomitant treatment with thyroid preparations; risk of suicide; surgical intervention; pregnancy, breast-feeding; road users; blood count, hepatic and

renal function tests during long-term therapy.
Adverse effects: Anticholinergic or mild CNS effects; sinus tachycardia, postural hypotension; Occasionally, disturbances of micturition, mania or hypomania, symptoms of delirium, activation of psychotic symptoms, arrhythmias, conduction disorders, allergic skin reactions; blood dyscrasias, hepatitis.
Advice to patients: See Label 2 in Appendix 6.
Nursing considerations: See under Amitriptyline.
Dose:By mouth, Adult, initially 25-75 mg daily for out-patients and 75 mg daily for hospitalised patients: increased stepwise to 150-200 mg daily. Maintenance, 50-100 mg daily. Elderly and children: initially, 10 mg daily. See lit. for details.

POM **Imipramine** *(EDL 25.2)*
Tablets, Imipramine HCl 10 mg, 25 mg

POM **APO-IMIPRAMINE**® *(Lahams)*
Tablet, Imipramine HCl 25 mg; light brown, f-c tab. marked '25'.
25 mg - 1000.

POM **TOFRANIL**® *(Novartis)*
Tablet, Imipramine HCl 25 mg; red-brown s-c round tab. marked 'GEIGY'.
25 mg - 50; 1000.

MOCLOBEMIDE

Therapeutic category: MAOI, Antidepressant
Pharmacology: Moclobemide is a MAOI. It acts through reversible inhibition of monoamine oxidase type A (RIMA). he metabolism of norepinephrine and serotonin is decreased leading to increased concentrations of these neuronal transmitters in the cerebral neurotransmitter system.
Moclobemide relieves symptoms such as dysphoria, exhaustion, lack of drive and inability to concentrate.
Indications: Treatment of depressive syndromes; it improves the quality of sleep but does not impair alertness.
Contra-indications: Known hypersensitivity to the drug; acute confusional states; paediatrics (clinical data still lacking).
Precautions: Thyrotoxicosis or pheochromocytoma.
Adverse effects: Nervousness, sleep disturbances, dizziness, agitation, feelings of anxiety, dry mouth, nausea, feeling of fullness, diarrhoea, constipation.
Advice to patients: See label 21 in Appendix 6.
Dose: By mouth, initially, 150 mg twice daily; reduced to 150 mg once daily if the patient's response is good.
In severe depression, up to 600 mg daily in divided Doses; Doses should not be raised until after the first week.
To be taken at the end of meals.

POM **AURORIX**® *(Swipha)*
Tablet, Moclobemide 150 mg; scored tab.
150 mg - 30.

PAROXETINE

Therapeutic category: Antidepressant; SSRI
Pharmacology: Paroxetine is a potent and selective inhibitor of 5-hydroxytryptamine re-uptake (5-HT, serotonin) and its antidepressant action and efficacy in the treatment of OCD and panic disorder is thought to be related to its specific inhibition of 5-HT re-uptake brain neurones. Paroxetine is chemically unrelated to the tricyclic, tetracyclic and other available antidepressants.
The principal metabolites are polar conjugated products of oxidation and methylation which are readily cleared and have no pharmacological activity. It is well absorbed after oral dosing and undergoes first-pass metabolism; elimination half-life is variable but is generally about one day. Steady state systemic levels attained by 7-14 days after starting treatment and pharmacokinetics do not appear to change during long-term therapy.
Paroxetine inhibits the hepatic cytochrome p450 enzyme and this may enhanc plasma levels of those co-administered drugs which are metabolised by this isozyme such as certain tricyclic antidepressants, phenothiazine neuroleptics and type 1c anti-arrhythmics. Long-term treatment with Paroxetine has shown antidepressant efficacy is maintained for periods of at least one year.
Indications: *Adults*: Treatment of symptoms of depressive illness of all types including reactive and severe depression accompanied by anxiety; following an initial satisfactory response, continued therapy is effective in preventing relapse of depression. Treatment of symptoms and prevention of relapse of obsessive compulsive disorder (OCD), generalized anxiety disorder, and also panic disorder with or without agoraphobia. Treatment of social anxiety disorder/social phobia and post-traumatic stress disorder.
Children and adolescents: Not recommended for treatment of children with depression.

Contra-indications: Known hypersensitivity to paroxetine and excipients. Avoid co-administration with MAOIs or within 2 weeks of terminating treatment with MAOIs, and also thioridazine.

Precaution: MAOIs: not recommended for use in combination with MAOIs or within two weeks of terminating treatment with MAO inhibitors; History of mania; Patients receiving oral anticoagulants; Cardiac conditions; Epilepsy; Seizures; ECT; Use during pregnancy and lactation; Ability to drive/use machines may be impaired.

Interactions: *Food/antacids*: no effect on absorption and pharmacokinetics of Paroxetine; *Tryptophan*: may cause 'serotonin syndrome' resulting in a combination of agitation, restlessness and GI symptoms including diarrhoea; *Drug metabolising enzyme inducers/inhibitors*: may affect metabolism and pharmacokinetics of Paroxetine; *Alcohol*: avoid concomitant use; *MAOIs*; *Lithium*: monitor lithium levels when co-administered; *Phenytoin/anticonvulsants*: may increase incidence of adverse effects; *Warfarin*: may result in increased bleeding in the presence of unaltered prothrombin times.

Adverse effects: Most commonly nausea, somnolence, sweating, tremor, asthenia, dry mouth, insomnia, sexual dysfunction (including impotence and ejaculation disorder(s), dizziness, constipation, diarrhoea and decreased appetite; Also dizziness, vomiting, diarrhoea, restlessness, hallucinations and hypomania, rash, including urticaria accompanied by pruritus or angio-oedema have been reported; Extrapyramidal reactions have been reported infrequently; Dystonic movement face, tongue and eyes have also been reported; rarely abnormalities of liver function tests and hyponatraemia; dry mouth, constipation, somnolence may occur.

Advice to patients: Abrupt discontinuation of therapy may cause dizziness, sensory disturbance (e.g. paraesthesia), anxiety, sleep disturbances including vivid dreams), agitation, tremor, nausea, sweating and confusion; gradual discontinuation by dose-tapering or alternate day dosing should be considered.

Dose: To be administered once daily in the morning with food; tablet should be swallowed whole, not chewed.

By mouth, Adults, *Depression, generalized anxiety disorder, post traumatic stress disorder*, 20 mg daily; may be increased weekly in 10 mg increments, up to a max. 50 mg per day.

Social Anxiety Disorder/Social Phobia, 20 mg dailymay be increased weekly in 10 mg increments as required, up to a max. 50 mg/day.

Obsessive Compulsive Disorder, Initially 20 mg daily; may be increased weekly in 10 mg increments to 40 mg daily; up to a max. 50 mg daily.

Panic disorder, Initially 10 mg daily increased weekly in 10 mg increments to 40 mg daily according to the patient's response; up to a max. 50 mg per day.

Elderly: Increased plasma concentrations of Paroxetine occur in elderly. Dosing should commence at the adult starting dose and may be increased in weekly 10 mg increments to a max. 40 mg daily according to the patient's response.

Children: Not recommended.

Renal/hepatic impairment: Increased plasma concentrations of Paroxetine occur in patients with severe renal impairment (creatinine clearance < 30 ml/min) or hepatic impairment. The recommended dose is 20 mg a day. Incremental dosage, if required, should be restricted to the lower end of the range.

Note: A low initial starting dose is recommended to avoid worsening of panic symptomatology during early treatment of panic disorder. Dosage should be reviewed and adjusted if necessary within 2-3 weeks of initiation of therapy and thereafter as judged clinically appropriate. Treatment may last several months for depression and may be even longer for OCD and panic disorder to ensure patient is free of symptoms.

POM **SEROXAT®** *(GSK)*

Tablet (20 mg), Paroxetine (as HCl) 20 mg; white, film-coated, modified oval, tablet marked 'Seroxat 20' on one side and scored on the reverse.

Pack - 2 x 15's.

Tablet (30 mg), Paroxetine (as HCl) 30 mg; blue, film-coated, modified oval, tablet marked 'Seroxat 30' on one side and scored on the reverse.

Pack - 2 x 15's.

SERTRALINE

Therapeutic category: SSRI, Antidepressant.

Pharmacology: The principal belief of the monoamine theory of depression is that depressive symptoms arise because of central deficiency of one or both the neurotransmitters serotonin (5-HT) and noradrenaline

(norepinephrine). By selectively blocking serotonin reuptake, sertraline increases the availability of this neurotransmitter and this accounts for its antidepressant activity. It is devoid of stimulant, sedative or anticholinergic activity. It has no affinity for muscarinic (cholinergic), serotonergic, dopaminergic, adrenergic, histaminergic, GABA or benzodiazepine receptors. They do not cause weight gain. Sertraline is slowly absorbed after oral administration. Food slightly increases sertraline bioavailability and it is recommended that sertraline capsules be administered with meals. It is extensively metabolised in the liver and less than 0.2% is excreted unchanged in the urine. It has elimination half-life of about 26 hours and is thus suitable for once-daily administration.

Other specific serotonin reuptake inhibitors include citalopram, fluoxetine, fluvoxamine and paroxetine.

Indications: Treatment of symptoms of depression in patients with or without a history of mania; prophylaxis against recurrence of depression.

Contra-ndications: Hypersensitivity to sertraline.

Precautions: MAOI (sertraline should not be used in combination with a MAOI or within 14 days of discontinuing treatment with a MAOI); hepatic insufficiency (use a lower or less frequent Dose); renal insufficiency (proportion of unchanged drug excreted in the urine is small and may not necessitate dosage adjustment); children, pregnancy, breast–feeding; driving a car or operating machinery.

Adverse effects: Nausea, diarrhoea/loose stools, dyspepsia, tremor, dizziness, insomnia, somnolence, sweating, dry mouth and male sexual dysfunction (principally ejaculatory delay).

Advice to patients: See Label 21 in Appendix 6. Notify physician if you are currently on another antidepressant drug; alert physician if you are pregnant or intend becoming pregnant while on this drug; avoid alcoholic drinks; weight loss may occur, but it is usually minimal.

Nursing considerations: •Administer with food or milk to reduce GI upset; ensure that drug is crushed if patient cannot swallow.

•Give increased fluid and bulk in diet if constipation occurs.

•Relieve dry mouth by giving sips of water, sugarless gum or hard candy.

•Provide safety measures and assist with ambulation, especially in elderly.

•Advise patient not to discontinue drug abruptly after prolonged use as nausea, headache, malaise may occur.

•Caution patients on activities requiring alertness as drug may cause drowsiness, dizziness, blurred vision; and to make position changes slowly to avoid fainting, especially in elderly.

Dose: By mouth, initially 50 mg once daily (either in the morning or evening); increased if necessary in 50 mg increments to a max. 200 mg daily over a period of weeks.Maintenance Dose, 50-100 mg; Doses of 150 mg or above should not be used for more than 8 weeks.

Elderly, usual adult dose.

Note: Not recommended for use in children and lactation.

POM **SERLIFT®** *(Ranbaxy)*
*Tablet*s, Sertraline (as HCl) 25 mg, 50 mg; f-c tabs.
25 mg - 10 x 10's (in blister)
50 mg - 10 x 10's (in blister).

POM **ZOLOFT®** *(Pfizer)*
Capsule, Sertraline (as HCl) 50 mg; orange/yellow capsules in blister pack.
50 mg - 15.

1.4.2 Drugs used in bipolar disorders

Treatment of bipolar disorders has to take account of three stages: treatment of the acute episode, continuation phase and prophylaxis to prevent further episodes. **Lithium** is effective in acute mania but symptomatic control of the florid symptoms with an antipsychotic or benzodiazepine is often necessary whilst waiting for the antimania drug to exert its effect. Benzodiazepines may be given during the initial stages until lithium becomes effective but they should not be used for long periods because of the risk of dependence. Lithium may be given concurrently with antipsychotics and treatment with the antipsychotic should be tailed off as lithium becomes effective. Alternatively, lithium therapy may be delayed until the patient's mood is stabilized with the antipsychotic. However, there is a risk of neurotoxicity and increased extrapyramidal disorders when lithium and antipsychotics are used concurrently (Appendix 1). Lithium is the mainstay of treatment but its narrow therapeutic range is a disadvantage. **Sodium valproate** is effective and **carbamazepine** may also be used.

Treatment of depressive episodes in

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bipolar disorders will mostly involve combination treatment using either lithium or sodium valproate together with a tricyclic antidepressant. Increased adverse effects are a problem which may compromise treatment.

Lithium prophylaxis should usually only be undertaken with specialist advice and the likelihood of recurrence considered. Long-term lithium therapy has been associated with thyroid disorders and mild cognitive and memory impairment. Patients should continue the treatment for longer than 3 to 5 years only if benefit persists.

Withdrawal appears to produce high levels of relapse. If lithium is to be discontinued, the Dose should be reduced gradually over a few weeks and patients should be warned of possible relapses if discontinued abruptly.

Lithium salts have a narrow therapeutic/toxic ratio and should only be prescribed if there are facilities for monitoring serum lithium concentrations. Doses are adjusted to achieve serum-lithium concentrations of 0.4–1 mmol/litre (lower end of range for maintenance therapy and the elderly) on samples taken 12 hours after the preceding Dose. The optimum range for each patient should be determined.

Overdosage, usually with serum-lithium concentration of over 1.5 mmol/litre may be fatal and toxic effects include coarse tremor, ataxia, dysarthria, nystagmus, renal impairment and convulsions. If any of these effects occur, treatment should be stopped, serum-lithium concentration determined and in mild overdosage large amounts of sodium and fluid should be given to reverse the toxicity; in severe toxicity, haemodialysis may be required.

For patients who are unresponsive to or intolerant of lithium, carbamazepine may be used in the prophylaxis of bipolar illness particularly in those with rapid cycling affective disorders (more than four affective episodes per year).

LITHIUM

Indications: Treatment and prophylaxis of mania, prophylaxis of bipolar disorder and recurrent depression.

Contra-indications: Renal impairment (Appendix 4); cardiac insufficiency; conditions with sodium imbalance such as Addison disease.

Precautions: Measure serum-lithium concentration about 4 days after starting treatment, then weekly until stabilized, then at least every 3 months; monitor thyroid function every 6–12 months on stabilized regimens—risk of hypothyroidism (see below); monitor renal function; maintain adequate fluid and sodium intake; reduce Dose or discontinue in diarrhoea, vomiting and intercurrent infection (especially if associated with profuse sweating); pregnancy (Appendix 2); breastfeeding (Appendix 3); elderly (reduce Dose); diuretic treatment, myasthenia gravis; surgery; if possible, avoid abrupt withdrawal (see notes above); **interactions**: Appendix 1.

Patient advice: Patients should maintain adequate fluid intake and should avoid dietary changes which may reduce or increase sodium intake. Patients should be advised to seek medical attention if symptoms of hypothyroidism (for example, feeling cold, lethargy) develop (women are at greater risk).

Note: Different preparations vary widely in bioavailability; a change in the preparation used requires the same precautions as initiation of treatment.

Adverse effects: Gastrointestinal disturbances, fine tremor, renal impairment (particularly impaired urinary concentration and polyuria), polydipsia, weight gain and oedema (may respond to Dose reduction); hyperparathyroidism and hypercalcaemia reported; signs of intoxication include blurred vision, muscle weakness, increasing gastrointestinal disturbances (anorexia, vomiting, diarrhoea), increased CNS disturbances (mild drowsiness and sluggishness, increasing to giddiness with ataxia, coarse tremor, lack of co-ordination, dysarthria) and require withdrawal of treatment; with severe overdosage (serum concentrations above 2 mmol/litre), hyperreflexia and hyperextension of the limbs, convulsions, toxic psychoses, syncope, renal failure, circulatory failure, coma, occasionally death; goitre, raised antidiuretic hormone concentration, hypothyroidism, hypokalaemia, ECG changes, exacerbation of psoriasis and kidney changes may occur

Nursing considerations: •Give with meals to decrease GI upset.

•Ensure adequate fluid intake of 2-3 litres daily to prevent dehydration during the initial treatment period; salt intake should also be adjusted to compensate for losses through sweating or diarrhoea.

•Teach patient to avoid tasks requiring psychomotor

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co-ordination until the CNS effects are known.
•Advise patient to report to physician at the earliest signs of toxicity namely diarrhoea, vomiting, drowsiness, muscular weakness, ataxia. He should expect transient nausea, polyuria, thirst, and discomfort during first few days of therapy.
•Monitor therapy; regular lithium blood level determinations are mandatory due to the narrow therapeutic margin of safety.
•Monitor blood glucose closely in diabetics.

Dose: *Treatment of mania* (general guidelines only, see also note below) by mouth , ADULT initially 0.6–1.8 g daily (elderly 300–900 mg daily)
Prophylaxis of mania, bipolar disorder and recurrent depression (general guidelines only, see also note below), by mouth , ADULT initially 0.6–1.2 g daily (elderly 300–900 mg daily).

Note: Dosage of lithium depends on the preparation chosen since different preparations vary widely in bioavailability. Dosage should be adjusted to achieve a serum-lithium concentration of 0.4–1 mmol/litre (lower end of range for maintenance therapy and in elderly) on samples taken 12 hours after a Dose and 4–7 days after starting treatment then every week until dosage has remained unchanged for 4 weeks, then every 3 months thereafter.

DOSAGE REGIMENS: For Dose information for a specific preparation, consult manufacturer's literature

POM **Lithium** *(WMF 24.2.2)*
Tablet or Capsule, Lithium carbonate 300 mg.

POM **Lithium** *(EDL 25.3)*
Tablet or Capsule, Lithium carbonate 300 mg.

CARBAMAZEPINE

Indications: Prophylaxis of bipolar disorder unresponsive to or intolerant of lithium; epilepsy, trigeminal neuralgia (section 1.7.1).

Contra-indications: Atrioventricular conduction abnormalities; history of bone-marrow depression; porphyria.

Precautions: Hepatic impairment (Appendix 5); renal impairment (Appendix 4); cardiac disease (see also Contraindications); skin reactions (see Adverse effects); history of blood disorders (blood counts before and during treatment); glaucoma; pregnancy (Appendix 2 (neural tube screening)); breastfeeding (Appendix 3); avoid sudden withdrawal; **interactions**: Appendix 1.

BLOOD, HEPATIC OR SKIN DISORDERS: Patients or their carers should be told how to recognize signs of blood, liver or skin disorders, and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, bruising or bleeding develop. Leukopenia which is severe, progressive and associated with clinical symptoms requires withdrawal (if necessary under cover of suitable alternative)

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Dizziness, drowsiness, headache, ataxia, blurred vision, diplopia (may be associated with high plasma concentrations); gastrointestinal intolerance including nausea and vomiting, anorexia, abdominal pain, dry mouth, diarrhoea or constipation; commonly, mild transient generalized erythematous rash (withdraw if worsens or is accompanied by other symptoms); leukopenia and other blood disorders (including thrombocytopenia, agranulocytosis and aplastic anaemia); cholestatic jaundice, hepatitis, acute renal failure, Stevens-Johnson syndrome (erythema multiforme), toxic epidermal necrolysis, alopecia, thromboembolism, arthralgia, fever, proteinuria, lymph node enlargement, arrhythmias, heart block and heart failure, dyskinesias, paraesthesia, depression, impotence, male infertility, gynaecomastia, galactorrhoea, aggression, activation of psychosis, photosensitivity, pulmonary hypersensitivity, hyponatraemia, oedema, disturbances of bone metabolism with osteomalacia also reported; confusion and agitation in elderly

Nursing considerations: •Give with food or milk to minimize GI distress.
•Relieve dry mouth with frequent sips of water, gum or hard candy.
•Advise patient to avoid driving or potentially hazardous activities that require mental alertness.
•Observe patient for excessive sedation; do not discontinue suddenly when treating seizures or status epilepticus.

Dose: *Prophylaxis of bipolar disorder*, by mouth, ADULT initially 400 mg daily in divided Doses increased until symptoms are controlled to a maximum of 1.6 g daily; usual maintenance range 400–600 mg daily.

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POM **Carbamazepine** *(WMF 24.2.2)*
Tablets, Carbamazepine 100 mg, 200 mg.

See section 1.7.1 for the proprietary preparations of Carbamazepine.

SODIUM VALPROATE

Indications: Acute mania; epilepsy (section 1.7.1)
Contra-indications: Active liver disease, family history of severe hepatic dysfunction; pancreatitis; porphyria.
Precautions: Monitor liver function before and during therapy (Appendix 5), especially in patients at most risk (those with metabolic disorders, degenerative disorders, organic brain disease or severe seizure disorders associated with mental retardation); ensure no undue potential for bleeding before starting and before major surgery or anticoagulant therapy; renal impairment (Appendix 4); pregnancy (Appendix 2 (neural tube screening)); breastfeeding (Appendix 3); systemic lupus erythematosus; false-positive urine tests for ketones; avoid sudden withdrawal; **interactions**: Appendix 1.

BLOOD OR HEPATIC DISORDERS: Patients or their carers should be told how to recognize signs of blood or liver disorders, and advised to seek immediate medical attention if symptoms including malaise, weakness, anorexia, lethargy, oedema, vomiting, abdominal pain, drowsiness, jaundice, or spontaneous bruising or bleeding develop.

PANCREATITIS: Patients or their carers should be told how to recognize signs of pancreatitis and advised to seek immediate medical attention if symptoms such as abdominal pain, nausea and vomiting develop; discontinue sodium valproate if pancreatitis diagnosed.
Adverse effects: Gastrointestinal irritation, nausea, increased appetite and weight gain, hyperammonaemia; ataxia, tremor; transient hair loss (regrowth may be curly); oedema, thrombocytopenia, inhibition of platelet aggregation; impaired hepatic function and rarely fatal hepatic failure (see Precautions—withdraw treatment immediately if malaise, weakness, lethargy, oedema, abdominal pain, vomiting, anorexia, jaundice, drowsiness); sedation reported and also increased alertness; behavioural disturbances; rarely pancreatitis (measure plasma amylase if acute abdominal pain), extrapyramidal symptoms, leukopenia, pancytopenia, red cell hypoplasia, fibrinogen reduction; irregular periods, amenorrhoea, gynaecomastia, hearing loss, Fanconi syndrome, dementia, toxic epidermal necrolysis, Stevens-Johnson syndrome (erythema multiforme), vasculitis, hirsutism, and acne reported.
Dose: *Acute mania*, by mouth, ADULT initially 750 mg daily in divided Doses, increased as quickly as possible to achieve the optimal response (maximum 60 mg/kg daily).

POM **Sodium Valproate** *(WMF 24.2.2)*
Tablets, Sodium valproate 200 mg, 500 mg; enteric-coated tablets (Gastro-resistant tablets).

See section 1.7.1 for the proprietary preparations of Carbamazepine.

1.5 Obsessive-compulsive disorders and panic attacks

Obsessive-compulsive disorders can be treated with a combination of pharmacological, behavioural and psychological treatments.
Antidepressants such as **clomipramine** which inhibit reuptake of serotonin have been found to be effective. Panic attacks may be treated with behavioural or cognitive therapy. If this management fails, drug therapy may be tried. Some tricyclic antidepressants including clomipramine, or SSRIs can reduce frequency of attacks or prevent them completely.
Benzodiazepines may be used in panic attacks resistant to antidepressants.

CLOMIPRAMINE

Indications: Phobic and obsessional states; panic attacks.
Contra-indications: Recent myocardial infarction, arrhythmias (especially heart block); manic phase in bipolar disorders; severe liver disease; children; porphyria.
Precautions: Cardiac disease (see Contraindications above), history of epilepsy; pregnancy (Appendix 2); breastfeeding (Appendix 3); elderly; hepatic impairment (Appendix 5); thyroid disease; phaeochromocytoma; history of mania, psychoses (may aggravate psychotic symptoms); angle-closure

glaucoma, history of urinary retention; concurrent electroconvulsive therapy; avoid abrupt withdrawal; anaesthesia (increased risk of arrhythmias and hypotension); **interactions**: Appendix 1
SKILLED TASKS. May impair ability to perform skilled tasks, for example operating machinery, driving.
Adverse effects: Sedation, dry mouth, blurred vision (disturbance of accommodation, increased intra-ocular pressure), constipation, nausea, difficulty in micturition; cardiovascular adverse effects particularly with high dosage including ECG changes, arrhythmias, postural hypotension, tachycardia, syncope; sweating, tremor, rash and hypersensitivity reactions (urticaria, photosensitivity); behavioural disturbances; hypomania or mania, confusion (particularly in elderly), interference with sexual function, blood sugar changes; increased appetite and weight gain (occasional weight loss); endocrine adverse effects such as testicular enlargement, gynaecomastia and galactorrhoea; convulsions, movement disorders and dyskinesias, fever, agranulocytosis, leukopenia, eosinophilia, purpura, thrombocytopenia, hyponatraemia (may be due to inappropriate antidiuretic hormone secretion); abnormal liver function test.
Dose: *Phobic and obsessional states*, by mouth, ADULT initially 25 mg daily, usually at bedtime (ELDERLY 10 mg daily) increased over 2 weeks to 100–150 mg daily; CHILD not usually recommended

POM **Clomipramine** *(WMF 24.4)*
Capsules, Clomipramine HCl 10 mg, 25 mg.

See section 1.4.1 for the proprietary preparations of Clomipramine.

1.6 Antiparkinson Drugs

1.6.1 Drugs used in parkinsonism
1.6.2 Drugs used in essential tremor and related disorders

1.6.1 Drugs used in parkinsonism

The use of pharmacotherapy will depend upon the degree of incapacity of the patient and is generally not justified until symptoms compromise working ability and social relationships; although levodopa is used in the early stages in some patients. Close supervision is then needed to ensure that treatment regimens are tolerated and that appropriate changes are made to the regimen as the disease progresses.
The most effective form of therapy is a combination of **levodopa** and a peripheral dopa-decarboxylase inhibitor, such as **carbidopa**. The response to levodopa with carbidopa is a compromise between increased mobility and adverse effects. Dyskinesias may be Dose limiting and increasingly frequent with increased duration of treatment. Many factors including tolerance and progression of the disease may result in complications after 2–5 years of treatment. 'End-of-Dose' deterioration occurs when there is a reduced duration of benefit from a Dose, resulting in disability and dystonias. The 'on-off' phenomenon is characterized by sudden swings from mobility to episodes of akinesia, tremor and rigidity lasting from a few minutes to several hours. Amelioration of these effects can sometimes be achieved by administering levodopa in a sustained-release preparation or in a greater number of fractionated Doses throughout the day. Psychiatric symptoms inducing disruption of sleep, vivid dreams and hallucinations are characteristic adverse effects that may occur at any time, especially in the elderly, and may require Dose reduction or withdrawal of levodopa.
Treatment for idiopathic parkinsonism is often initiated with a dopamine receptor agonist such as **bromocriptine** [not on WHO Model List]. Supplementary use of amantadine [not on WHO Model List], bromocriptine or the monoamine-oxidase-B inhibitor, selegiline [not on WHO Model List] can be of value either to enhance the effect of levodopa or to reduce 'end-of-Dose' fluctuations and 'on-off' effects.
Anticholinergic (more correctly termed antimuscarinic) drugs such as **biperiden** are usually sufficient in drug-induced parkinsonism.

LEVODOPA

Indications: Idiopathic Parkinson's disease; post-encephalitic Parkinsonism; symptomatic Parkinsonism due to carbon monoxide or manganese poisoning; arteriosclerotic

Parkinsonism; other drug - induced Parkinsonism except those due to phenothiazines or neuroleptic - induced Parkinsonism.

Contra-indications: Severe psychoses, closed-angle glaucoma.

Precautions: Cardiovascular, endocrine, hepatic, pulmonary or renal disease; psychiatric disturbances; open-angle glaucoma; history of gastric or duodenal ulceration; skin melanoma; discoloration of urine and other body fluids; pregnancy, breast-feeding.

Adverse effects: GI and cardiovascular disturbances, psychiatric symptoms; polyuria, incontinence, difficult micturition.

Advice to patients: See Labels 14 and 21 in Appendix 6.

Nursing considerations: •Give with meals to decrease GI upset.

•Warn patient of possible dizziness and orthostatic hypotension; teach patient to get up slowly and dangle legs before getting out of bed.

•Instruct patient to avoid Vtamin B_6 preparations, Vitamin fortified foods containing vitamin B_6 as they can reverse the effect of Levodopa.

•Advise patient not to stop medication abruptly; may precipitate parkinsonian crisis.

•Observe patient closely for muscle twithing and blepharospasm (twitching of eyelids), which are signs of overdose (report to doctor immediately).

•When given in combination with a dopa decarboxylase inhibitor such as carbidopa or benserazide, the amount of levodopa needed is reduced by 75% thereby reducing the incidence of adverse effects.

Dose: By mouth, initially 125-500 mg daily in divided Doses; increased gradually, at intervals of 2-3 days, to a maximum 4 g daily in divided Doses.

POM **Levopoda** *(EDL 9.1)*
Tablet or Capsule, Levodopa 250 mg.

LEVODOPA plus BENSERAZIDE

Indications: Treatment of Parkinson's disease, Symptomatic parkinsonism (Postencephalic, arteriosclerotic, toxic), except drug-induced parkinsonism.

Contra-indications: Patients under 25 years; pregnancy; endocrine, renal, hepatic and cardiac diseases with severe decompensation; psychoses and the more severe psychoneurosis.

Precautions:Discontinueother antiparkinsonian drugs gradually; history of myocardial infarction, coronary insufficiency or cardiac arrhythmia (perform periodic cardiovascular checks including ECG).

Adverse effects: Mental disturbances including insomnia, agitation or more rarely depression and psychotic reactions; abnormal involuntary movements.

Advice to patients: See Labels 14, 21 and 25 in Appendix 6.

Nursing considerations: •See under Levodopa.

Dose: By mouth, 125 mg 3 times daily; increasing by 125 mg daily until the required therapeutic Dose is obtained. See lit. for details.

POM **Levodopa plus Benserazide** *(EDL 9.1)*
Capsules, Levodopa 50, 100, 200 mg plus benserazide 12.5, 25, 50 mg respectively.

POM **MADOPAR®** *(Swipha)*
Tablet, Levodopa 200 mg, benserazide 50 mg; pink doubly scored tab. marked with maker's symbol.
250 mg - 30.

LEVODOPA plus CARBIDOPA

Carbidopa is a representative peripheral dopa decarboxylase inhibitor. Various drugs can serve as alternatives.

Indications: All forms of parkinsonism other than drug-induced.

Contra-indications: Concurrent use of monoamine oxidase inhibitors; angle-closure glaucoma; confirmed or suspected malignant melanoma.

Precautions: Pulmonary disease, peptic ulceration, cardiovascular disease (including previous myocardial infarction); diabetes mellitus, osteomalacia, open-angle glaucoma, history of melanoma (risk of activation), psychiatric illness (avoid if severe); close monitoring of hepatic, haematological, psychiatric, cardiovascular, and renal function required in long-term therapy; elderly: avoid rapid Dose increases; warn patients to resume normal activities gradually; avoid abrupt withdrawal; pregnancy (toxicity in animals) (Appendix 2), breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Nausea, anorexia and vomiting, particularly at the start of treatment; postural hypotension at the start of treatment, particularly in elderly and those receiving antihypertensives; excessive drowsiness and sudden onset of sleep (warn patient of these effects); confusion, vivid dreams, dizziness, tachycardia, arrhythmias; reddish discoloration of body fluids; insomnia, headache, flushing, gastrointestinal bleeding, peripheral neuropathy; taste disturbances, pruritis, rash, liver enzyme changes; psychiatric symptoms including

psychosis, depression, hallucinations, delusions and neurological disturbances including dyskinesias may be Dose-limiting; painful dystonic spasms ('end-of-Dose' effects) and ('on-off' effects) after prolonged treatment (see notes above); neuroleptic malignant syndrome, on sudden withdrawal; rarely hypersensitivity.

Nursing considerations: •Space doses evenly over the waking hours.
•See under Levodopa.

Dose: *Parkinsonism*, by mouth , ADULT expressed in terms of levodopa, initially 100 mg (with carbidopa 10 mg) twice daily, increased by 100 mg (with carbidopa 10 mg) every few days as necessary, to a maximum of levodopa 1.5 g

Administration: Optimum daily Dose must be determined for each patient by careful monitoring and be taken after meals.

POM **Carbidopa plus Levodopa** *(WMF 9.1)*
Tablets, Carbidopa 10 mg, Levodopa 100 mg; Carbidopa 25 mg, levodopa 250 mg.

POM **Carbidopa plus Levodopa** *(EDL 9.1)*
Tablet, Carbidopa 10 mg, Levodopa 100 mg; Carbidopa 25 mg, levodopa 250 mg.

BENZHEXOL

Synonym: Trihexyphenidyl Hydrochloride
Therapeutic category: Anticholinergic Agent; Anti-Parkinson's Agent.
Indications: Extrapyramidal syndrome (but not tardive dyskinesia) induced by drugs such as phenothiazines and reserpine; adjunctive treatment of Parkinson's disease.
Contra-indications: Hypersensitivity to benzhexol or any component; narrow-angle glaucoma; pyloric or duodenal obstruction; achalasia; myasthenia gravis.
Precautions: Urinary retention; cardiac, renal or hepatic disorders; elderly; hot weather or during exercise.
Adverse effects: Constipation, dry mouth; decreased sweating; dry nose, throat or skin; less commonly decreased flow of breast milk, difficulty in swallowing, orthostatic hypotension, tachycardia, drowsiness, blurred vision, weakness, difficult urination, nausea, vomiting, loss of memory, rash.
Advice to patients: Take after meals or with food if GI upset occurs; do not discontinue drug abruptly; notify physician if adverse GI effects, rapid or pounding heartbeat, confusion, eye pain, rash, fever or heat intolerance occurs. Observe caution when performing hazardous tasks or those that require alertness such as driving, as drug may cause drowsiness. Avoid alcohol and other CNS depressants. May cause dry mouth - adequate fluid intake or chewing gum may relieve. Difficult urination or constipation may occur - notify physician if effects persist; may increase susceptibility to heat stroke.

Nursing considerations: •Tolerated best if given in 3 daily doses and with food; high doses may be divided into 4 doses, at meal times and at bed time.
•Patients may be switched to sustained-action capsules when stabilised on conventional dosage forms.

Dose: Adult, by mouth, initially 1-2 mg daily; increased by 2 mg increments at intervals of 3-5 days.
Maintenance Dose: 5-15 mg daily in 3-4 divided Doses.

POM **Benzhexol** *(EDL 9.1)*
Tablets, Benzhexol HCl 2 mg, 5 mg.

POM **APO-TRIHEX®** *(Lahams)*
Tablets, Benzhexol HCl 2 mg, white scored tab. marked 'APO TRM'; 5 mg, white, scored tab. marked 'APO 5'.
2 mg - 500
5 mg - 100, 500.

BIPERIDEN

Biperiden is a representative anticholinergic drug. Various drugs can serve as alternatives.

Indications: Drug-induced extrapyramidal symptoms (but not tardive dyskinesias) and adjunctive treatment of parkinsonism.
Contra-indications: Angle-closure glaucoma; untreated urinary retention; prostatic hypertrophy; myasthenia gravis; gastrointestinal obstruction.
Precautions: Elderly; cardiovascular disease, hepatic or renal impairment; avoid abrupt withdrawal; pregnancy and breastfeeding; **interactions**: Appendix 1
SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.
Adverse effects: Drowsiness, dry mouth, constipation, blurred vision; hesitancy of micturition, dizziness, tachycardia, arrhythmias; confusion, excitement, agitation, hallucinations, and psychiatric disturbances with high dosage, especially in the elderly and other susceptible patients, may require withdrawal of treatment; impaired memory.
Nursing considerations: •Administer with or after meals to minimize GI upset; may give with fluids other than water.

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•Give I.V. injection slowly. Keep patient in a recumbent position as parenteral dose may cause transient postural hypotension and coordination disturbances.
•Relieve dry mouth with ice cubes, cool drinks or hard sweets.
•Warn patient to avoid activities that require alertness, as the drug may cause drowsiness.
•Teach patient not to stop taking drug abruptly; to be tapered off over 1 week.
•Notify physician if urinary hesitancy or retention occurs.
•Teach patient to avoid cold or cough medications with lcohol and antihistamines except otherwise instructed by physician.
•Observe patient closely for adverse reactions especially in the elderly and debilitated patients (inform the doctor immediately). Because of possibility of dizziness, help patient into bed.
•May increase susceptibility to heat stroke; advise patient to limit activities during hot weather.

Dose: *Drug-induced extrapyramidal symptoms, parkinsonism*, by mouth, ADULT , as biperiden hydrochloride, initially 1 mg twice daily, increased gradually to 2 mg 3 times daily; usual maintenance Dose 3–12 mg daily in divided Doses
Drug-induced extrapyramidal symptoms, parkinsonism, by IM injection or slow IV injection , Adult , as biperiden lactate, 2.5–5 mg repeated as necessary to maximum 20 mg in 24 hours

POM **Biperiden** *(WMF 9.1)*
Tablet, Biperiden HCl 2 mg
Injection (Solution for injection), Biperiden lactate 5 mg per ml; in 1ml amp.

POM **Biperiden** *(EDL 9.1)*
Tablet, Biperiden HCl 2 mg
Injection: Biperiden lactate 5 mg per ml; in 1ml amp.

BROMOCRIPTINE

Indications: Parkinsons disease, but not drug-induced extrapyramidal symptoms; endocrine disorders, section 10.6.
Contra-indications, Precautions, etc: See Bromocriptine in section 10.6.
Dose: By mouth, 1.25mg daily, preferably in the evening, for the 1st week; increased gradually by 1.25 mg/day each week in 2-3 divided Doses for 6 - 8 weeks. A further increase by 2.5mg/day each week may be required to achieve adequate therapeutic response; usual range is 10 - 40 mg per day. To be taken with food.

See section 10.6 for the preparations of Bromocriptine.

1.6.2 Drugs used in essential tremor and related disorders

ESSENTIAL TREMOR
It can be treated with beta-blockers such as **propranolol** (120 mg daily) (section 1.8) which may be of value if the tremor results in physical or social disability.

DYSTONIAS
If no identifiable cause is found and the patient does not go into spontaneous remission, a trial of **levodopa** should be given to determine whether the patient has dopamine-responsive dystonia. If there is no response within three months, the drug should be withdrawn and small Doses of an anticholinergic drug such as **biperiden** should be given. The dosage may be increased gradually and up to 16 mg daily may be tolerated. In patients who fail to respond to either levodopa or an anticholinergic, other drugs including diazepam, baclofen, carbamazepine or phenothiazines may be of value. Psychological treatments have also been used successfully in the management of dyskinesias.

CHOREA
Choreiform movements can be induced by certain drugs including levodopa, phenytoin and antipsychotic drugs. Huntington disease is the most common of the hereditary choreas. Drug treatment is symptomatic and does not alter the progression of the disease. The aim of therapy is to reduce dopaminergic transmission which results from excessive or enhanced cholinergic activity. Antipsychotic drugs antagonize dopamine and usually lessen the chorea temporarily. Tetrabenazine [not included on WHO Model List], the dopamine-depleting drug, is used to control movement disorders in Huntington chorea and related disorders.

TICS
Tics which resemble choreiform movements are commonly associated with anxiety. However, in the more complex multiple tic disorder, Tourette syndrome, treatment with antipsychotic drugs may be required.

TARDIVE DYSKINESIA

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It is associated with chronic administration of antipsychotic drugs. It is characterized by involuntary, repetitive, choreiform movement of the cheek, mouth and fingers. The first step of treatment should always be discontinuation of the antipsychotic drug or dosage reduction if the underlying psychotic disorder permits.

1.7 Anticonvulsants (Antiepileptics)

1.7.1 Control of epilepsy

1.7.1 Control of epilepsy

Treatment should always be started with a single drug, but the choice of an anticonvulsant can only be made on an individual basis and will depend on the efficacy of the drug and the patient's tolerance of treatment. If a drug fails to control the seizures after it has been used in full therapeutic dosage for an adequate period, or if it is not tolerated, it should be gradually substituted with another with the first drug being withdrawn only when the new regimen is mainly established. If monotherapy is ineffective, two drugs should be given in combination and several regimens may need to be tried before the most appropriate is found.

Initial Dose of the drug of choice should be determined on the basis of the degree of urgency, the size and age of the patient. It should be increased gradually until an effective response is obtained. All antiepileptics commonly produce neurological adverse effects at too high a Dose, and patients should be monitored closely for adverse effects to help in accurate Dose titration. Except for phenytoin, it is rarely useful to measure plasma-drug concentrations as an aid to Dose adjustment. Non-compliance because of inappropriate dosing and overdosing is a major impediment to effective antiepileptic treatment. Patients should ideally remain under supervision throughout treatment.

WITHDRAWAL

Treatment is normally continued for a minimum of two years after the last seizure. Withdrawal should be extended over a period of several months because abrupt withdrawal can lead to complications such as status epilepticus. In patients receiving several antiepileptic drugs, only one drug should be withdrawn at a time. Many adult patients relapse once treatment is withdrawn and it may be justified to continue treatment indefinitely, particularly when the patient's livelihood or lifestyle can be endangered by recurrence of a seizure.

PREGNANCY AND BREASTFEEDING

Untreated epilepsy during pregnancy may cause harm to the fetus; there is therefore no justification for abrupt withdrawal of treatment although withdrawal of therapy may be an option if the patient has been seizure-free for at least 2 years; resumption of treatment may be considered after the first trimester. If antiepileptics are continued in pregnancy, monotherapy with the lowest effective Dose is preferred, with adjustment made to take account of changes in plasma levels associated with pregnancy. There is an increased risk of birth defects with the use of anticonvulsants, particularly **carbamazepine**, **valproate** and **phenytoin**. However, if there is good seizure control, there is probably no advantage in changing pregnant patients' antiepileptic drugs. In view of the risks of neural tube and other defects, patients who may become pregnant should be informed of the risks and referred for advice, and pregnant patients should be offered counselling and antenatal screening. To counteract the risk of neural tube defects, adequate **folate** supplements are advised for women before and during pregnancy. In view of the risk of neonatal bleeding associated with **carbamazepine**, **phenobarbital** and **phenytoin**, prophylactic **phytomenadione** (vitamin K_1) is recommended for the neonate and the mother before delivery. Antiepileptic drugs can be continued during breastfeeding (see also Appendix 3).

DRIVING

Regulations are in place in many countries which may, for example, restrict driving by patients with epilepsy to those whose seizures are controlled. Further, antiepileptic drugs may cause CNS depression, particularly in the early stages of treatment and patients affected by adverse effects such as drowsiness or dizziness should not operate machinery or drive.

Choice of antiepileptic in management of convulsive disorders

GENERALIZED TONIC-CLONIC, SIMPLE PARTIAL AND COMPLEX PARTIAL SEIZURES

Carbamazepine, **phenobarbital**, **phenytoin**, and **valproate** are widely used in the treatment of these conditions. However, each of these drugs is associated with Dose-related and idiosyncratic adverse effects and monitoring of haematological and hepatic function is often advised, particularly for carbamazepine and valproate.

ABSENCE SEIZURES

Both **ethosuximide** and **valproate** are widely used in the treatment of absence seizures (petit mal) and are usually well tolerated. However, ethosuximide can, rarely, cause lupus erythematosus and psychoses which call for immediate, but cautious, discontinuation. Absence seizures are commonly associated with tonic-clonic seizures and valproate is preferred since it is effective in both disorders.

TONIC SEIZURES, ATONIC SEIZURES AND ATYPICAL ABSENCE SEIZURES

Phenobarbital or **phenytoin** is widely used for tonic seizures, **valproate** or **clonazepam** for atonic seizures, and **clonazepam** for atypical absence seizures.

MYOCLONIC SEIZURES

Valproate is widely used and most effective for juvenile myoclonic seizures. However, both valproate and this type of seizure are associated with a high relapse rate and it is often necessary to continue therapy indefinitely. Other myoclonic seizures are often resistant to treatment and some do not have an epileptic basis. **Valproate** or **clonazepam** can be of value in this case and other antiepileptic drugs may be useful in intractable cases. Both drugs are generally well accepted, although tolerance to clonazepam has been reported.

INFANTILE SPASM (INFANTILE MYOCLONIC EPILEPSY)

Infantile spasms, which are often associated with severe brain damage, can be resistant to antiepileptic drugs. **Clonazepam** is sometimes of value in resistant cases.

FEBRILE CONVULSIONS

Brief febrile convulsions usually respond to sponging with tepid water and by giving an antipyretic such as paracetamol (section 1.8.1). Recurrent febrile convulsions or prolonged convulsions (those lasting 15 minutes or longer) are treated with **diazepam**, either rectally in solution or by intravenous injection, to prevent possible brain damage.

Intermittent prophylaxis , with diazepam administered at the onset of fever, may prevent recurrence of febrile convulsions, but only in a small proportion of children. Use of antiepileptics for continuous prophylaxis is controversial; it is probably indicated in only a small proportion of children including those whose first seizure occurred during the first 14 months of life, or who already have evident neurological abnormalities, or who have had previous prolonged or focal convulsions. **Phenobarbital** may be used for this purpose but careful clinical monitoring and dosage adjustment are necessary in order to minimize the risk of adverse effects. **Valproate**, although effective, is not recommended because of the greater risk of hepatotoxicity in young children.

Status epilepticus

Status epilepticus is a medical emergency which carries a high mortality rate. Initial management includes positioning the patient to avoid injury, supporting respiration including provision of oxygen, maintaining blood pressure, and the correction of any hypoglycaemia; maintenance of the airway and assisted ventilation are crucial even when the seizures are controlled, because the drugs used in its management may also depress respiration.

Intravenous **diazepam** or **clonazepam** are often effective in status epilepticus. Diazepam, which acts rapidly, should be administered first and should be followed immediately by a loading Dose of **phenytoin** which has a longer-acting effect. When cannulation is impossible, diazepam may be administered rectally as a solution (absorption from suppositories is too slow for treatment of status epilepticus). Intravenous **phenobarbital** is also effective but is more likely to cause respiratory depression; it is used in refractory cases but should be avoided in patients who have recently received oral phenobarbital. Rectal paraldehyde may

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also be used; it causes little respiratory depression and is therefore useful where facilities for resuscitation are poor.

If seizures continue despite treatment, general anaesthesia may be required. The underlying cause must be identified and remedied in all cases.

Nursing Considerations:- Anticonvulsants

•Give with food or milk to reduce GI upset.

•Maintain good oral hygiene for hydantoins e.g. phenytoin sodium.

•Monitor patient's blood, liver and kidney parameters as indicated and notify doctor of any abnormalities.

•Notify doctor of abnormal changes in behaviour and mood.

•Discontinue drug if you notice allergic reactions (including red, raised rash), blood dyscrasia (including fever, sore throat, bruising, rash, jaundice); report promptly to doctor.

•Advise patient to avoid driving or other activities that require alertness.

CARBAMAZEPINE

Therapeutic category: Neurotropic and psychotropic agent

Indications: Generalized tonic-clonic and partial seizures; trigeminal neuralgia; bipolar disorder (section 1.4.2).

Contra-indications: Atrioventricular conduction abnormalities; history of bone-marrow depression; porphyria.

Precautions: Hepatic impairment (Appendix 5); renal impairment (Appendix 4); cardiac disease (see also Contraindications); skin reactions (see Adverse effects); history of blood disorders (blood counts before and during treatment); glaucoma; pregnancy (important see notes above; Appendix 2); breastfeeding (see notes above; Appendix 3); avoid sudden withdrawal; **interactions**: Appendix 1

BLOOD, HEPATIC OR SKIN DISORDERS: Patients or their carers should be told how to recognize signs of blood, liver or skin disorders, and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, bruising or bleeding develop. Leukopenia which is severe, progressive and associated with clinical symptoms requires withdrawal (if necessary under cover of suitable alternative).

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING; SEE ALSO NOTES ABOVE.

Advice to patients: Take with food, may cause drowsiness, periodic blood test monitoring required; notify physician if you observe bleeding, bruising, jaundice, abdominal pain, pale stools, mental disturbances, fever, chills, sore throat, or mouth ulcers (these are early toxic signs and symptoms).

Adverse effects: Dizziness, drowsiness, headache, ataxia, blurred vision, diplopia (may be associated with high plasma levels); gastrointestinal intolerance including nausea and vomiting, anorexia, abdominal pain, dry mouth, diarrhoea or constipation; commonly, mild transient generalized erythematous rash (withdraw if worsens or is accompanied by other symptoms); leukopenia and other blood disorders (including thrombocytopenia, agranulocytosis and aplastic anaemia); cholestatic jaundice, hepatitis, acute renal failure, Stevens-Johnson syndrome (erythema multiforme), toxic epidermal necrolysis, alopecia, thromboembolism, arthralgia, fever, proteinuria, lymph node enlargement, arrhythmias, heart block and heart failure, dyskinesias, paraesthesia, depression, impotence, male infertility, gynaecomastia, galactorrhoea, aggression, activation of psychosis, photosensitivity, pulmonary hypersensitivity, hyponatraemia, oedema, disturbances of bone metabolism with osteomalacia also reported; confusion and agitation in elderly.

Nursing considerations: •Give with food or milk to minimize GI distress.

•Relieve dry mouth with frequent sips of water, gum or hard candy.

•Advise patient to avoid driving or potentially hazardous activities that require mental alertness.

•Observe patient for excessive sedation; do not discontinue suddenly when treating seizures or status epilepticus.

Dose: *Generalized tonic-clonic seizures, partial seizures*, by mouth , ADULT initially 100 mg twice daily, increased gradually according to response to usual maintenance Dose of 0.8–1.2 g daily in divided Doses; ELDERLY reduce initial Dose; CHILD 10–20 mg/kg daily in divided Doses.

Trigeminal neuralgia, by mouth , ADULT initially 100 mg 1–2 times daily increased gradually according to response; usual Dose 200 mg 3–4 times daily with up to 1.6 g daily in some patients.

Note: Plasma concentration for optimum response 4–12 mg/litre (17–50 micromol/litre).

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POM **Carbamazepine** *(WMF 5.1)*
Tablets, Carbamazepine 100 mg, 200 mg.

POM **Carbamazepine** *(EDL 5)*
Tablets, Carbamazepine 100 mg, 200 mg.

POM **APO-CARBAMAZEPINE®** *(Lahams)*
Tablet, Carbamazepine 200 mg; white, double-scored tab. marked 'APO 200'.
200 mg - 500.

POM **CARBATOL®** *(Supreme Pharm.)*
Tablet, Carbamazepine 200 mg.
200 mg - 30.

POM **CARZEPIN®** *(Hovid)*
Tablet, Carbamazepine 200 mg
200 mg - 500.

POM **TEGRETOL®** *(Novartis)*
Tablets, Carbamzepine 200 mg; white scored tab. marked 'GEIGY' and 'GK'.
200 mg - 20; 100.

POM **TEGRETOL CR®** *(Novartis)*
Tablets, Carbamazepine 200 mg, 400 mg; s–r, f–c divisible tabs.
200 mg - 50
400 mg - 30.

CLONAZEPAM

DRUG SUBJECT TO INTERNATIONAL CONTROL UNDER THE CONVENTION ON PSYCHOTROPIC SUBSTANCES (1971)

Clonazepam is a representative benzodiazepine anticonvulsant. Various drugs can serve as alternatives.
Clonazepam is a complementary drug.

Indications: Atonic seizures; myoclonic seizures; atypical absence seizures; absence seizures resistant to ethosuximide or valproate; infantile spasms.

Contra-indications: Respiratory depression; acute pulmonary insufficiency; myasthenia gravis.

Precautions: Respiratory disease; hepatic impairment (Appendix 5); renal impairment (Appendix 4); elderly and debilitated; pregnancy (see notes above; Appendix 2); breastfeeding (see notes above; Appendix 3); avoid sudden withdrawal; porphyria; **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING; EFFECTS OF ALCOHOL ENHANCED; SEE ALSO NOTES ABOVE.

Advice to patients: See Label 2 in Appendix 6.

Adverse effects: Drowsiness, lethargy, ataxia, paradoxical aggression, irritability and mental changes; rarely blood disorders, abnormal hepatic function tests, excessive salivation.

Nursing considerations: •Raise bed rails, initiate safety measures, assist with ambulation.
•Instruct patient to avoid alcohol and other CNS depressants; and to avoid alcohol and other CNS depressants, may cause increased sedation.
•Observe patient for excessive sedation, respiratory depression.
•Avoid abrupt discontinuation after prolonged use.

Dose: *Epilepsy* (see Uses above), by mouth, ADULT initially 1 mg at night for 4 nights, increased gradually over 2–4 weeks to a usual maintenance Dose of 4–8 mg daily in divided Doses; ELDERLY (or debilitated patients) initial Dose 500 micrograms increased as above; CHILD up to 1 year initially 250 micrograms increased as above to 0.5–1 mg daily in divided Doses; 1–5 years initially 250 micrograms increased to 1–3 mg daily in divided Doses; 5–12 years initially 500 micrograms increased to 3–6 mg daily in divided Doses.

POM **Clonazepam** *(WMF 5.1)*
Tablet, Clonazepam 500 micrograms.

POM **Clonazepam** *(EDL 5)*
Tablets, Clonazepam 0.5 mg, 2 mg.
Injection, Clonazepam 1 mg per ml; in 1 ml. amp.

DIAZEPAM

DRUG SUBJECT TO INTERNATIONAL CONTROL UNDER THE CONVENTION ON PSYCHOTROPIC SUBSTANCES (1971).

Diazepam is a representative benzodiazepine anticonvulsant. Various drugs can serve as alternatives.

Therapeutic category: Sedative/anticonvulsant.

Indications: Status epilepticus; emergency management of recurrent seizures; febrile convulsions; seizures associated with poisoning and drug withdrawal; adjunct in acute alcohol withdrawal; premedication (section 3.2); anxiety disorders (section 1.1.2)

Contra-indications: Respiratory depression; acute pulmonary insufficiency; sleep apnoea; severe hepatic impairment; myasthenia gravis; avoid injections containing benzyl alcohol in neonates.

Precautions: Respiratory disease, muscle

weakness, history of alcohol or drug abuse, marked personality disorder; pregnancy (see notes above; Appendix 2); breastfeeding (see notes above; Appendix 3); reduce Dose in elderly or debilitated and in hepatic impairment (avoid if severe, Appendix 5), renal impairment (Appendix 4); avoid prolonged use and abrupt withdrawal; when given intravenously facilities for reversing respiratory depression with mechanical ventilation must be at hand (see below); porphyria; **interactions**: Appendix 1.

PRECAUTIONS FOR INTRAVENOUS INFUSION: Intravenous infusion of diazepam is potentially hazardous (especially if prolonged) calling for close and constant observation and best carried out in a specialist centre with intensive care facilities. Prolonged intravenous infusion may lead to accumulation and delay recovery.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING; SEE ALSO NOTES ABOVE.

Adverse effects: Drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, salivation changes, gastrointestinal disturbances, skin reactions, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention; blood disorders and jaundice; hypotension and apnoea, pain and thrombophlebitis (with injection).

Nursing considerations: See Diazepam in Section 1.1.2.

Dose: *Status epilepticus or emergency management of recurrent epileptic seizures*, by slow intravenous injection (at rate of 5 mg/minute), ADULT 10–20 mg, repeated if necessary after 30–60 minutes; may be followed by intravenous infusion to maximum 3 mg/kg over 24 hours; by slow intravenous injection , CHILD 200 to 300 micrograms/kg (or 1 mg per year of age); by rectum as solution, ADULT and CHILD over 10 kg, 500 micrograms/kg, ELDERLY 250 micrograms/kg; repeated if necessary every 12 hours; if convulsions not controlled, other measures should be instituted.

Febrile convulsions (preferred treatment), by rectum as solution [injection solution may be used], CHILD over 10 kg, 500 micrograms/kg (maximum 10 mg), with Dose repeated if necessary

Febrile convulsions (alternative treatment), by slow intravenous injection , CHILD 200–300 micrograms/kg (or 1 mg per year of age)

Drug or alcohol withdrawal, by slow intravenous injection (at rate of 5 mg/minute), ADULT 10 mg; higher Doses may be required depending on severity of symptoms

Seizures associated with poisoning, by slow intravenous injection (at rate of 5 mg/minute), ADULT 10–20 mg.

POM **Diazepam** *(WMF 5.1)*

Injection, (Solution for injection), Diazepam 5 mg/ml; in 2-ml ampoule.

Rectal solution, Diazepam 2 mg/ml, in 1.25- and 2.5-ml tube; 4 mg/ml, in 2.5-ml tube [not included on WHO Model List].

POM **Diazepam** *(EDL 5)*

Injection, Diazepam 5 mg per ml; in 2 ml amp.

See Diazepam in Section 1.1.2 for the proprietary preparations.

ETHOSUXIMIDE

Ethosuximide is a complementary antiepileptic drug.

Indications: Absence seizures.

Precautions: Hepatic or renal impairment; blood counts and hepatic and renal function tests recommended; pregnancy (see notes above; Appendix 2); breastfeeding (see notes above; Appendix 3); avoid sudden withdrawal; porphyria; **interactions**: Appendix 1.

BLOOD DISORDERS: Patients or their carers shoul be told how to recognize signs of blood disorders, and advised to seek immediate medical attention if symptoms such as fever, sore throat, mouth ulcers, bruising or bleeding develop.

SKILLED TASKS: MAY IMPAIR ABILITTO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING; SEE ALSO NOTES ABOVE.

Advice to patients: See Label 2 in Appendix 6.

Adverse effects: Gastrointestinal disturbances including anorexia, hiccups, nausea and vomiting, epigastric pain (particularly during initial treatment); weight loss, drowsiness, dizziness, ataxia,

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headache, depression, mild euphoria; rarely, rash including Stevens-Johnson syndrome (erythema multiforme), systemic lupus erythematosus, disturbances of liver and renal function (see Precautions), haematological disorders including leukopenia, agranulocytosis, aplastic anaemia, thrombocytopenia, pancytopenia; gum hyperplasia, swelling of tongue, irritability, hyperactivity, sleep disturbances, night terrors, aggressiveness, psychosis, increased libido, myopia, vaginal bleeding, also reported.

Nursing considerations: •Administer with food or milk to minimise GI upset.

•Assist with ambulation; warn patient to avoid activities requiring alertness and psychomotor co-ordination.

•Instruct patient not to discontinue drug abruptly as this may cause absence seizure.

•Observe patient for excessive sedation.

Dose: *Absence seizures*, by mouth , ADULT and CHILD over 6 years initially 500 mg daily, increased by 250 mg at intervals of 4–7 days to a usual Dose of 1–1.5 g daily (occasionally, up to maximum of 2 g daily); CHILD under 6 years initially 250 mg daily, increased gradually to usual Dose of 20 mg/kg daily Patient Advice. Daily Doses of 1 g and above should be taken as 2 or more divided Doses.

Note: Plasma concentration for optimum response 40–100 mg/litre (300–700 micromol/litre).

POM **Ethosuximide** *(WMF 5.1)*
Capsule, Ethosuximide 250 mg.
Syrup, Ethosuximide 250 mg/5 ml.

POM **Ethosuximide** *(EDL 5)*
Tablet or Capsule, Ethosuximide 250 mg.
Syrup, Ethosuximide 250 mg per 5 ml.

PARALDEHYDE

Therapeutic category: Hypnotic/ anticonvulsant.

Indications: Status epilepticus.

Precautions: Bronchopulmonary disease or hepatic impairment, colitis, road users, avoid plastic syringes.

Adverse effects: Injection is painful; skin rashes.

Nursing considerations: •Administer I.M. injection in a Z-track method deep into a mass of muscle, to prevent tissue sloughing.

•Observe closely for respiratory depression; advise patient to avoid driving and other activities that require alertness.

•May cause drug depecdence and severe withdrawal symptoms.

•Avoid contact with rubber and plastic; use glass syringe and bottle for parental dose.

•Do not use paraldehyde if it has a brownish colour or an odour of acetic acid, or if the container has been open longer than 24 hours. Always use fresh supply and avoid exposure to air.

Dose: By deep I.M. injection, as a single Dose, Adult , 5-10 ml; up to a max. 20 ml daily (do not give more than 5 ml at any one site).
Child (up to 3 months), as a single Dose, 0.5 ml; 3 - 6 months, 1 ml; 6 -12 months, 1.5 ml; 1-2 years, 2 ml; 3-5 years, 3-4 years, 6-12 years, 5-6 ml.
By I.V. infusion, not recommended.
By rectum, Adult, 5-10 ml; administered as a 10% enema in normal saline. May also be diluted with arachis oil or olive oil 1:2 and given as retention enema.
Child, as for I.M. Dose.

POM **Paraldehyde** *(EDL. 5)*
Injection, Paraldehyde in 5 ml, 10 ml amps.

PHENOBARBITAL

DRUG SUBJECT TO INTERNATIONAL CONTROL UNDER THE CONVENTION ON PSYCHOTROPIC SUBSTANCES (1971).

Therapeutic category: Sedative/ anticonvulsant

Indications: Generalized tonic-clonic seizures; partial seizures; neonatal seizures; febrile convulsions; status epilepticus (see notes above).

CONTRAINDICATIONS: Porphyria; absence seizures.

Precautions: Elderly, debilitated, children (may cause behavioural changes); impaired renal function (Appendix 4) or hepatic function (Appendix 5), respiratory depression (avoid if severe); pregnancy (see notes above; Appendix 2); breastfeeding (see notes above; Appendix 3); avoid sudden withdrawal; **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING; SEE ALSO NOTES ABOVE.

Advice to patients: See Label 2 in Appendix 6.

Adverse effects: Sedation, mental depression, ataxia, nystagmus; allergic skin reactions including rarely, exfoliative dermatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome (erythema multiforme); paradoxical excitement, restlessness and confusion in the elderly;

irritability and hyperactivity in children; megaloblastic anaemia (may be treated with folic acid); osteomalacia; status epilepticus (on treatment withdrawal); hypotension, shock, laryngospasm and apnoea (with intravenous injection).

Nursing considerations: •Institute safety measures to avoid injuries; observe patient for excessive sedation and respiratory depression.

•Warn patient not to discontinue drug abruptly but to inform physician immediately if adverse reactions occur.

•Teach patient that drug may cause physical and psychological dependence and he/she should not alter dose without notifying physician.

Dose: *Generalized tonic-clonic seizures*, partial seizures, by mouth, ADULT 60–180 mg at night; CHILD up to 8 mg/kg daily

Febrile convulsions, by mouth, CHILD up to 8 mg/kg daily.

Neonatal seizures, by intravenous injection (dilute injection 1 in 10 with water for injections), neonate 5–10 mg/kg every 20–30 minutes up to plasma concentration of 40 mg/litre.

Status epilepticus, by intravenous injection (dilute injection 1 in 10 with water for injections), ADULT 10 mg/kg at a rate of not more than 100 mg/minute (up to maximum total Dose of 1 g); CHILD 5–10 mg/kg at a rate of not more than 30 mg/minute.

Note: For therapeutic purposes phenobarbital and phenobarbital sodium may be considered equivalent in effect. Plasma concentration for optimum response 15–40 mg/litre (65–170 micromol/litre).

POM **Phenobarbital** *(WMF 5.1)*
Tablets, Phenobarbital 15 mg, 30 mg, 60 mg, 100 mg.
Elixir (Oral solution), Phenobarbital 15 mg/5 ml
Injection (Concentrate for solution for injection), Phenobarbital sodium 200 mg/ml [not included on WHO Model List].

POM **Phenobarbitone** *(EDL 5)*
Tablets, Phenobarbitone 15 mg, 30 mg, 60 mg.
Elixir, Phenobarbitone 15 mg per 5 ml.

POM **Phenobarbitone** *(Emzor)*
Tablets, Phenobarbitone 15 mg, 30 mg, 60 mg; white biconvex tabs.
Pack - 100; 1000.

POM **Phenobarbitone** *(Mopson)*
Tablet, Phenobarbitone 30 mg.
Pack - 1000.
Syrup, Phenobarbitone 15 mg per 5 ml.
Pack - 60 ml.

POM **Phenobarbitone** *(Vitabiotics)*
Tablets, Phenobarbitone 30 mg.
30 mg - 1000's.

PHENYTOIN SODIUM

Indications: Generalized tonic-clonic seizures; partial seizures; status epilepticus.

Contra-indications: Porphyria; avoid parenteral use in sinus bradycardia, sino-atrial block, second- and third-degree heart block, Stokes-Adams syndrome.

Precautions: Hepatic impairment (reduce Dose; Appendix 5); pregnancy (important, see notes above; Appendix 2); breastfeeding (see notes above; Appendix 3); diabetes mellitus; monitor blood counts; hypotension and heart failure (caution with parenteral use); intravenous administration—resuscitation facilities must be available; injection solution alkaline (irritant to tissues); **interactions**: Appendix 1.

BLOOD OR SKIN DISORDERS: Patients or their carers should be told how to recognize signs of blood or skin disorders and advised to seek immediate medical attention if symptoms such as sore throat, rash, mouth ulcers, bruising or bleeding develop. Leukopenia which is severe, progressive or associated with clinical symptoms requires withdrawal (if necessary under cover of suitable alternative)

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING; SEE NOTES ABOVE

Adverse effects: Gastric intolerance, headache, sleeplessness, agitation (during initial phase); sedation, confusion, blurred vision, ataxia, nystagmus, diplopia, slurred speech, cerebellar-vestibular symptoms, behavioural disorders, hallucinations, hyperglycaemia (may be signs of overdosage); gingival hyperplasia, acne, coarse facies, hirsutism, fever, hepatitis, neurological changes (peripheral neuropathy, choreiform movements, impaired cognition, increased seizure frequency); osteomalacia, rickets (associated with reduced plasma calcium levels); lymph-node enlargement; rashes

(discontinue; if mild re-introduce cautiously, but discontinue if recurrence); very rarely, Stevens-Johnson syndrome (erythema multiforme), systemic lupus erythematosus, toxic epidermal necrolysis; rarely blood disorders including megaloblastic anaemia (may be treated with folic acid), leukopenia, thrombocytopenia, agranulocytosis with or without bone marrow depression; intravenous administration—cardiovascular and CNS depression (particularly if administered too rapidly) with arrhythmias, hypotension and cardiovascular collapse, alterations in respiratory function (including respiratory collapse).

Advice to patients: See Labels 21 and 27 in Appendix 6.

Nursing considerations: •Give orally, after meals, in divided doses to prevent averse GI reactions; advise patient not to stop drug abruptly (seizures may occur) and also not to change brand or dosageform without notifyig physician.

•Discontinue drug if rash appears and notify the physcian.

•Stress the importance of oral hygiene and regular dental examintion to minimise the development of gingival hyperplasia.

•Caution patient on the use of other drugs or alcoholic beverages without first seeking the physician's advice. Alcohol may diminish the effect of the drug

•Patient should avoid activities that require mental alertness and physical coordination until the CNS effects of the drug are established.

•Drug may colour urine pink, red, or reddish-brown.

Dose: *Generalized tonic-clonic seizures*, partial seizures, by mouth , ADULT initially 3–4 mg/kg daily (as a single Dose or in 2 divided Doses), increased gradually at intervals of 2 weeks as necessary (with plasma-phenytoin concentration monitoring); usual Dose 200–500 mg daily; CHILD initially 5 mg/kg daily in 2 divided Doses; usual Dose range 4–8 mg/kg daily (maximum 300 mg).

Note: Plasma concentration for optimum response 10–20 mg/litre (40–80 micromol/litre).

Patient Advice: Preferably taken with or after food.

Status epilepticus, by slow intravenous injection or by intravenous infusion (with blood pressure and ECG monitoring), ADULT 15 mg/kg at a rate of not more than 50 mg/minute, as a loading Dose; maintenance Doses of about 100 mg by mouth or by slow intravenous injection should be given thereafter at intervals of 6–8 hours, monitored by measurement of plasma concentrations; rates and Dose reduced according to weight; CHILD 15 mg/kg as a loading Dose at rate of 1 mg/kg/minute (not exceeding 50 mg/minute); neonate 15–20 mg/kg as a loading Dose at rate of 1–3 mg/kg/minute

Dilution and Administration: According to manufacturer's directions.

POM **Phenytoin Sodium** *(WMF 5.1)*
Tablets, Phenytoin sodium 25 mg, 50 mg, 100 mg.
Capsules, Phenytoin sodium 25 mg, 50 mg, 100 mg.
Injection (Solution for injection), Phenytoin sodium 50 mg/ml; in 5-ml ampoule.

POM **Phenytoin Sodium** *(EDL 5)*
Tablets or Capsules, Phenytoin sodium 25 mg, 50 mg, 100 mg.

POM **EPANUTIN®** *(Pharma-Deko)*
Capsules, Phenytoin sodium 25 mg (white/purple cap.), 50 mg (white/pink cap.) and 100 mg (white/orange cap.). All marked with cap. name and strength.

POM **EPITOIN®** *(Hovid)*
Capsule, Phenytoin sodium 100 mg
100 mg - 1000.

SODIUM VALPROATE

Synonym: Valproate Sodium; Valproic Acid.

Indications: Generalized tonic-clonic seizures; partial seizures; atonic seizures; absence seizures; myoclonic seizures; acute mania (section 1.4.2).

Contra-indications: Active liver disease, family history of severe hepatic dysfunction; pancreatitis; porphyria.

Precautions: Monitor liver function before and during first 6 months of therapy (Appendix 5), especially in patients at most risk (children under 3 years of age, those with metabolic disorders, degenerative disorders, organic brain disease or severe seizure disorders associated with mental retardation, or multiple antiepileptic therapy); ensure no undue potential for bleeding before starting and before major surgery or anticoagulant therapy; renal impairment (Appendix 4); pregnancy (important see notes above; Appendix 2 (neural tube screening)); breastfeeding

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(see notes above; Appendix 3); systemic lupus erythematosus; false-positive urine tests for ketones; avoid sudden withdrawal; **interactions**: Appendix 1

BLOOD OR HEPATIC DISORDERS: Patients or their carers should be told how to recognize signs of blood or liver disorders, and advised to seek immediate medical attention if symptoms including loss of seizure control, malaise, weakness, anorexia, lethargy, oedema, vomiting, abdominal pain, drowsiness, jaundice, or spontaneous bruising or bleeding develop.

PANCREATITIS: Patients or their carers should be told how to recognize signs of pancreatitis and advised to seek immediate medical attention if symptoms such as abdominal pain, nausea and vomiting develop; discontinue sodium valproate if pancreatitis diagnosed.

Adverse effects: Gastrointestinal irritation, nausea, increased appetite and weight gain, hyperammonaemia; ataxia, tremor; transient hair loss (regrowth may be curly); oedema, thrombocytopenia, inhibition of platelet aggregation; impaired hepatic function and rarely fatal hepatic failure (see Precautions—withdraw treatment immediately if malaise, weakness, lethargy, oedema, abdominal pain, vomiting, anorexia, jaundice, drowsiness or loss of seizure control); sedation reported and also increased alertness; behavioural disturbances; rarely pancreatitis (measure plasma amylase if acute abdominal pain), extrapyramidal symptoms, leukopenia, pancytopenia, red cell hypoplasia, fibrinogen reduction; irregular periods, amenorrhoea, gynaecomastia, hearing loss, Fanconi syndrome, dementia, toxic epidermal necrolysis, Stevens-Johnson syndrome (erythema multiforme), vasculitis, hirsutism and acne reported.

Advice to patients: Take with food or milk; do not chew, break or crush the tablet or capsule to avoid local irritation of the mouth and throat; do not administer with carbonated drinks as it may irritate the mouth and throat; report any sore throat, fever or fatigue, bleeding or bruising that is severe or that persists; may cause drowsiness, impair judgement or co-ordination.

Nursing considerations: •Administer tablets or capsules whole; give elixir alone and do not dilute it. •Instruct patient not to discontinue drug abruptly after a long period of use, since convulsions may occur.

Dose: *Generalized tonic-clonic seizures, partial seizures, absence seizures, atonic seizures; myoclonic seizures*, by mouth , ADULT initially 600 mg daily in 2 divided Doses, preferably after food, increased by 200 mg daily at 3-day intervals to maximum of 2.5 g daily in divided Doses; usual maintenance Dose 1–2 g daily (20–30 mg/kg daily); CHILD up to 20 kg, initially 20 mg/kg daily in divided Doses, may be increased provided plasma concentrations monitored (above 40 mg/kg daily also monitor clinical chemistry and haematological parameters); CHILD over 20 kg, initially 400 mg daily in divided Doses, increased until control (usually in range of 20–30 mg/kg daily); maximum 35 mg/kg daily.

Note: Plasma concentrations in therapeutic range of 40–100 mg/litre (280 to 700 micromol/litre); not generally considered useful in assessing control, but higher levels associated with increased incidence of adverse effects; indicator of compliance, Dose change or co-medication.

POM **Sodium Valproate** *(WMF 5.1)*
Gastro-resistant tablets (Enteric-coated tablets), Sodium valproate 200 mg, 500 mg.

POM **Sodium Valproate** *(EDL 5)*
Tablets, Sodium valproate 100 mg, 200 mg, 500 mg.
Elixir, Sodium valproate 200 mg per 5 ml.

POM **EPILIM®** *(Sanofi)*
Tablets, Sodium Valprote 200 mg, 500 mg; both e-c tabs.
200 mg – 100
500 mg – 100
Tablet (Crushable), Sodium Valproate 100 mg.
100 mg – 100
Syrup, Sodium Valproate 200 mg per 5 ml; red syrup.
Pack – 300 ml
Liquid, Sodium Valproate 200 mg per 5 ml; sugar-free red liquid.
Pack - 300 ml.

1.8 Analgesics

1.8.1 Non-opioid analgesics and antipyretics
1.8.2 Opioid analgesics

Pain can be classified as acute or chronic. Acute pain is usually of short duration and the cause often identifiable (disease,

trauma). Chronic pain persists after healing is expected to be complete, or is caused by a chronic disease. Pain may be modified by psychological factors and attention to these is essential in pain management. Drug treatment aims to modify the peripheral and central mechanisms involved in the development of pain. Neurogenic pain generally responds poorly to conventional analgesics; treatment can be difficult and includes the use of carbamazepine (section 1.7.1) for trigeminal neuralgia and amitriptyline (section 1.4.1) for diabetic neuropathy and postherpetic neuralgia.

Non-opioid analgesics (section 1.8.1) are particularly suitable for pain in musculoskeletal conditions whereas the opioid analgesics (section 1.8.2) are more suitable for moderate to severe visceral pain. Those non-opioid analgesics which also have anti-inflammatory actions include salicylates and NSAIDs (nonsteroidal anti-inflammatory drugs); they can reduce both pain and inflammation of chronic inflammatory disorders such as rheumatoid arthritis, but they do not alter or modify the disease process itself. For the management of rheumatoid arthritis DMARDs (disease-modifying antirheumatic drugs) may favourably influence the outcome of the disease (section 2.1.2). The pain and inflammation of an acute attack of gout is treated with a NSAID or colchicine (section 2.2.1); a xanthine-oxidase inhibitor (section 2.2.2) is used for long-term control of gout.

1.8.1 Non-opioid analgesics and antipyretics

Non-opioid analgesics with anti-inflammatory activity include salicylates such as acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs such as ibuprofen. Non-opioid analgesics with little or no anti-inflammatory activity include paracetamol.

Acetylsalicylic acid

The principal effects of **acetylsalicylic acid** are anti-inflammatory, analgesic, antipyretic and antiplatelet. Oral Doses are absorbed rapidly from the gastrointestinal tract; rectal absorption is less reliable but suppositories are useful in patients unable to take oral dosage forms. Acetylsalicylic acid is used for the management of mild to moderate pain such as headache, acute migraine attacks (section 1.9), transient musculoskeletal pain and dysmenorrhoea, and for reducing fever. Although it may be used in higher Doses in the management of pain and inflammation of rheumatoid arthritis, other NSAIDs are preferred because they are likely to be better tolerated. Acetylsalicylic acid is also used for its antiplatelet properties (section 5.6). Adverse effects with analgesic Doses are generally mild but include a high incidence of gastrointestinal irritation with slight blood loss, bronchospasm and skin reactions in hypersensitive patients, and increased bleeding time. Anti-inflammatory Doses are associated with a much higher incidence of adverse reactions, and they also cause mild chronic salicylism which is characterized by tinnitus and deafness. Acetylsalicylic acid should be avoided in children under 16 years, unless specifically indicated (for example juvenile arthritis), because of an association with Reye syndrome (encephalopathy and liver damage); it should particularly be avoided during fever or viral infection in children and adolescents.

Paracetamol

Paracetamol is similar in analgesic and antipyretic efficacy to acetylsalicylic acid. It is used for mild to moderate pain including headache and acute migraine attacks (section 1.9) and for reducing fever, including post-immunization pyrexia. Paracetamol is particularly useful in patients in whom salicylates or other NSAIDs are contraindicated, such as asthmatics and those with a history of peptic ulcer, or for children under the age of 16 years in whom salicylates should be avoided because of the risk of Reye syndrome. It is generally preferred to acetylsalicylic acid, particularly in the elderly, because it is less irritant to the stomach. Unlike acetylsalicylic acid and other NSAIDs, paracetamol has little anti-inflammatory activity which limits its usefulness for long-term treatment of pain associated with inflammation; however it is useful in the management of osteoarthritis, a condition with only a small inflammatory component. In normal Doses adverse effects are rare, but overdosage with a single Dose of 10–15 g is particularly dangerous because it may cause

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hepatocellular necrosis and, less frequently, renal tubular necrosis.

ASPIRIN

Synonym: Acetylsalicylic Acid; ASA.

Therapeutic category: Analgesic; Anti-inflammatory Agent; Antipyretic; NSAID.

Indications: Mild to moderate pain including dysmenorrhoea, headache; pain and inflammation in rheumatic disease and other musculoskeletal disorders (including juvenile arthritis); pyrexia; acute migraine attack (section 1.9); antiplatelet (section 5.6).

Contra-indications: Hypersensitivity (including asthma, angioedema, urticaria or rhinitis) to acetylsalicylic acid or any other NSAID; children and adolescents under 16 years (Reye syndrome—see also notes above); gastrointestinal ulceration; haemophilia and other bleeding disorders; not for treatment of gout.

Precautions: Asthma, allergic disease; impaired renal or hepatic function (Appendices 4 and 5); pregnancy (Appendix 2); breastfeeding (Appendix 3); elderly; G6PD-deficiency; dehydration; **interactions**: Appendix 1.

Adverse effects: Generally mild and infrequent for lower Doses, but common with anti-inflammatory Doses; gastrointestinal discomfort or nausea, ulceration with occult bleeding (occasionally major haemorrhage); also other haemorrhage (including subconjunctival); hearing disturbances such as tinnitus (rarely deafness), vertigo, confusion, hypersensitivity reactions (angioedema, bronchospasm and rash); increased bleeding time; rarely oedema, myocarditis, blood disorders (particularly thrombocytopenia).

Advice to patients: See Label 21 in Appendix 6.

Nursing considerations: •Administer with food, milk, antacid, or large glass of water to minimize GI distress.

•Watch for bleeding gums or any signs of GI bleeding particularly in patients on large doses and/or prolonged therapy.

•Co-administration with alcohol, steroids or other NSAIDs may increase risk of GI bleeding.

•Teach patient to avoid other OTC medications unless on doctor's or pharmacist's supervision.

•Advise patient to notify physician if ringing in ears or persistent GI pain occurs.

•Encourage patient to use soft tooth brush.

Dose: *Mild to moderate pain, pyrexia*, by mouth with or after food, ADULT 300–900 mg every 4–6 hours if necessary; maximum 4 g daily; CHILD under 16 years not recommended.

Mild to moderate pain, pyrexia, by rectum, ADULT 600–900 mg inserted every 4 hours if necessary; maximum 3.6 g daily; CHILD under 16 years not recommended.

Inflammatory arthritis, by mouth with or after food, ADULT 4–8 g daily in divided Doses in acute conditions; up to 5.4 g daily may be sufficient in chronic conditions

Juvenile arthritis, by mouth with or after food, CHILD up to 130 mg/kg daily in 5–6 divided Doses in acute conditions; 80–100 mg/kg daily in divided Doses for maintenance.

OTC **Acetylsalicylic acid** *(WMF 2.1.1)*
Tablets, Acetylsalicylic acid 300 mg.
Dispersible tablets (Soluble tablets), Acetylsalicylic acid 300 mg [not included on the WHO Model List].
Suppositories, Acetylsalicylic acid 150 mg, 300 mg [300-mg strength not included on the WHO Model List].

OTC **Aspirin** *(EDL 2.3)*
Tablet (or Capsule), Acetylsalicylic acid 300 mg, 500 mg.

OTC **ALAGBIN® Plus** *(P.Z.)*
Tablet, Aspirin 500 mg, caffeine anhydrous 30 mg.
Pack - 20; 200

OTC **ALKA-SELTZER®** *(Gemini)*
Tablet (soluble), Acetylsalicylic acid 324 mg.
324 mg – 30

OTC **ANACIN®** *(SKG)*
Tablet, Acetylsalicylic acid 300 mg; white biconvex tab. marked with a broad arrow on both sides.
300 mg - 72 x 2.

OTC **Aspirin** *(BCN)*
Tablet, Acetylsalicylic acid 300 mg.
300 mg - 1000.

OTC **Aspirin** *(Chemo-Pharma)*
Caplet, Acetylsalicylic acid 300 mg
300 mg - 1000.

OTC **Aspirin** *(Gemini)*
Tablet, Acetylsalicylic acid 300 mg.
300 mg - 30; 100.

OTC **Aspirin** *(Juhel)*
Tablet, Acetylsalicylic acid 300 mg.
300 mg - 1000.

OTC **Aspirin** *(May & Baker)*
Tablet, Acetylsalicylic acid 300 mg.
300 mg - 1000.

OTC **Aspirin** *(Novel)*
Tablet, Acetylsalicyclic acid 300 mg; white shallow concave tab.
300 mg - 1000.

OTC **Aspirin** *(Ranbaxy)*
Tablet, Acetylsalicylic acid 300 mg.
300 mg – 1000.

OTC **Aspirin** *(Ulticare-Lyka)*
Caplet, Acetylsalicylic acid 300 mg.
300 mg – 1000.

OTC **CAFENOL**® *(GSK)*
Tablet, Acetylsalicylic acid 300 mg; white scored tab. marked 'CAFENOL'.
300 mg - 60; 200.

OTC **DISPRIN**® *(Reckitt Benckiser).*
Soluble Tablet, Aspirin 300 mg; white scored tab. marked 'DISPRIN'.
300 mg -3.

OTC **DRASTIN**® **Plus***(P.Z.)*
Tablet, Aspirin 420 mg, caffeine anhydrous 30 mg.
Pack - 30; 100; 150.

OTC **EMPIRIN**® *(Emzor)*
Tablet, Acetylsalicylic acid 300 mg; white plain biconvex tab.
300 mg – 1000.

OTC **HEDEX**® *(GSK)*
Tablet, Acetylsalicylic acid 500 mg; white capsule-shaped tab.

OTC **NASMOPRIN**® *(NASDMU)*
Tablet, Acetylsalicylic acid 300 mg; white shallow concave tab. marked "NASMOPRIN" on one side and "NASDMU" on the reverse.
Pack - 1000.

OTC **PHENSIC**® *(GSK)*
Tablet, Acetylsalicylic acid 300 mg; white tab. marked 'PHENSIC' on both sides.
300 mg – 4 x 15 (in blister).
Dose: Adult and child over 12 years, 600 mg every 3-4 hours as required; not exceeding 3.6 g in 24 hours.

OTC **PROPON**® *(Pharchem)*
Tablet, Acetylsalicylic acid 500 mg.
500 mg – 1000.
Dose: By mouth, Adult, 500 mg 3 times daily.

OTC **TOPTABS**® *(SKG)*
Tablet, Acetylsalicylic acid 350 mg, caffeine 30 mg.
300 mg – 50.
Dose: By mouth, Adult, 1 - 2 tabs up to 4 times daily.

POM **VASOPRIN**® *(Juhel)*
Tablet, Acetyl Salicylic Acid B.P. 75 mg.
Pack - 30; 100; 500.
Indications: Reduces the risk of episodes in patients with overt cardiovascular diseases and for the temporary relief of minor aches and pains associated with a cold, headache, toothache, muscular aches and to reduce fever.
Dose: *In cardiovascular therapy*, 1-2 tabs daily. *For pains*, 4-8 tabs every 4 hours as needed. Do not exceed 48 tablets in 24 hours. Drink a full glass of water with each Dose.

ASPIRIN plus CODEINE

Indications: Headache, rheumatic and nerve pain; colds and feverish conditions.
Precautions: Peptic ulcer disease; avoid alcohol. Prolonged use of high Doses of Codeine can lead to dependence.
Adverse effects: Constipation, nausea, vomiting, dizziness, drowsiness.
Advice to patients: See Label 21 in Appendix 6.
Nursing considerations: •Teach patient of potential to abuse and physical dependency may occur.
•Teach him/her to avoid OTC products such as salicylates, alcohol in cough products and cold preparations unless prescribed by the doctor.
• See also under Aspirin.
Dose: Adult and children over 12 years, 1-2 tablets up to 4 times a day if necessary; not exceeding 8 tablets within 24 hours. Not recommended for children under 12 years.

OTC **BEECODEEN**® *(BCN)*
Tablet, Aspirin B.P. 400 mg, codeine phosphate B.P. 8 mg.
Pack - 50; 1000.

PARACETAMOL

Synonym: Acetaminophen.
Therapeutic category: Non-narcotic analgesic and antipyretic.
Indications: Mild to moderate pain including dysmenorrhoea, headache; pain

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relief in osteoarthritis and soft tissue lesions; pyrexia including post-immunization pyrexia; acute migraine attack (section 1.9).

Precautions: Hepatic impairment (Appendix 5); renal impairment; alcohol dependence; breastfeeding (Appendix 3); **overdosage**: section 19.2.1; **interactions**: Appendix 1.

Adverse effects: Rare but rashes and blood disorders reported; important: liver damage (and less frequently renal damage) following overdosage.

Advice to patients: See Label 29 in Appendix 6.

Nursing considerations: •Give with food or milk to reduce GI upset if necessary.
•Large doses, prolonged use or excessive consumption of alcohol can cause liver damage.
•Warn patient to avoid use in high fever, fever persisting longer than 3 days, or recurrent fever without consulting a doctor.
•Teach patient symptoms of overdosage namely nausea, vomiting, abdominal pain; to report to doctor immediately.

Dose: *Post-immunization pyrexia*, by mouth, INFANT 2–3 months, 60 mg followed by a second Dose, if necessary, 4–6 hours later; warn parents to seek medical advice if pyrexia persists after second Dose.
Mild to moderate pain, pyrexia, by mouth, ADULT 0.5–1 g every 4–6 hours, maximum 4 g daily; CHILD under 3 months see note below, 3 months–1 year 60–125 mg, 1–5 years 120–250 mg, 6–12 years 250–500 mg, these Doses may be repeated every 4–6 hours if necessary (maximum 4 Doses in 24 hours).
Mild to moderate pain, pyrexia, by rectum, ADULT 0.5–1g; CHILD 1–5 years 125–250 mg, 6–12 years 250–500 mg; Doses inserted every 4–6 hours if necessary, maximum 4 Doses in 24 hours.

Note: Infants under 3 months should not be given paracetamol unless advised by a doctor; a Dose of 10 mg/kg (5 mg/kg if jaundiced) is suitable.

OTC **Paracetamol** *(WMF 2.1.1)*
Tablets, Paracetamol 500 mg
Dispersible tablets (Soluble tablets), Paracetamol 120 mg, 500 mg [not included on WHO Model List].
Oral solution, Paracetamol 120 mg/5 ml, 125 mg/5 ml, 250 mg/5 ml [120 mg/5 ml and 250 mg/5 ml strengths not included on WHO Model List].
Suppositories, Paracetamol 60 mg, 100 mg, 125 mg, 250 mg, 500 mg [only 100-mg strength included on WHO Model List].

OTC **Paracetamol** *(EDL 2.3)*
Tablets or Capsules, Paracetamol 125 mg, 500 mg.
Suspension or Syrup, Paracetamol 125 mg per 5 ml.
Suppository, Paracetamol 100 mg.

OTC **ACAMOL®** *(Dizpharm)*
Tablet, Paracetamol 500 mg.
500 mg - 20; 1000
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml, 2 L.

OTC **BARBIMOL®** *(Juhel)*
Paediatric tablet, Paracetamol BP 125 mg; orange scored biconvex tablet marked 'P/125' and 'Juhel' on the reverse.
125 mg – 10 x 10's.
Syrup, Paracetamol BP 125 mg per 5 ml.
Pack – 60 ml in amber bottle.

OTC **CAPOL®** *(GSK)*
Tablet, Paracetamol 500 mg.
500 mg - 20; 100; 500.
Suspension, Paracetamol 125 mg per 5 ml
Pack - 60 ml.

OTC **CHEMADOL®** *(Chemiron)*
Tablet, Paracetamol 500 mg
Syrup, Paracetamol 120 mg per 5 ml.

OTC **DAGA®** *(NGC)*
Tablet, Paracetamol 500 mg; yellow flat/round scored tab. marked 'DAGA' and 'Hoechst logo'.
500 mg - 200.
Syrup, Paracetamol 125 mg per 5 ml.
Pack - 60 ml.

OTC **DAGA® Plus** *(NGC)*
Tablet, Paracetamol, caffeine.

OTC **DEPENDOL®** *(Strides Vital)*
Tablet, Paracetamol 500 mg; white tab. marked 'P/500' on one side.
500 mg - 96.

OTC **DOLVIRAN-P®** *(Gemini)*
Tablet, Paracetamol 500 mg
500 mg - 20.

OTC **EMCAP®** *(Emzor)*
Caplet, Paracetamol 500 mg; white scored

capsule-shaped tab. marked 'EMZOR'.
500 mg - 100; 1000.
Caplet (Extra), Paracetamol 500 mg, caffeine 30 mg.
Pack - 200.

OTC **FAPDOL**® *(Food & Pharma)*
Tablet, Paracetamol 500 mg.
500 mg - 100; 1000.
Syrup, Paracetamol 125 mg per 5 ml
Pack - 60 ml.

OTC **FEBRILIX**® *(BCN)*
Syrup, Paracetamol 125 mg per 5 ml.
Pack - 60 ml.

OTC **FEVAMOL**® *(David)*
Tablet, Paracetamol 500 mg.
Syrup, Paracetamol 125 mg per 5 ml.

OTC **GATMOL**® *(Gateway)*
Tablet, Paracetamol 500 mg.
500 mg - 100; 200;1000.

OTC **IMOCETA**® *(Chris-Ejik)*
Tablet, Paracetamol 500 mg.
500 mg - 10, 1000.

OTC **LEADAMOL**® *(Leady-pharma)*
Tablet, Paracetamol 500 mg.
Syrup, Paracetamol 125 mg per 5 ml.

OTC **LOFEV**® *(Interpharma)*
Tablet, Paracetamol 500 mg.
500 mg - 10 x 10's.

OTC **LOTEMP**® *(Unique)*
Tablet, Paracetamol 500 mg.
500 mg - 4 x 24; 1000.
Caplet, Paracetamol 500 mg.
500 mg - 10 x 10; 1000.
Syrup, Paracetamol 125 mg per 5 ml.
Pack - 60 ml.

OTC **M & B 5**® *(May & Baker)*
Tablet, Paracetamol 500 mg.
500 mg - 20; 200.
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml.

OTC **MANTRA**® *(Jawa)*
Caplet, Paracetamol 500 mg.

OTC **MATHEWDOL**® *(Daily Need)*
Syrup, Paracetamol Syrup B.P.
Pack - 60 ml.

OTC **MERACAF**® *(Justeen)*
Tablet, Paracetamol 500 mg, Caffeine 25 mg.
Pack – 2 x 10's.

OTC **MICPOL**® *(Mopson)*
Suspension, Paracetamol 120 mg per 5 ml.
Pack - 60 ml, 2 L.

OTC **MIRA-PARA**® *(Mirapharm)*
Elixir, Paracetamol 125 mg per 5 ml.

OTC **Moko Paracetamol** *(New Healthway)*
Syrup, Paracetamol Syrup 120 mg per 5 ml.
Pack - 60 ml.

OTC **NACEMOL**® *(NASDMU)*
Tablet, Paracetamol 500 mg; white scored tab. marked 'P/500' on one side and 'NASDMU' on the reverse.
500 mg - 96; 1000.

OTC **NOVADEX**® *(SKG)*
Tablet, Paracetamol 500 mg; white scored tab. marked 'P500' on one side and 'NOVADEX' on the reverse.
500 mg - 50 x 2; 100; 100.
Elixir, Paracetamol 125 mg per 5 ml; red strawberry flavoured syrup.
Pack - 60 ml; 2 L.

OTC **PADOX**® *(Chemo-Pharma)*
Syrup, Paracetamol 125 mg per 5 ml
Pack - 60 ml.

OTC **PAINAX**® *(Evans)*
Tablet, Paracetamol 500 mg; white/pink scored tab. marked 'LX'.
500 mg - 20; 100; 1000.

OTC **PAINKIL**® *(Farmex-Meyer)*
Tablet, Paracetamol 500 mg;
500 mg - 10; 20.
Syrup, Paracetamol 125 mg per 5 ml
Pack - 60 ml

OTC **PANADOL**® *(GSK)*
Tablet, Paracetamol 500 mg; white round flat tab. marked 'PANADOL' on both sides.
500 mg - 20; 100; 500.
Chewable tablet (Children's), Paracetamol 125 mg; pink cherry flavoured tab.
125 mg - 20; 100.

OTC **PANDA**® *(Afrab Chem)*
Tablet, Paracetamol 500 mg.
500 mg - 96; 1000.
Syrup, Paracetamol 125 mg per 5 ml.
Pack - 60 ml amber bottle.
Drops, Paracetamol 100 mg per ml.

Pack - 15 ml amber bottle with dropper.

OTC **Paracetamol** *(BCN)*
Tablet, Paracetamol 500 mg
500 mg - 1000.
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 4 L.

OTC **Paracetamol** *(Chemo-Pharma)*
Tablet, Paracetamol 500 mg; scored tab. marked 'P.500' on one side and 'CHEMO' on the reverse.
500 mg - 1000

OTC **Paracetamol** *(Emzor)*
Tablet, Paracetamol 500 mg; white scored tab. marked EMZOR.
500 mg - 96; 1000.
Syrup, Paracetamol 125 mg per 5 ml; clear pink syrup.
Pack - 60 ml: 2 L.

OTC **Paracetamol** *(Farmex-Meyer)*
Tablet, Paracetamol 500 mg.
500 mg - 1000.

OTC **Paracetamol** *(Juhel)*
Tablet, Paracetamol 500 mg.
500 mg - 96; 1000.

OTC **Paracetamol** *(Leady)*
Tablet, Paracetamol 500 mg; white scored tab. marked 'LP500'.
500 mg - 100; 1000.
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml; 2 L.

OTC **Paracetamol** *(Mopson)*
Tablet, Paracetamol 500 mg.
500 mg - 1000.
Caplet, Paracetamol 500 mg; white or yellow caplet.
500 mg - 1000.
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml, 2 L.

OTC **Paracetamol** *(Neimeth)*
Tablet, Paracetamol 500 mg.
500 mg - 20.
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml.

OTC **Paracetamol** *(Novel)*
Tablet, Paracetamol 500mg; white scored tab. marked P.500 on one side and 'NOVEL' on the reverse.
500mg - 96, 1000.
Caplet, Paracetamol 500mg; white or pink caplet marked P/500 on one side and 'NOVEL' on the reverse.
Pack - 1000.

OTC **Paracetamol** *(Panvij Biotec)*
Tablet, Paracetamol 500 mg; white or yellow scored tab. marked 'P' and '500'.
500mg - 10 x 10; 100 x 10.

OTC **Paracetamol** *(Pharchem)*
Tablet, Paracetamol 500 mg.
500 mg - 1000.

OTC **Paracetamol** *(Ulticare-Lyka)*
Caplet, Paracetamol 500 mg.
500 mg - 1000.

OTC **PARADANA®** *(Dana)*
Tablet, Paracetamol 500 mg.
500 mg - 8 x 12's; 1000's.

OTC **PARAFEN®** *(Justeen)*
Tablet, Paracetamol 500 mg, Caffeine 30 mg.
Pack – 200's.

OTC **PARAKAF®** *(Diamond Remedies)*
Caplet, Paracetamol 500 mg; white tab. marked 'PARAKAF' on both sides.
500 mg - 2 x 10.
Caplet (Extra), Paracetamol 500 mg, caffeine (anhydrous) 30 mg.
Pack - 200.

OTC **PARAMEDROL®** *(Transpharm)*
Tablet, Paracetamol 500 mg; white uncoated tab.
500 mg - 12 x 8 (in blisters); 100; 250; 500;1000.

OTC **PARAMEX®** *(Farmex-Meyer)*
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml.

OTC **PASTIN® Extra** *(Juhel)*
Tablet, Paracetamol 500 mg, caffeine 30 mg.
Pack - 200; 1000.

OTC **PENSTOP®** *(Rajrab)*
Tablet, Paracetamol 500 mg; white scored tab.
500 mg - 20; 100; 1000.
Elixir, Paracetamol 120 mg per 5 ml; pink flavoured elixir.
Pack - 100 ml; 2 L.

OTC **PENTAMOL®** *(Morison)*
Elixir, Paracetamol 120 mg per 5 ml.
Pack - 60 ml.

OTC **PENTAX®** *(Vitabiotics)*

Syrup, Paracetamol 125 mg per 5 ml
Pack - 60 ml.

OTC **PENTAX Plus**® *(Vitabiotics)*
Tablet, Paracetamol 500 mg, Caffeine 25 mg.
Pack - 20.

OTC **PHARDOL**® *(Pharma-Deko)*
Suppository, Paracetamol 125 mg; white or off-white suppositories in white rotoplast shells.
125 mg - 10.
Dose: Child under one year (10kg b.wt.), insert one suppository in the anus; 1-5 years (20kg b.wt.), insert two suppositories in the anus one after the other. Adjust Dose according to b.wt.

OTC **PR**® *(BCN)*
Tablet, Paracetamol 500 mg; white thick biconvex tab.
500 mg - 50; 200.

OTC **REMIDOL**® *(Ranbaxy)*
Tablet, Paracetamol 500 mg.
500 mg - 12 x 8.

OTC **ROBERT PARACETAMOL**® *(P.Z.)*
Tablet, Paracetamol 500 mg.
500 mg - 20; 100.
Syrup, Paracetamol 125 mg per 5 ml
Pack - 60 ml.

OTC **SARIDON P**® *(Swipha)*
Tablet, Paracetamol 500 mg; white scored tab. marked 'SARIDON-P'.
500 mg - 20; 100; 200.
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml.

OTC **SETAMOL**® *(Hovid)*
Tablet, Paracetamol 500 mg; f-c tab.
500 mg - 10 x 10.

OTC **STRIMOL**® **Extra** *(Strides Vital)*
Tablet, Paracetamol, Caffeine.
Pack – 200's.

OTC **THERACIN**® *(Therapeutic)*
Tablet, Paracetamol 500 mg; white scored tab. marked 'THERACIN'.
500 mg - 20; 100; 1000.
Syrup, Paracetamol 120 mg per 5 ml.
Pack - 60 ml; 100 ml; 200 ml; 1L; 2 L.

OTC **ULTIMOL**® *(Ulticare-Lyka)*
Syrup, Paracetamol 125 mg per 5 ml; cherry flavoured syrup.
Pack - 60 ml.

OTC **ZIMOL**® **Extra** *(Justeen)*
Tablet, Paracetamol 500 mg, Caffeine 30 mg.
Pack – 20 x 10's.

Paracetamol + Diphenhydramine
OTC **Moko Teething Mixture** *(New Healthway)*
Syrup, DiphenhydramineHCl 6.25 mg, paracetamol 120 mg per 5 ml.
Pack – 100 ml

PARACETAMOL plus CHLORMEZANONE

Therapeutic category: Analgesic/muscle relaxant.
Indications: Relief of pain and muscle spasm associated with inflammatory and degenerative processes; trauma; neuritic and vasomotor pain, premenstrual tension and dysmenorrhoea.
Precautions: Reduce Dose if drowsiness occurs; additive effects may occur with alcohol or other CNS-acting drugs; use in pregnancy and lactation not established.
Adverse effects: Drowsiness, drug rash, dizziness, flushing, nausea, depression, oedema, inability to void, weakness, excitement, tremor, confusion, and headache; rarely, urticaria due to the paracetamol component.
Advice to patients: See Label 2 or 19 in Appendix 6.
Dose: Adult, 1-2 tabs 3-4 times daily depending on the severity of pain; max. of 8 tabs daily.
Child (7-12 years), ½ tab. 3-4 times daily; starting with the lowest dosage and increasing as needed.

POM **BESEROL**® *(GSK)*
Tablet, Paracetamol 450 mg, chlormezanone 100 mg.
Pack - 20; 100; 500.

PARACETAMOL plus IBUPROFEN plus CAFFEINE

Therapeutic category: Analgesic; Antipyretic; Anti-inflammatory.
Indications: For the relief of pains of minor and middle intensity such as headache, neuralgia, myalgia, arthalgia, toothache, dysmenorrhea; less effective in postoperative and postpartum pain; as antipyretic in the treatment of fever; relief of signs and symptoms of rheumatoid arthritis and osteoarthrisits.
Contra-indications: Hypersensitivity to Ibuprofen, Paracetamol & Caffeine; individuals with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other

NSAIDs.

Adverse effects: Large doses taken for a long period can cause gastic distress, hemolytic anaemia, agranulocytosis, urticaria,rash, fever, hypoglycemia, drowsiness, severe hepatic damage and may lead to death.

Dose: Adults: 4 to 6 capsules per day i.e. two capsules to be taken two or three times daily.
Children: 5 years and above 1-2 capsules per day.

POM **IBEX®** *(Medreich)*
Capsule, Ibuprofen B.P. 200 mg, paracetamol B.P. 325 mg, caffeine B.P. 30 mg.
Pack - 24's (in blister).

PROPYPHENAZONE plus CAFFEINE

Therapeutic category: Analgesic/antipyretic.

Indications: Symptomatic treatment of pains including headache of various origin; toothache and pain after dental extraction; neuralgia - facial, intercostal, sciatic, etc.; acute pain in rheumatic disease, e.g. in degenerative joint disease, arthritis, and other musculo-skeletal disorders; pain following trauma or surgery; dymenorrhoea; muscle pain, pain in colds or influenza.

Precautions: Not for prolonged treatment; pregnancy, breast feeding; severe kidney or liver disorders.

Adverse effects: Dizziness, nausea, blood dyscrasias; very rarely hypersensitivity reactions.

Dose: By mouth, Adult: 1-2 tabs once or twice daily; max. 6 tabs daily.
Child (above 6 years): 1 tab. at a time; max. 1-3 tabs daily according to age.

OTC **OPTALIDON®** *(Swissco)*
Tablet, Propyphenazone 125 mg, caffeine 25 mg.

1.8.2 Opioid analgesics

Morphine is effective in relieving moderate to severe pain, particularly of visceral origin; there is a large variation in patient response. Weaker opioids such as codeine are suitable for mild to moderate pain.

Morphine remains the most valuable analgesic for severe pain. In addition to pain relief it confers a state of euphoria and mental detachment; repeated administration may cause dependence and tolerance, but this should not be a deterrent in the control of pain in terminal illness (see also section 12.4). Regular use may also be appropriate for certain cases of non-malignant pain, but specialist supervision is required. In normal Doses common adverse effects include nausea, vomiting, constipation and drowsiness; larger Doses produce respiratory depression and hypotension.

Codeine is an opioid analgesic much less potent than morphine and much less liable, in normal Doses, to produce adverse effects including dependency. It is effective for mild to moderate pain but is too constipating for long-term use.

TRAMADOL

Tramadol is an analgesic with a dual mode of action. It is an opioid analgesic with a low affinity for opioid receptors. It is also believed to act by blocking the reuptake of noradrenaline and serotonin at synapses in the descending neural pathways which inhibit pain responses in the spinal cord. A significant part of the analgesic effect of tramadol may be attributed to non–opioid properties. Tramadol is an effective analgesic in moderate to severe pain arising from a variety of causes. Due to its dual mode of action, tramadol may have less pronounced opioid adverse effects at therapeutic Doses. Sedation, nausea and dry mouth are common adverse effects caused by tramadol. It causes less respiratory depression than parenteral morphine, nalbuphine, buprenorphine or pentazocine. It may also be less likely to induce constipation than other opioid analgesics. The drug has little euphoric effect and is thought to have a lower potential for abuse than other opioids.

Tramadol (***Tramal®***) is available as 50mg capsules and as an injection for intramuscular or intravenous administration.

CODEINE

Drug subject to international control under the Single Convention on Narcotic Drugs (1961).

Indications: Mild to moderate pain; diarrhoea (section 4.3.2).

Contra-indications: Respiratory depression, obstructive airways disease, acute asthma attack; where risk of paralytic ileus.

Precautions: Renal and hepatic impairment (Appendices 4 and 5); dependence; pregnancy (Appendix 2); breastfeeding (Appendix 3); **overdosage**: section 19.2.2; **interactions**: Appendix 1.

Adverse effects: Constipation particularly troublesome in long-term use; dizziness,

nausea, vomiting; difficulty with micturition; ureteric or biliary spasm; dry mouth, headaches, sweating, facial flushing; in therapeutic Doses, codeine is much less liable than morphine to produce tolerance, dependence, euphoria, sedation or other adverse effects.

Dose: *Mild to moderate pain*, by mouth, ADULT 30–60 mg every 4 hours when necessary to a maximum of 240 mg daily; CHILD 1–12 years, 0.5–1 mg/kg every 4–6 hours when needed.

CD **Codeine** *(WMF 2.2)*
Tablets, Codeine phosphate 30 mg.

With Paracetamol plus caffeine
POM **PAINCODIN®** *(Farmex)*
Caplet, Paracetamol BP 500 mg, Codeine phosphate hemihydrate 8 mg, Caffeine BP 30 mg.
Pack – 2 x 10's.
Indications: Headache, backache, toothache, rheumatic pain, fever; pains of cold and flu, migraine sorethroat, neuralgia and menstrual pain.
Dose: Adults and children (over 12 years), 2 caplets every 4 hours; not more than 8 caplets in a day.

DIHYDROCODEINE

Indications: Moderate to severe pain especially indicated in painful conditions where an alert patient is desired, viz. sciatica, osteoarthritis, chronic rheumatoid arthritis, arthritis of the spine, peripheral vascular disease, post–herpetic neuralgia, paget's disease, malignant disease, post–operative pain.
Contra-indications: Respiratory depre- ssion; obstructive airways disease.
Precautions: Asthma (avoid during an attack); reduce Dose in elderly, hypothyroidism, chronic hepatic disease and in renal insufficiency; avoid alcohol; pregnancy; history of drug dependence or abuse.
Adverse effects: Constipation, nausea, vomiting, headache and vertigo.
Advice to patients: See Labels 2 and 21 in Appendix 6.
Dose: By mouth, 30mg (1 tab) every 4-6 hours, preferably with or after food.
Child (4-12 years): 0.5-1 mg per kg b.wt every 4-6 hours.
Child (under 4 years): Not recommended.
By intramuscular or deep subcutaneous injection, up to 50 mg every 4–6 hours. Injection should be restricted to patients unable to be treated with the tablets.

CD **Dihydrocodeine** *(EDL 2.1)*
Tablet, Dihydrocodeine tartrate 30 mg.
Injection, Dihydrocodeine tartrate 50 mg per ml; in 1 ml amp.

MORPHINE

Drug subject to international control under the Single Convention on Narcotic Drugs (1961).
Indications: Severe pain (acute and chronic); myocardial infarction, acute pulmonary oedema; adjunct during major surgery and postoperative analgesia (section 3.5).
Contra-indications: Acute respiratory depression, acute alcoholism, where risk of paralytic ileus; raised intracranial pressure or head injury (interferes with respiration, also affects pupillary responses vital for neurological assessment); avoid injection in phaeochromocytoma.
Precautions: Renal and hepatic impairment (Appendices 4 and 5); reduce Dose or avoid in elderly and debilitated; dependence (severe withdrawal symptoms if withdrawn abruptly); hypothyroidism; convulsive disorders; decreased respiratory reserve and acute asthma; hypotension; prostatic hypertrophy; pregnancy (Appendix 2) and breastfeeding (Appendix 3); **overdosage**: section 19.2.2; **interactions**: Appendix 1.
Advice to patients: Avoid alcohol, may cause drowsiness, impaired judgement or coordination; may cause physical and psychological dependence with prolonged use.
Adverse effects: Nausea, vomiting (particularly in initial stages) constipation; drowsiness; also dry mouth, anorexia, spasm of urinary and biliary tract; bradycardia, tachycardia, palpitations, euphoria, decreased libido, rash, urticaria, pruritus, sweating, headache, facial flushing, vertigo, postural hypotension, hypothermia, hallucinations, confusion, dependence, miosis; larger Doses produce respiratory depression and hypotension
Nursing considerations: •Administer I.V. slowly over 3-5 minutes preferably as a dilute solution with sterile water.
•Monitor respiratory and mental status, B.P., CNS depression. Do not give drug if respirations are below 12 /minute.
•Assist with ambulation; patient should avoid activities requiring alertness.
•Laxative or stool softener may be administered to

relieve constipation.

Dose: *Acute pain*, by subcutaneous injection (not suitable for oedematous patients) or by intramuscular injection ADULT 10 mg every 4 hours if necessary (15 mg for heavier well-muscled patients); INFANT up to 1 month 150 micrograms/kg, 1–12 months 200 micrograms/kg; CHILD 1–5 years 2.5–5 mg, 6–12 years 5–10 mg.

Chronic pain, by mouth or by subcutaneous injection (not suitable for oedematous patients) or by intramuscular injection 5–20 mg regularly every 4 hours; Dose may be increased according to need; oral Dose should be approximately double corresponding intramuscular Dose

Myocardial infarction, by slow intravenous injection (2 mg/minute), 10 mg followed by a further 5–10 mg if necessary; elderly or debilitated patients, reduce Dose by half

Acute pulmonary oedema, by slow intravenous injection (2 mg/minute), 5–10 mg.

Note: The Doses stated above refer equally to morphine sulfate and HCl.

CD **Morphine** *(WMF 2.2)*
Tablets, Morphine sulfate 10 mg.
Oral solution, Morphine HCl or sulfate 10 mg/5 ml.
Injection (Solution for injection), Morphine sulfate 10 mg/ml, 1-ml ampoule.

CD **Morphine** *(EDL 2.1)*
Injection, Morphine (as sulph. or HCl) 10 mg per ml; in 1 ml amp.

PENTAZOCINE

Indications: Moderate to severe pain.
Contra-indications: Respiratory depression, raised intracranial pressure and head injury. Narcotic dependence.
Precautions: Respiratory depression, obstructive respiratory conditions, or cyanosis; renal or hepatic impairment; Pregnancy; myocardial infarction.
Adverse effects: Sedation, dizziness and occasional euphoria, lightheadedness, nausea and vomiting, visual disturbances, constipation and respiratory disturbances.
Advice to patients: Avoid alcohol, may cause drowsiness, impaired judgement or coordination; may cause physical and psychological dependence with prolonged use; will cause withdrawal in patients currently dependent on narcotics.
Nursing considerations: •Give I.M. deeply into large muscle mass, rotate sites; S.C. may cause necrosis with repeated inj; Avoid intra-arterial injection.
•Provide safety measures and assist with ambulation; patient should avoid activities requiring alertness.
•Monitor respiratory and mental status, B.P., CNS depression.
•May give antiemetic for nausea, vomiting.
Dose: Adult, 30 mg I.M., S.C. or I.V., 3-4 hourly, up to a max. of 360 mg daily. Child: (3-12 years), 0.5-1 mg per kg b.wt, I.M., up to 30mg, 4-6 hourly, if necessary. Child: (Under 3 years), not recommended. See lit. for details.

CD **Pentazocine** *(EDL 2.1)*
Injection, Pentazocine (as lactate) 30 mg per ml; in 1 ml amp.

CD **FORTWIN®** *(Ranbaxy)*
Injection, Pentazocine lactate 30 mg per ml. Pack - 100 x 1 ml.

CD **SOSEGON®** *(GSK)*
Injection, Pentazocine (as lactate) 30 mg per ml; clear odourless to pale yellow solution. Pack - 5.

PETHIDINE

Synonym: Meperidine HCl.
Indications: Moderate to severe pain including postoperative pain and the pain of labour.
Contra-indications, Precautions, etc.: See under morphine.
Advice to patients: Avoid alcohol, may cause drowsiness.
Nursing considerations: •Keep patient lying down for 1 hr after IM/SC inj. I.V. injection should be given preferably as a dilute solution; S.C injection is very painful.
•Provide safety measures and assist with ambulation.
•Laxative or stool softener may be administered to relieve constipation.
•Advise ambulatory patients to avoid activities that require mental alertness; make position changes slowly to avoid orthostatic hypotension.
•Inform patient to avoid alcohol containing preparations except on doctor's order.
•Monitor respiratory and cardiovascular status, B.P., CNS depression. Withhold the drug and notify physician if respirations are below 12/minute or if there is change in pupil size.
Dose: By I. M. or S.C. injection, 25-100 mg, repeated 3-4 hourly if necessary; up to 150 mg in severe pain. Reduce Dose in I.V. injection.

Child: by I.M. injection, 0.5-2 mg/kg b.wt.

CD **Pethidine** *(EDL 2.1)*
Injection, Pethidine HCl 50 mg per ml; in 1ml, 2 ml amps.

CD **Pethilorfan** *(EDL 2.1)*
Injection, Pethidine HCl 50 mg, levallorphan tartrate 0.625 mg per ml; in 1 ml, 2 ml amps.

TRAMADOL

Pharmacology: See notes above.
Indications: Acute and chronic pains of moderate to severe intensity due to all kinds of cancer, and pains due to diagnostic procedure or operation.
Contra-indications: History of hypersensitivity to tramadol or any of the components; acute addiction with alcohol, hypnotics, analgesics, opioids, or other CNS acting drugs; concurrent use with MAOIs; pregnancy, lactation.
Precautions: Impaired renal or hepatic function (reduce Dose); history of epilepsy or those susceptible to seizures; elderly patients and those with chronic respiratory disorders; may impair ability to drive or operate machinery especially in conjunction wiht alcohol.
Adverse effects: Sedation, nausea and dry mouth; sweating, headache, dizziness, asthenia, restlessness, somnolence. Less commonly palpitations, respiratory depression, convulsions (usually after rapid I.V. injection).
Advice to patients: Avoid driving or operating machinery until the full effect of drug wears off.
•May give with antiemetic if nausea, vomiting occurs.
•Provide safety measures and assist with ambulation.
•Advise ambulatory patients to avoid activities that require mental alertness as drowsiness, dizziness and confusion may occur; make position changes slowly to avoid orthostatic hypotension.
•Inform patient to avoid alcohol containing preparations except on doctor's order.
•Monitor patient for CNS changes and allergic reactions; teach patient to report the same if they occur.
Dose: By mouth, Adult, 50-100 mg every 4-6 hours; not exceeding 400 mg/day.
By I.V. or I.M. injection (over 2-3 minutes), 50-100 mg every 4-6 hours; may be increased to a max. 400 mgdaily depending on age and severity of pain.
Not recommended for children.

CD **ZIPAN**® *(Silva Hill).*
Injection, Tramadol HCl 100 mg per ml; colourless and transparent liquid in colourless 2 ml ampoule.
Pack - 2 ml x 10 Amp.

1.9 Drugs Used in the Treatment of Migraine

1.9.1 Acute migraine attack
1.9.2 Migraine prophylaxis

Chronic recurrent headache is associated with many disorders, both somatic and psychogenic. An accurate diagnosis must consequently be made before appropriate treatment can be initiated for migraine. Untreated, migraine attacks last for several hours and sometimes for as long as 3 days. Migraine headache is frequently accompanied by episodes of gastrointestinal disturbance including nausea and vomiting. The headache may be preceded or accompanied by aura (classical migraine) which is characterised by visual disturbances such as flickering lines and fragmented vision or sensory disturbances such as tingling or numbness; rarely, hemiparesis or impaired consciousness may occur. Migraine without aura (common migraine) is the more common form occurring in about 75% of patients who experience migraine.
Emotional or physical stress, lack of or excess sleep, missed meals, menstruation, alcohol and specific foods including cheese and chocolate are often identified as precipitating factors; oral contraceptives may increase the frequency of attacks. Avoidance of such precipitating factors can be of great benefit in preventing or reducing the frequency of attacks and should be addressed in detail. Women taking combined oral contraceptives who experience an onset or increase in frequency of headaches should be advised of other contraceptive measures.
The two principal strategies of migraine management are treatment of acute attacks and prophylactic treatment.

1.9.1 Acute migraine attack

1.9.1.1 Analgesics
1.9.1.2 Ergot alkaloid
1.9.1.3 Antiemetic

Treatment of acute attacks may be non-specific using simple analgesics, or specific using an ergot alkaloid such as

ergotamine. If nausea and vomiting are features of the attack, an antiemetic drug may be given. Treatment is generally by mouth; some drugs are available as suppositories which may be administered if the oral route is not effective (poor oral bioavailability, or absorption from the gut impaired by vomiting) or not practicable (patient unable to take drugs orally).

Simple analgesics including NSAIDs (nonsteroidal anti-inflammatory drugs) can be effective in mild to moderate forms of migraine if taken early in the attack; most migraine headaches respond to **paracetamol**, **acetylsalicylic acid** or an NSAID such as **ibuprofen**. Peristalsis is often reduced during migraine attacks and, if available, a dispersible or effervescent preparation of the drug is preferred because of enhanced absorption compared with a conventional tablet. The risk of Reye syndrome due to acetylsalicylic acid in children can be avoided by giving paracetamol instead. Frequent and prolonged use of analgesics by migraine sufferers may lead to analgesic-induced headache.

Ergotamine should be considered only when attacks are unresponsive to non-opioid analgesics. It is poorly absorbed when taken orally or sublingually. Rectal suppositories may offer an advantage when other routes of administration are unsatisfactory. To be fully effective ergotamine must be taken in adequate amounts as early as possible during each attack. Adverse effects limit how much ergotamine can be used in a single attack and consequently the recommended dosage should never be exceeded, and at least four days should elapse between successive treatments. Even normal dosage can lead to dependence, tolerance to adverse effects and to a withdrawal syndrome on discontinuing the drug. To avoid dependence the frequency of administration should be limited to no more than twice a month. Adverse effects include nausea, vomiting, diarrhoea and vertigo; chronic ergotism is characterized by severe peripheral vasoconstriction which can lead to gangrene in the extremities. The severity of adverse effects prevents the use of ergotamine for migraine prophylaxis.

An antiemetic such as **metoclopramide**, given as a single Dose orally or by intramuscular injection at the onset of a migraine attack, preferably 10–15 minutes before the analgesic or ergotamine, is useful not only in relieving nausea but also in restoring gastric motility, thus improving absorption of the antimigraine drug.

Products which contain barbiturates or codeine are undesirable, particularly in combination with ergotamine, since they may cause physical dependence and withdrawal headaches.

1.9.1.1 Analgesics

ASPIRIN

Indications: Acute migraine attacks; tension headache; pyrexia, mild to moderate pain and inflammation (section 1.8.1); antiplatelet (section 5.6).

Contra-indications: Hypersensitivity (including asthma, angioedema, urticaria or rhinitis) to acetylsalicylic acid or any other NSAID; children and adolescents under 16 years (Reye syndrome); gastrointestinal ulceration; haemophilia; not for treatment of gout.

Precautions: Asthma, allergic disease; impaired renal or hepatic function (Appendices 4 and 5); pregnancy (Appendix 2); breastfeeding (Appendix 3); elderly; G6PD-deficiency; dehydration; **interactions**: Appendix 1.

Adverse effects: Generally mild and infrequent but high incidence of gastrointestinal irritation with slight asymptomatic blood loss, increased bleeding time; bronchospasm and skin reactions in hypersensitive patients; see also section 1.8.1.

Dose: *Treatment of acute migraine attack*, by mouth preferably with or after food, ADULT 300–900 mg at first sign of attack, may be repeated every 4–6 hours if necessary; maximum 4 g daily; CHILD under 16 years not recommended

Treatment of acute migraine attack, by rectum, ADULT 600–900 mg inserted at first sign of attack, may be repeated every 4 hours if necessary; maximum 3.6 g daily; CHILD under 16 years not recommended.

POM **Acetylsalicylic acid** *(WMF 7.1)*

Tablets, Acetylsalicylic acid 300 mg, 500 mg.

Dispersible tablet, Acetylsalicylic acid 300 mg [not included on WHO Model List].

RETURN

Suppositories, Acetylsalicylic acid 300 mg [not included on WHO Model List].

See section 1.8.1 for the proprietary preparations of Aspirin.

PARACETAMOL

Indications: Acute migraine attacks, tension headache; mild to moderate pain, pyrexia (section 1.8.1).

Precautions: Hepatic impairment (Appendix 5); renal impairment; alcohol dependence; pregnancy (Appendix 2) and breastfeeding (Appendix 3); **overdosage**: section 19.2.1; **interactions**: Appendix 1.

Adverse effects: Rare, but rashes, blood disorders; **important**: liver damage (and less frequently renal damage) following overdosage.

Dose: *Treatment of acute migraine attack*, by mouth, ADULT 0.5–1 g at first sign of attack, may be repeated every 4–6 hours if necessary, maximum 4 g daily; CHILD 6–12 years 250–500 mg at first sign of attack, may be repeated every 4–6 hours if necessary, maximum 4 Doses in 24 hours.

Treatment of acute migraine attack, by rectum , ADULT and CHILD over 12 years 0.5–1 g at first sign of attack, may be repeated every 4–6 hours if necessary, maximum 4 Doses in 24 hours; CHILD 6–12 years 250–500 mg at first sign of attack, may be repeated every 4–6 hours if necessary, maximum 4 Doses in 24 hours.

POM **Paracetamol** *(WMF 7.1)*
Tablets, Paracetamol 300 mg, 500 mg
Dispersible tablets, Paracetamol 500 mg [not included on WHO Model List].
Suppositories, Paracetamol 250 mg, 500 mg [not included on WHO Model List].

IBUPROFEN

Indications: Acute migraine attacks, tension headache; mild to moderate pain and inflammation, pyrexia (section 2.1.1)

Contra-indications: Hypersensitivity (including asthma, angioedema, urticaria or rhinitis) to acetylsalicylic acid or any other NSAID; active peptic ulceration.

Precautions: Hepatic or renal impairment (Appendices 4 and 5); preferably avoid if history of peptic ulceration; cardiac disease; elderly; pregnancy and breastfeeding (Appendices 2 and 3); coagulation defects; allergic disorders; **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances including nausea, diarrhoea, dyspepsia, gastrointestinal haemorrhage; hypersensitivity reactions including rash, angioedema, bronchospasm; headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, tinnitus, renal failure; rarely hepatic damage; very rarely exfoliative dermatitis, purpura; prolonged administration, see section 2.1.1.

Dose: *Treatment of acute migraine attack*, by mouth preferably with or after food, ADULT 400–600 mg at first sign of attack, may be repeated every 6–8 hours if necessary, maximum 2.4 g daily; CHILD 8–12 years 200 mg at first sign of attack, may be repeated every 6–8 hours if necessary.

POM **Ibuprofen** *(WMF 7.1)*
Tablets, Ibuprofen 200 mg, 400 mg.

1.9.1.2 Ergot alkaloid

ERGOTAMINE

DRUG SUBJECT TO INTERNATIONAL CONTROL UNDER THE UNITED NATIONS CONVENTION AGAINST ILLICIT TRAFFIC IN NARCOTIC DRUGS AND PSYCHOTROPIC SUBSTANCES (1988)

Therapeutic category: Adrenergic Blocking Agent; Ergot Alkaloid.

Indications: Treatment of acute migraine attacks unresponsive to analgesics.

Contra-indications: Pregnancy (Appendix 2) and breastfeeding (Appendix 3); children; peripheral vascular disorders, coronary artery disease, obliterative vascular disease and Raynaud syndrome, severe hypertension, sepsis; severe renal or hepatic dysfunction (Appendices 4 and 5); hyperthyroidism; porphyria.

Precautions: Elderly; daily rebound headaches indicative of ergotamine dependence; discontinuation after regular normal dosage may result in withdrawal headache; risk of peripheral vasospasm (advise patient to stop medication immediately if numbness or tingling in extremities or anginal pain develops and to contact doctor); **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, vertigo, abdominal pain, diarrhoea, muscle

cramps, increased headache; precordial pain, myocardial ischaemia; rarely myocardial infarction; repeated high dosage may cause ergotism with gangrene and confusion; pleural and peritoneal fibrosis may occur with excessive use.

Advice to patients: See Labels 18 and 26 in Appendix 6.

Nursing considerations: •Do not crush sublingual drug product; give by sublingual route during early stage of attack, for rapid absorption.
•Administer oral product with or after meals to reduce GI symptoms.
•Provide a quiet, low-light environment to help patient relax
•Teach patient to report symptoms such as nausea, vomiting, numbness or tingling, and chest, muscle or abdominal pain to the physician.
•Advise patient to comply to drug schedule and never exceed recommended dosage.
.•Advise patient to avoid prolonged exposure to cold which can aggravate adverse effects.
•Ergotamine rebound or increased frequency and duration of headache may oocur if the drug is stopped.
•Avoid during pregnancy because drug is teratogenic.

Dose: *Treatment of acute migraine attack*, by mouth or by rectum , ADULT 1–2 mg at first sign of attack, maximum 4 mg in 24 hours; do not repeat at intervals of less than 4 days, maximum 8 mg in any one week; not to be used more than twice in any 1 month; CHILD not recommended.

POM **Ergotamine** *(WMF 7.1)*
Tablets, Ergotamine tartrate 1 mg
Suppositories, Ergotamine tartrate 2 mg [not included on WHO Model List].

POM **Ergotamine** *(EDL 7)*
Tablet, Ergotamine tartrate 2 mg.

ERGOTAMINE plus CAFFEINE

Indications: Acute attacks of migraine and related types of vascular headache.

Contra-indications: Hypersensitivity to the drug; impaired 'peripheral' circulation, obliterative vascular disease; coronary heart disease, severe hypertension; renal or hepatic insufficiency; septic conditions; pregnancy, breastfeeding.

Precautions: Withdraw the drug if tingling in the fingers or toes occur; not to be taken for preventive treatment or frequently over a prolonged period of time.

Adverse effects: Nausea, vomiting, paraesthesia, pain, weakness in the extremities, peripheral vasoconstriction.

Advice to patients: See Label 18 in Appendix 6.

Nursing considerations: See under Ergotamine.

Dose: Adult, initially 2 tabs; then, 1 tab. half-hourly up to a max. 6 tabs per attack or per day; max. 10 tabs weekly.
See lit. for details.

POM **Ergotamine plus Caffeine** *(EDL 7)*
Tablet, Ergotamine tartrate 1 mg, Caffeine 100 mg.

POM **Ergotamine plus Caffeine plus Cyclizine** *(EDL 7)*
Tablet, Ergotamine tartrate 2 mg, Caffeine hydrate 100 mg, Cyclizine HCl 50 mg.

POM **CAFERGOT®** *(Swissco)*
Tablet, Ergotamine tartrate 1 mg, Caffeine 100 mg; white s-c tab.

POM **MIGRIL®** *(SKG Pharma)*
Tablet, Ergotamine tartrate 1 mg, caffeine hydrate 100 mg, cyclizine HCl 50 mg; scored tab.

Dose: Adult, as soon as possible after warning or attack of migraine, 1 tab. initially; then, ½ tab. if necessary half–hourly; max. 4 tabs. per attack (8 mg Ergotamine) and 6 tabs weekly (12 mg Ergotamine).

1.9.1.3 Antiemetic

METOCLOPRAMIDE

Indications: Nausea and vomiting associated with migraine; nausea and vomiting in gastrointestinal disorders and cytotoxic therapy (section 4.5)

Contra-indications: Gastrointestinal obstruction, haemorrhage or perforation; 3–4 days after gastrointestinal surgery; phaeochromocytoma.

Precautions: Hepatic or renal impairment (Appendices 4 and 5); elderly; children and young adults; pregnancy (Appendix 2) and breastfeeding (Appendix 3); epilepsy; porphyria; **interactions**: Appendix 1.

Adverse effects: Extrapyramidal effects (especially in children and young adults); drowsiness, restlessness, diarrhoea; prolonged administration, see section 4.5.

Dose: *Nausea and vomiting of migraine*, by mouth or by intramuscular injection, ADULT single Dose of 10–20 mg at first sign of attack preferably 10–15 minutes before antimigraine drug; ADOLESCENT single Dose of 5–10 mg (5 mg if body weight less than 60 kg).

POM **Metoclopramide** *(WMF 7.1)*
Tablet, Metoclopramide HCl 10 mg
Injection (Solution for injection), Metoclopramide HCl 5 mg/ml, 2-ml ampoule.

1.9.2 Migraine prophylaxis

Prophylactic treatment should be considered for patients in whom treatment of acute migraine attacks with analgesics or ergotamine is ineffective, or in whom attacks occur more than once a month, or for those with less frequent but severe or prolonged attacks. Prophylaxis can reduce the severity and frequency of attacks but does not eliminate them completely; additional symptomatic treatment is still needed. However, long-term prophylaxis is undesirable and treatment should be reviewed at 6-monthly intervals. Of the many drugs that have been advocated beta-adrenoceptor antagonists (beta-blockers) are most frequently used. **Propranolol**, a non-selective beta-blocker and other related compounds with similar profile such as **atenolol** are generally preferred. The potential for beta-blockers to interact with ergotamine should be borne in mind. Tricyclic antidepressants, such as **amitriptyline** (section 1.4.1) or calcium-channel blocking drugs such as **verapamil** (section 5.5) may be of value.

PIZOTIFEN

Indications: Prophylactic (interval) treatment of vascular headaches such as typical and atypical migraine, vasomotor headaches, cluster headache (Horton syndrome).
Precautions: Road users, narrow-angle glaucoma, urinary retention due to the slight anticholinergic effect; pregnancy, breast-feeding.
Adverse effects: Sedative; rarely dizziness, dry mouth, constipation; nervousness in children.
Advice to patients: See Label 2 in Appendix 6.
Dose: Adult, initially 0.5 mg daily; inc. up to 3-4.5 mg daily in 3 divided doses in refractory cases. Maintenance, 1.5 mg daily in a single or in divided doses. Child: initially 0.5 mg daily; increased up to 1.5 mg in divided doses or 1 mg as a single dose at night.
Note: Not effective in acute migraine attacks.

POM **Pizotifen** *(EDL7)*
Tablets, Pizotifen (as hydrogen malate) 0.5 mg, 1.5 mg.
Elixir, Pizotifen (as hydrogen malate) 0.25 mg per ml.

POM **SANDOMIGRAN®** *(Novartis)*
Tablets, Pizotifen (as hydrogen malate) 0.5 mg (Ivory s-c tab. marked 'SMG'), 1.5 mg (Ivory s-c tab. marked 'SMG' and '1.5').
Elixir, Pizotifen (as hydrogen malate) 0.25 mg per 5 ml.

PROPRANOLOL

Propranolol is a representative beta-adrenoceptor antagonist. Various drugs can serve as alternatives.
Indications: Prophylaxis of migraine.
Contra-indications: Asthma or history of obstructive airways disease, uncontrolled heart failure, Prinzmetal angina, marked bradycardia, hypotension, sick sinus syndrome, second- or third-degree atrioventricular block, cardiogenic shock, metabolic acidosis, severe peripheral arterial disease; phaeochromocytoma.
Precautions: First-degree atrio-ventricular block; renal impairment (Appendix 4); liver disease (Appendix 5); pregnancy and breastfeeding (Appendices 2 and 3); portal hypertension; diabetes mellitus; myasthenia gravis; history of hypersensitivity (increased reaction to allergens, also reduced response to epinephrine (adrenaline)); **interactions**: Appendix 1.
Adverse effects: Bradycardia, heart failure, hypotension, conduction disorders, bronchospasm, peripheral vaso-constriction, exacerbation of intermittent claudication and Raynaud phenomenon, gastrointestinal disturbances, fatigue, sleep disturbances including nightmares; rarely, rash, dry eyes (reversible), exacerbation of psoriasis.
Dose: *Prophylaxis of migraine*, by mouth ADULT initially 40 mg 2–3 times daily, increased by same amount at weekly intervals if necessary; usual range 80–160 mg daily; CHILD under 12 years, 20 mg 2–3 times daily.

POM **Propranolol** *(WMF 7.1)*
Tablets, Propranolol HCl 20 mg, 40 mg, 80 mg, 160 mg [80 mg and 160 mg not included on WHO Model List].

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1.10 Drugs used in the treatment of obesity

ORLISTAT

Therapeutic category: Anti-obesity agent.

Pharmacology: Orlistat is the hydrated form of a naturally occuring molecule (lipstatin). The hydration leads to an improved stability profile. It is a potent reversible inhibitor of gastric and pancreatic lipases, which acts locally in the GIT lumen and inhibits the cleavage of triglycerides. It therefore prevents the absorption of up to 30% of ingested dietary fat. The fat is excreted in the faeces, producing hypocaloric state and weight loss almost exclusively by the reduction of visceral and subcutaneous fat. The efficacy of orlistat depends on the presence of dietary fat, which is why it should be taken with meals. Cessation of treatment leads rapidly to a normalization of fat absorption.

Indications: For long term weight control (Weight loss, Weight maintenance, Prevention of weight regain) when used in conjunction with a moderately hypocaloric diet in obese patients with a body mass index (BMI, patient's body-weight divided by the square of patient's height) greater or equal to 30 kg/m^2 or over weight patients (BMI > 28 kg/m^2) with associated risk such as diabetes, hypertension and dislipidaemia.

In type 2 diabetic patients who are overweight (BMI > 28 kg/m^2) or obese BMI > 30 kg/m^2, Orlistat in conjuction with a mildly hypocaloric diet provides additional glycaemic control when used in combination with other antidiabetic agents.

Contra-indications: Chronic malasoption syndromes, cholestasis and in patients with known hypersensitivity to orlistat or any of the other components of the capsule.

Adverse effects: Abdominal pain/discomfort, flatulence, liquid stools, soft stools, rectal pain/ discomfort. The incidence of these side effects inceases the higher the fat content of the diet and thus faeces.

Dose: 120 mg capsule with each meal; to be taken immediately before, during or up to one hour after the meal.

Note: The patient should be on nutritionally balanced, mildly hypocaloric diet.

POM **XENICAL**® *(Swipha)*
Capsule, Orlistat 120 mg.
120 mg - 84 (in blisters).

2. Drugs for musculoskeletal and joint diseases

RETURN

2.1 Antirheumatic drugs
2.1.1 Nonsteroidal anti–inflammatory drugs (NSAIDs)
2.1.2 Disease-modifying antirheumatic drugs (DMARDs)
2.1.3 Other antirheumatic drugs
2.2 Drugs used in gout
2.2.1 Acute gout
2.2.2 Chronic gout
2.3 Skeletal muscle relaxants (antispasmodics)
2.4 Muscle relaxants (peripherally acting) and cholinesterase inhibitors
2.4.1 Muscle relaxants
2.4.2 Cholinesterase inhibitors
2.5 Topical antirheumatic drugs

Rheumatoid arthritis and other inflammatory disorders

A non-steroidal anti-inflammatory drug (NSAID) is indicated when pain and stiffness are due to inflammatory rheumatic disease. Drugs are also used to influence the disease process itself (section 2.1.2). For rheumatoid arthritis these disease-modifying antirheumatic drugs (DMARDs) include penicillamine, gold salts, antimalarials (chloroquine and hydroxychloroquine), drugs that affect the immune response, and sulfasalazine; corticosteroids may also be of value (section 10.3). Drugs which may affect the disease process in psoriatic arthritis include sulfasalazine, gold salts, azathioprine, methotrexate (section 2.1.2). For long-term control of gout uricosuric drugs and allopurinol (section 2.2) may be used.

Osteoarthritis and soft-tissue disorders

In osteoarthritis (sometimes called degenerative joint disease or osteoarthrosis) non-drug measures such as weight reduction and exercise should be encouraged. For pain relief in osteoarthritis and soft-tissue disorders, **paracetamol** (section 1.8.1) is often adequate and should be used first. Alternatively a low-dose of a NSAID (e.g. **ibuprofen** up to 1.2 g daily) may be used. If pain relief with either drug is inadequate, both paracetamol (in a full dose of 4 g daily) and a low-dose of a NSAID may be required; if necessary the dose of the NSAID may be increased or a low dose of an opioid analgesic given with paracetamol.

Topical treatment including application of a NSAID or **capsaicin** 0.025% may provide some pain relief in osteoarthritis.

Intra-articular **corticosteroid** injections may produce temporary benefit in osteoarthritis, especially if associated with soft-tissue inflammation.

Hyaluronic acid and its derivatives are available for osteoarthritis of the knee. **Sodium hyaluronate** (Synject®) is injected intra-articularly to supplement natural hyaluronic acid in the synovial fluid. These injections may reduce pain over 1–6 months but they are associated with short-term increase in knee inflammation.

2.1 Antirheumatic drugs

2.1.1 Nonsteroidal anti–inflammatory drugs (NSAIDs)
2.1.2 Disease-modifying antirheumatic drugs (DMARDs)
2.1.3 Other antirheumatic drugs

2.1.1 Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs, including **ibuprofen**, have analgesic, anti-inflammatory and antipyretic properties. In single doses NSAIDs have analgesic activity comparable to that of paracetamol. In regular full dosage, they have a lasting analgesic and anti-inflammatory effect, which makes them useful for continuous or regular pain due to inflammation. Differences in anti-inflammatory activity between different NSAIDs are small but there is considerable variation in individual patient response and in the incidence and type of adverse effects. Ibuprofen has

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fewer adverse effects than other NSAIDs but its anti-inflammatory properties are weaker. Diclofenac and naproxen (neither of which is included on the WHO Model List) combine moderately potent anti-inflammatory activity with a relatively low incidence of adverse effects (but incidence is higher than that for ibuprofen).

Ibuprofen is used in the treatment of mild to moderate pain and in the management of pain and inflammation in rheumatoid arthritis and juvenile arthritis. It may also be of value in the less well-defined conditions of back pain and soft-tissue disorders. Ibuprofen is also used to reduce pain in children. With all NSAIDs caution should be exercised in the treatment of the elderly, in allergic disorders, during pregnancy and breastfeeding. In patients with renal, cardiac or hepatic impairment, the dose should be kept as low as possible and renal function should be monitored. NSAIDs should not be given to patients with active peptic ulceration and should preferably not be used in those with a history of the disease. The commonest adverse effects are generally gastrointestinal including nausea, vomiting, diarrhoea, and dyspepsia; hypersensitivity reactions including anaphylaxis, bronchospasm, and rash have been reported, as has fluid retention.

ASPIRIN

See under Section 1.8.1

CELECOXIB

Pharmacology: Celecoxib is a nonsteroidal anti-inflammatory drug that exhibits anti-inflammatory, analgesic, and antipyretic activities in animal models. The mechanism of action of celecoxib is believed to be due to inhibition of prostaglandin synthesis, primarily via inhibition of cyclooxygenase-2 (COX-2), and at therapeutic concentrations in humans, celecoxib does not inhibit the cyclooxygenase-1 (COX-1) isoenzyme. In animal colon tumor models, celecoxib reduced the incidence and multiplicity of tumors.

Peak plasma levels of celecoxib occur approximately 3 hours after an oral dose. When celecoxib capsules were taken with a high fat meal, peak plasma levels were delayed for about 1-2 hours with an increase in total absorption (AUC) of 10-20%. Celecoxib, at doses up to 200 mg bid can be administered without regard to timing of meals. Higher doses (400 mg bid) should be administered with food to improve absorption. Celecoxib metabolism is primarily mediated via cytochrome P450 2C9. Three metabolites, a primary alcohol, the corresponding carboxylic acid, and its glucuronide conjugate, have been identified in human plasma. These metabolites are inactive as COX-1 or COX-2 inhibitors. Celecoxib is eliminated predominantly by hepatic metabolism with little (<3%) unchanged drug recovered in the urine and feces.

The use of celecoxib in patients with severe hepatic impairment is not recommended. Significant interactions may occur when celecoxib is administered together with drugs that inhibit P450 2C9.

Indications: Symptomatic treatment of inflammation and pain in osteoarthritis and rheumatoid arthritis. Management of acute pain; treatment of primary dysmenorrhea. For the regression and reduction in number of adenomatous colorectal polyps, which may lead to the development of colorectal cancer in patients with familial adenomatous polyposis (PAP); as an adjunct to usual care (e.g., endoscopic surveillance, surgery).

Contra-indications: Hypersensitivity to any ingredient of the product; known sulfonamide hypersensitivity. Patients who have experienced asthma, urticaria or allergic-type reactions after taking acetylsalicyclic acid or NSAIDs.

Use in pregnancy: Celecoxib, as with other drugs inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus and should be avoided during the third trimester of pregnancy. Celebrex should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Use in Lactation: Not recommended

Precautions: Patients with compromised cardiac function and other conditions predisposing to fluid retention. Patients with severe kidney disease and severe liver disease.

Interactions: Patients who are known to be poor CYP2C9 metabolisers should be administered Celecoxib with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

Anticoagulant activity should be monitored in patients taking warfarin or similar agents, particularly in the first few days after initiating or changing the dose of celecoxib. Bleeding events in association with increases in prothrombin time have been reported, predominantly in the elderly, in patients receiving celecoxib concurrently within

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warfarin.

Celecoxib should be introduced at the lowest recommended dose in patients receiving the CYP2C9 inhibitor fluconazole. Caution is advised when co-administering celecoxib with other CYP2C9 inhibitors.

Antacids (aluminium and magnesium) reduce the extent of absorption of celecoxib by 10% which produced no clinically relevant effect.

Adverse effects: Gastrointestinal disorders, abdominal pain, diarrhea, dyspepsia.

Advice to patients: Patients should promptly report signs or symptoms of gastrointestinal ulceration or bleeding, skin rash, unexplained weight gain, or edema to their physicians.

Patients should be informed of the warning signs and symptoms of hepatotoxicity (*e.g.*, nausea, fatigue, lethargy, pruritus, jaundice, right upper quadrant tenderness, and "flu-like" symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy.

Patients should also be instructed to seek immediate emergency help in the case of an anaphylactoid reaction.

In late pregnancy celecoxib should be avoided because it may cause premature closure of the ductus arteriosus.

Dose: For osteoarthritis and rheumatoid arthritis, the lowest dose of celecoxib should be sought for each patient. These doses can be given without regard to timing of meals.

Osteoarthritis: For relief of the signs and symptoms of osteoarthritis the recommended oral dose is 200 mg/day administered as a single dose or as 100 mg twice per day.

Rheumatoid Arthritis: For relief of the signs and symptoms of rheumatoid arthritis the recommended oral dose is 100-200 mg twice per day.

Management of Acute Pain and Treatment of Primary Dysmenorrhea: The recommended dose of celecoxib is 400 mg initially, followed by an additional 200 mg dose if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily as needed.

Familial Adenomatous Polyposis (FAP): Usual medical care for FAP patients should be continued while on celecoxib. To reduce the number of adenomatous colorectal polyps in patients with FAP, the recommended oral dose is 400 mg (2 × 200 mg capsules) twice per day to be taken with food.

Use in Elderly: No dosage adjustments is generally necessary. However, for elderly with a lower than average body weight (50 kg), it is advisable to initiate therapy at the lowest recommended dose.

Use in children: Celebrex has not been studied in subjects under 18 years old.

Overdosage: In the event of suspected overdose, appropriate supportive medical care should be provided.

POM **CELEBREX**® *(Pfizer)*
Capsule, Celecoxib 200 mg.
200 mg - 10's (in blister).

DICLOFENAC

Therapeutic category: Antirheumatic agent with anti-inflammatory and antipyretic properties.

Pharmacology: The active agent diclofenac belongs to the non-steroid anti-inflammatory group and exhibits marked antirheumatic, anti-inflammatory and analgesic properties. Diclofenac inhibits prostaglandin synthetase and has an inhibitory action on platelet aggregation. It is suitable for the treatment of rheumatic states and non-rheumatic, inflammatory pain.

Pharmacokinetics - After oral administration, diclofenac is rapidly and completely absorbed. The plasma concentrations are linearly dose-dependent. Plasma protein binding amounts to more than 97%. Peak plasma concentrations are attained 1-4 hours after taking the enteric-coated tablets. The therapeutic plasma concentration range is 0.7-2 mcg/ml.

Diclofenac undergoes first-pass metabolism. Elimination is about 2/3 renal and about 1/3 via the bile in metabolized form (about 90% of the administered dose in 96 hours). The greater amount of the hydroxyl-glucuronide and sulphated metabolites are biologically inactive. Only about 1% is renally excreted in unchanged form.

The plasma half-life is about 2 hours and is not affected by kidney failure.

The pharmacokinetics do not vary with the age of patients.

Indications: Inflammatory and degenerative forms of rheumatism; acute musculoskeletal disorders; acute gout; post-operative and post-traumatic inflammation and swelling; painful and/ or inflammatory conditions in gynaecology e.g. dysmenorrhoea; renal and biliary colic; as an adjunct in severe painful inflammatory infections of the ear, nose, or throat.

Contra-indications: Avoid use in the presence of peptic ulcers, pregnancy, lactation, hypersensitivity (e.g. with asthma attacks, skin reactions, acute rhinitis) to acetylsalicylic acid or other non-steroid anti-inflammatory agents, severe disorders of liver function or haemopoietic disorders.

Precautions: Patients with evidence of peptic ulcers in their history, those with unexplained gastrointestinal disorders, those with liver or kidney damage and those with high blood pressure as well as elderly patients require attentive medical supervision.

Patients who suffer from asthma, hayfever, nasal polyps or chronic airways infections and patients with hypersensitivity to analgesics and rheumatism drugs of all types are threatened with asthma attacks when using diclofenac (so called analgesics intolerance, analgesic-induced asthma).

Adverse effects: Gastrointestinal upsets, upper abdominal pain, eructation, nausea, diarrhoea, light-headedness or headaches at the start of treatment. These adverse effects are generally mild and usually regress after a few days. Hypersensitivity reactions such as skin rash and pruritus, asthma attacks and a tendency to oedema may arise.

Advice to patients: See Label 21 in Appendix 6.

Nursing considerations: •Administer whole with, do not crush tablets; give with food or milk to minimize GI distress.

•Give with a full glass of water to enhance absorption, keep patient upright for 30 min.

•Advise patient to report any signs of blood in stool and to avoid other medications namely aspirin, other NSAIDs, alcohol, paracetamol, unless prescribed.

•Teach patient symptoms of peptic ulceration which are common with NSAIDs; relieve symptoms with antacid.

•Advise patient to avoid driving or any hazardous activities if dizziness, drowsiness occurs.

Dose: By mouth, 75-150 mg daily in 2-3 divided doses depending on the indication; up to 200 mg in dysmenorrhoea and migraine attacks.
By deep I.M. injection, 75 mg once daily or 75 mg twice daily in severe cases for not more than 2 days.
Child (above 1 year): 0.5-2 mg/kg daily.

POM **Diclofenac** *(EDL 2.4)*
Tablets, Diclofenac 25 mg, 100 mg.
Injection, Diclofenac 25 mg per ml.

POM **ABITREN**® *(Dizpharm)*
Tablet, Diclofenac sodium 100 mg; s-r tab.
100 mg - 10, 20.

POM **CATAFLAM**® *(Novartis)*
Tablet, Diclofenac potassium 50 mg; brown tab. marked 'PP' and 'CG'.
50 mg - 10; 100.
Injection, Diclofenac potassium 25 mg per ml; in 3 ml amp.

POM **CLOFENAC**® *(Hovid)*
Tablets, Diclofenac 50 mg, 100 mg.
50 mg - 20; 100
100 mg - 20; 100.
Tablet (SR), Diclofenac sodium 100 mg; s-r, pink, f-c tab.
100 mg - 10 x 10 (in blisters); 100 (in polyethylene bottle).

POM **DICLOGESIC**® *(Supreme)*
Retard Tablet, Diclofenac 100 mg.
100 mg - 10.

POM **DICLOSAL**® *(Strides Vital)*
Injection, Diclofenac 75 mg per 3 ml; in ampoule.
Pack – 3 ml x 10's.

POM **GROFENAC**® (*Supreme)*
Tablet, Diclofenac sodium 50 mg
50 mg - 20.
Retard tablet, Diclofenac sodium 100 mg; f -c tab.
100 mg - 10 x 10.
Injection, Diclofenac sodium 25 mg per ml; in 3 ml amp.
3 ml - 5.

POM **KALFEN**® *(Justeen)*
Injection, Diclofenac sodium 75 mg per 3 ml.
Pack – 3 ml x 5's.

POM **OFENIN**® *(Beta Drugs)*
Injection, Diclofenac sodium C.P. 75 mg per 3 ml; in ampoules.
Pack – 3-ml x 5 amps; 3-ml x 10 amps; 3-ml x 100 amps.

POM **OLFEN**® *(Oculus)*
Lactabs, Diclofenac sodium B.P. 25 mg, 50 mg.
25 mg - 30
50 mg - 20.
Rectocaps, Diclofenac sodium B.P. 50 mg, 100 mg.
50 mg - 10
100 mg - 5.
Depocaps (SR), Diclofenac sodium B.P. 100 mg; as s-r pellets.
100 mg - 10; 20.
Injection, Diclofenac sodium B.P. 75 mg, Lido-

caine HCl 20 mg; in 2 ml amp.
Pack - 5 ampoules x 2 ml.
Dose: Adults: depending on the severity of the condition, the recommended dosage is between 50 and 150mg of active agent per day.
Lactab, Rectocap and Depocaps
Adults: the initial daily dose is usually 150mg; divided into 2-3 individual administrations (e.g 2 x 1 Lactab of 50mg per day or 1 x 1 Depocaps of 100mg per day during long term treatment). Both Lactab and Depocaps are taken unchewed with a glass of water before meals. To prevent nocturnal pain and morning stiffness, one Rectocaps rectal capsule (50 or 100mg) before retiring can be combined with the use of Lactab tablets during the day.
Child over one year old: 1-3 mg/kg/day
Ampoules
Adults: the injection solution is generally injected once daily as a deep intragluteal injection in the upper external quadrant. With severe pain states, up to 2 injections per day can be given with an interval of several hours, changing the injection sites. A change is made to Lactab tablets after the severe pain has faded.
Lactab tablets of 25 mg are available for *children over one year old*.
Gel, Diclofenac sodium B.P. 10 mg per g
Pack - 20 g; 50 g in tubes.
Pharmacology: Olfen gel is an anti-inflammatory and analgesic preparation for external application. It contains 1% diclofenac sodium in a cooling gel base that is well tolerated by the skin. Olfen gel has a pain-relieving, inflammation inhibiting and detumescent action in inflammations of rheumatic or traumatic origin. It improves or normalizes impaired function.
Pharmacokinetics - Diclofenac is absorbed through the skin after local application and its presence can be shown in the plasma. Absorption of the active ingredient is ca. 3.3% of the locally applied dosage. Diclofenac metabolites appearing after topical application are similar to those determined after oral administration.
Indications: For the local treatment of arthrosis, periarthropathy, localized forms of non-articular rheumatism syndrome (e.g. tendovaginitis, bursitis, tendinitis) as well as traumatically induced inflammations of tendons, ligaments, muscles and joints (e.g. contusions, sprains and strains).
Contra-indications: Hypersensitivity to diclofenac or to the gel base, to acetylsalicylic acid or to other nonsteroidal anti-inflammatory agents.
Due to insufficient clinical data, Olfen Gel is not recommended during pregnancy. Olfen Gel should not be used under occlusive, airtight dressings. Not to be taken by mouth.
Adverse effects: Occasionally itching, reddening of the skin, skin rash or smarting of the treated area. The incidence of systemic side effects cannot be excluded in the case of long-term application on large areas of skin.
Dose: Depending on the size of the area to be treated, 2-3 g of Olfen Gel should be applied to the skin 3-4 times daily and rubbed in lightly.
Olfen Gel should only be applied to intact surfaces of skin. Wounds, open injuries, eyes and mucous membranes should not come into contact with the preparation.
Olfen Gel may also be given in addition to further treatment with other dosage forms of Olfen.

POM **VOLTAREN®** *(Novartis)*
Tablet, Diclofenac sodium 25 mg; e–c tab.
25 mg - 30.
Retard tablet, Diclofenac sodium 100 mg.
100 mg - 10; 100
Injection, Diclofenac sodium 25 mg per ml; in 3 ml amp.
3 ml - 5.

POM **VOLTAREN SR®** *(Novartis)*
Tablet, Diclofenac sodium 75 mg; s–r tab.
75 mg - 30.

POM **VOLTAREN EMULGEL®** *(Oculus)*
Gel, Diclofenac diethylammonium 1.16% (equiv. to diclofenac sodium 1%); oily emulsion in an aqueous gel.
Pack - 20 g (in tube).
Indications: Localised rheumatic diseases; pain and inflammation due to sprains, strains, etc.
Dose: 2-4 mg applied locally to the skin 3-4 times daily and rubbed in gently.

DIFLUNISAL

Indications: Pain and inflammation associated with osteoarthritis and rheumatoid arthritis; pain and associated symptoms of primary dysmenorrhoea.
Contra-indications: Asthmatic attacks, urticaria, or rhinitis precipitated by salicylates or NSAIDS; active GI bleeding; hypersensitivity to diflusinal.
Precautions: History of GI haemorrhage or

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ulcers, renal impairment, pregnancy, breast feeding, children.

Adverse effects: Nausea, headache, GI pain, diarrhoea.

Advice to patients: See Label 21 in Appendix 6.

Nursing considerations: •Advise patient to swallow tablet whole, not to crush or chew.
•Instruct patient not to take aspirin with diflunisal.
•Avoid the use of diflunisal in children and adolescents with viral infections and flu, because of possible association with Reye's syndrome.

Dose: By mouth, 500 mg twice daily; adjusted according to the nature and intensity of pain; or initially 1000 mg as a single dose for faster onset of action.
Maintenance, not more than 1500 mg daily.

POM **Diflunisal** *(EDL 2.4)*
Tablet, Diflunisal 250 mg.

POM **DOLOBID®** *(Bolax/BPP)*
Tablet, Diflunisal 250 mg; peach f-c tab. marked 'DOLOBID'.
250 mg - 10; 50.

FENBUFEN

Indications: Rheumatoid arthritis and related conditions.

Contra-indications, Precautions, etc.: See under Indometacin.

Advice to patients: See Label 21 in Appendix 6.

Dose: By mouth, Adult, 300 mg in the morning and 600 mg at bedtime or 450 mg twice daily.

POM **Fenbufen** *(EDL 2.4)*
Tablets and Capsules, Fenbufen 300 mg, 450 mg.

IBUPROFEN

Indications: Pain and inflammation in rheumatic disease and other musculoskeletal disorders including juvenile arthritis; mild to moderate pain including dysmenorrhoea, headache; pain in children; acute migraine attack (section 1.9.1).

Contra-indications: Hypersensitivity (including asthma, angioedema, urticaria or rhinitis) to acetylsalicylic acid or any other NSAID; active peptic ulceration.

Precautions: Renal and hepatic impairment (Appendices 4 and 5); preferably avoid if history of peptic ulceration; cardiac disease; elderly; pregnancy and breastfeeding (Appendices 2 and 3); coagulation defects; allergic disorders; **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances including nausea, diarrhoea, dyspepsia, gastrointestinal haemorrhage; hypersensitivity reactions including rash, angioedema, bronchospasm; headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, tinnitus, photosensitivity, haematuria; fluid retention (rarely precipitating congestive heart failure in elderly), raised blood pressure, renal failure; rarely hepatic damage, alveolitis, pulmonary eosinophilia, pancreatitis, visual disturbances, erythema multiforme (Stevens-Johnson syndrome), toxic dermal necrolysis (Lyell syndrome), colitis, aseptic meningitis.

Advice to patients: See Label 21 in Appendix 6.

Nursing considerations: •If gastric upset occurs, administer drug with food, milk, or antacid (absorption of ibuprofen is enhanced in empty stomach).
•Do not give concomitantly with aspirin and aspirin-containing products, alcohol or steroids to minimise the risk of GI bleeding.
•Advise patient to avoid driving or any hazardous activities if dizziness, drowsiness, or confusion occurs.
•Teach patient symptoms of toxicity namely blurred vision, ringing or roaring in ears and to report same to the doctor.

Dose: *Mild to moderate pain, pyrexia, inflammatory musculoskeletal disorders*, by mouth with or after food, ADULT 1.2–1.8 g daily in 3–4 divided doses, increased if necessary to maximum 2.4 g daily (3.2 g daily in inflammatory disease); maintenance dose of 0.6–1.2 g daily may be sufficient.
Juvenile arthritis, by mouth with or after food, CHILD over 7 kg, 30–40 mg/kg daily in 3–4 divided doses.
Pain in children (not recommended for child under 7 kg), by mouth with or after food, 20–40 mg/kg daily in divided doses or 1–2 years 50 mg 3–4 times daily, 3–7 years 100 mg 3–4 times daily, 8–12 years 200 mg 3–4 times daily.

POM **Ibuprofen** *(WMF 2.1.3)*
Tablets, Ibuprofen 200 mg, 400 mg.

POM **Ibuprofen** *(EDL 2.4)*
Tablet or capsule, Ibuprofen 200 mg, 400 mg.

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POM **ACTIFEN®** *(Diamond Remedies)*
Tablet, Ibuprofen 200 mg; pink s-c tab. marked 'IBU 200'.
200 mg - 2 x 10.

POM **ADVIL®** *(Matbeny)*
Tablet/Caplet, Ibuprofen 200 mg; coated tab. and caplet.
200 mg - 10; 20.

POM **ARTOFEN®** *(Dizpharm)*
Tablet, Ibuprofen 200 mg
200 mg – 1000.

POM **ASKAFEN®** *(Diamond Remedies)*
Tablet, Ibuprofen 200 mg; s-c tab.
200 mg - 2 x 10.

POM **BRUFEN®** *(BCN)*
Tablets, Ibuprofen 200 mg (magenta s-c tab. marked 'BRUFEN'), 400 mg (magenta s-c tab. marked 'BRUFEN 400').
200 mg - 25; 100; 500.
400 mg - 25; 100; 250.

POM **BRUSTAN-N®** *(Ranbaxy)*
Tablet, Ibuprofen BP 400 mg; f-c tab.
400 mg - 24 x 10's.

POM **BUPROL®** *(Hovid)*
Tablets, Ibuprofen 200 mg, 400 mg; f-c tabs.
200 mg - 500; 10 x 100 blisters.
400 mg - 500; 1000

POM **GENAFEN®** *(Geneith)*
Tablet, Ibuprofen 400 mg.
400 mg – 10's (in blister).

POM **IBUGESIC®** *(Supreme)*
Tablets, Ibuprofen 200 mg, 400 mg.
200 mg - 20.
400 mg - 24.

POM **IBUNEX®** *(Titan)*
Tablet, Ibuprofen 200 mg.
200 mg – 1000.

POM **IBUPAIN FORTE®** *(Adler)*
Tablet, Ibuprofen 400 mg.
400 mg - 12.

POM **Ibuprofen** *(Emzor)*
Capsules and Tablets, Ibuprofen 200 mg, 400 mg.
200 mg - 20; 1000.

POM **Ibuprofen** (*Panvij Biotec*)
Tablets, Ibuprofen 200 mg (light pink coloured f-c tab.), 400 mg (light pink coloured f-c tab.).
200 mg - 10 x 10; 1000.
400 mg - 1 x 10; 10 x 10; 1000.

POM **INBU 200®** *(Strides Vital)*
Tablet, Ibuprofen 200 mg; pink s-c tab. marked 'IBU 200'.
200 mg – 2 x 10's; 1000's.

POM **INBU 400®** *(Strides Vital)*
Tablet, Ibuprofen 400 mg; pink s-c tab. marked 'IBU 400'.
400 mg – 2 x 15's; 1000's.

POM **LAM 200®** *(Dana)*
Tablet, Ibuprofen 200 mg; f-c tab.
200 mg – 10 x 10's.

POM **LAM 400®** *(Dana)*
Tablet, Ibuprofen 400 mg; f-c tab.
400 mg – 10 x 10's.

POM **RAFEN®** *(Rajat)*
Tablet, Ibuprofen BP 200 mg; s-c tab.
Pack – 2 x 10's (in blister).

POM **TABALON®** *(NGC)*
Tablet, Ibuprofen 400 mg; scored oblong tab.
400 mg - 20; 100.

POM **ZEDFEN®** *(Justeen)*
Tablet, Ibuprofen BP 400 mg.
400 mg – 1 x 10's.

INDOMETACIN

Synonym: Indomethacin.
Pharmacology: Indometacin is a non-steriodal drug with anti-inflammatory, antipyretic and analgesic properties. It is a potent inhibitor of prostaglandin synthesis; its mode of action may be due to a decrease of prostaglandins in peripheral tissues. See notes above.
Indications: Acute and chronic musculoskeletal and arthritic disorders such as rheumatoid arthritis, juvenile rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, lumbago, gout, degenerative joint disease of the limbs, inflammation and pain following orthopaedic surgery or dental procedures; fever, dysmenorrhoea.
Contra-indications: History of hypersensitivity to aspirin or other NSAIDs including those in whom asthmatic attacks, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAIDS. Children under 14 years; active peptic ulcer; pregnancy, breast-

feeding.

Precautions: May mask the signs and symptoms of infection (use with in existing infection). Fluid retention and peripheral oedema may occur with Indometacin like other NSAIDs (use cautiously in cardiac dysfunction, hypertension or other conditions pre-disposing to fluid retention). May prolong bleeding time, so use with caution in coagulation disorders. Severe hepatic reactions including jaundice and fatal hepatitis may occur with Indometacin as with other NSAIDs (discontinue therapy if abnormal liver test persists or worsens). Prolonged use may lead to renal disorders including acute nephritis with haematuria, proteinuria and occasionally nephrotic syndrome. May aggravate depression or other psychiatric disturbances, epilepsy and parkinsonism. May cause drowsiness and alteration in motor coordination (counsel patient on the possible effect on driving and performance of other skilled tasks). Prolonged use may cause corneal deposits and retinal disturbances including that of macula (advise patient to discontinue medication promptly and to notify physician if visual disturbances occur). History of gastro-intestinal ulceration or bleeding; elderly.

Adverse effects: GI reactions including nausea, diarrhoea, dyspesia, vomiting, abdominal pain or constipation; occasionally GI haemorrhage and ulceration (give with food or milk to minimize such effects). CNS effects namely headache, dizziness, and tinnitus; less commonly somnolence, fatigue and confusion. Others include renal failure, hepatic damage, hyperkalaemia, Stevens-Johnson syndrome. See also under Precautions.

Advice to patients: See Labels 21 and 25 in Appendix 6.

Nursing considerations: •Administer with food, milk, antacid, or large glass of water to minimize GI distress; to be swallowed whole.

•Teach patient symptoms of GI bleeding which are common with NSAIDs; he should report such signs to the doctor.

•Co-administration with alcohol, aspirin or steroids may increase the risk of GI bleeding.

•Tell patient to notify physician immmediately if any visual or hearing changes occur; may indicate toxicity.

•Advise patient to avoid driving or any hazardous activities if dizziness, drowsiness occurs.

•Indometacin is associated with high incidence of side efffects when used chronically and should not be used routinely as an analgesic or antipyretic.

•Monitor carefully for weight gain especially in the elderly and increased B.P. in hypertensive patients as indomethacin causes sodium retention.

Dose: By mouth, *moderate to severe rheumatoid arthritis (including acute flares of chronic disease), ankylosing spondylitis and osteoarthritis*, 25 mg 2-3 times daily; increased according to patient's needs by 25-50 mg at weekly intervals up to a max. 150-200 mg daily. After acute phase of disease is controlled, daily dose should be gradually reduced to the smallest effective dose.

Acute painful shoulder (bursitis or tendinitis), 75-150 mg daily in 3-4 divided doses. Discontinue the drug after inflammation has been controlled for several days. Usual course of therapy is 7-14 days.

Acute gout, 50 mg 3 times daily until pain is treatable, then rapidly reduce the dose to complete cessation of the drug.

Dysmenorrhoea, up to 75 mg daily as a single or in divided doses.

Child: Not recommended for children under 14 years.

POM **Indometacin** *(EDL 2.4)*
Capsule, Indometacin 25 mg.

POM **ARTHRACID®** *(Strides Vital)*
Capsule, Indometacin 25 mg.
25 mg - 10 x 10's.

POM **DOLOCIN®** *(Ranbaxy)*
Capsule, Indometacin 25 mg
25 mg - 10's; 1000's.

POM **DOLON®** *(Sam)*
Capsule, Indometacin 25 mg
25 mg - 10 x 10.

POM **INDOBETA-25®** *(Beta Drugs)*
Capsule, Indomethacin Capsules BP 25 mg.

POM **INDOCET®** *(Adler)*
Capsule, Indometacin 25 mg.
25 mg - 30.

POM **INDOGESIC®** *(Supreme)*
Capsule, Indometacin 25 mg.
25 mg - 30.

POM **Indometacin** *(Doyin)*
Capsule, Indometacin 25m g
25 mg - 10 x 10

POM **Indometacin** *(Emzor)*
Capsules and Tablets, Ibuprofen 200 mg, 400 mg.
200 mg - 20; 1000.

POM **INDOPAN®** *(Panvij Biotec)*

Capsule, Indometacin 25 mg; ivory/ivory cap. marked 'INDO' and '25'.
25 mg - 10 x 10; 1000.

POM **JECID**® *(Rajat)*
Capsule, Indometacin BP 25 mg
Pack – 10 x 10's (in blister); 1000's.

POM **METHACIN**® *(Hovid)*
Tablet, Indometacin 25 mg; f-c tab.
25 mg - 1000
Capsule, Indometacin 25 mg.
25 mg - 10 x 10; 500; 1000.

POM **ROMACID**® *(Geneith)*
Capsule, Indometacin 25 mg.
25 mg – 10's; 1000's.

KETOPROFEN

Indications: Rheumatoid arthritis, osteoarthritis, gout, ankylosing spondylitis, acute articular and periarticular disorders (bursitis, capsulitis, synovitis, tendinitis), fibrositis, cervical spondylitis, low back pain (strain, lumbago, sciatica), painful musculo-skeletal conditions and dysmenorrhoea.
Contra-indications, Precautions, etc.: See under Indometacin.
Advice to patients: See Label 21 in Appendix 6.
Nursing considerations: •Administer 30 minutes before or 2 hours after meals for best absorption (may give with food or milk if gastric upset occurs).
•Tell patient to notify physician immediately if any visual or hearing changes occur; may indicate toxicity.
•Co-administration with alcohol, aspirin, or steroids may increase the risk of GI bleeding.
•Teach patient the symptoms of GI bleeding and encourage him to report such to the doctor.
•Advise patient to avoid driving or any hazardous activities if dizziness, drowsiness occurs.
Dose: Adult, by mouth, 100-200 mg daily in 2-4 divided doses; 200 mg once daily for the s-r prep., to be taken with food, depending on patient weight and severity of symptoms.
By deep I.M. injection, 100 mg every 12 hours; up to a max. 200 mg in 24 hours.
Child: Not recommended for children below 12 years.
Note: Avoid I.V. use. Limit injection to the acute stage of a disease.

POM **Ketoprofen** *(EDL 2.4)*
Capsules, Ketoprofen 50 mg, 100 mg, 200 mg.

POM **APO-KETO SR**® *(Lahams)*
Tablet (Slow-release), Ketoprofen 200 mg; white, f-c tab. marked 'APO 200'.
200 mg - 100.

POM **KETONAL**® *(Taylek)*
Tablet Retard, ketoprofen 150 mg.
150 mg - 20.
Dose: Adult, by mouth, 150 mg twice daily; to be taken at 12 hourly intervals with food.
Injection, Ketoprofen 50 mg per ml; in 2 ml amp.
Pack - 10; 50.
Cream, Ketoprofen 50 mg per g.
Pack - 30 g; 100 g (in tubes).
Dose: Apply to the affected site 3-4 times daily.

POM **ORUCOTE**® *(May & Baker)*
Gel, Ketoprofen 2.5 g per 100 g; non-greasy, non-staining gel with cooling effect. Contains alcohol.
Indications: Acute, painful musculo-skeletal conditions caused by trauma such as sports injuries, sprains, strains and contusions.
Dose: Usually about 15 g per day; to be applied 2 to 4 times daily to the skin in the painful or inflamed region for up to 7 days. After application the affected area should be well massaged to ensure local absorption of the drug.
Note: To be avoided in patient with exudative dermatoses, eczema, sores and infected skin lesions or broken skin. Safety in children is not yet established.

POM **ORUJECT**® *(May & Baker)*
Injection, Ketoprofen 50 mg per ml; in 2 ml amp.

POM **ORUVAIL**® *(May & Baker)*
Capsule, Ketoprofen 200 mg; white/pink cap. marked 'ORUVAIL 200' in blue holding white pellets.
200 mg - 14;. 140.

MEFENAMIC ACID

Indications: Mild to moderate pain including headache, dental pain, postoperative and post-partum pain, dysmenorrhoea; rheumatic disorders such as osteoarthritis and rheumatoid arthritis.
Contra-indications: Hypersensitivity to mefenamic acid; cross-sensitivity to aspirin and other NSAIDs; intestinal ulceration or inflammatory bowel disease; avoid use in children below 14 years.
Precautions: Impaired renal or liver function;

elderly with dehydration and renal disease; diarrhoea or skin rash (discontinue); bronchial asthma or allergic disease; factors associated with peptic ulcer disease such as alcoholism, smoking, corticosteroid therapy; may cause drowsiness.

Adverse effects: GI disturbances; diarrhoea or skin rash (discontinue); peptic ulceration, GI bleeding, headache, drowsiness, dizziness, nervousness, visual disturbances, thrombocytopenia, haemolytic anaemia.

Advice to patients: See label 21 in Appendix 6. Administer after meals or with food, milk or antacids to reduce GI irritation.

Nursing considerations: •Administer with food to minimize GI irritation.
•Teach patient the symptoms of GI bleeding and encourage him to report such to the doctor.
•Co-administration with alcohol, aspirin, or steroids may increase the risk of GI bleeding.
•Patient should avoid hazardous activities until the CNS effects of the drug are established.
•Discontinue therapy if rash, visual disturbances, or diarrhoea develops.
•Do not use for more than a week at a time due to the increased risk of toxicity.

Dose: By mouth, Adult, initially 500 mg; followed by 250 mg every 6 hours as required.

POM **Mefenamic Acid** *(EDL 2.4)*
Tablets, Mefenamic acid 250 mg, 500 mg.

POM **HOSTAN®** *(Hovid)*
Tablet, Mefenamic acid 500 mg.
500 mg - 10 x 10; 500; 1000.

NAPROXEN

Indications: Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute musculoskeletal disorders and dysmenorrhoea, acute gout, juvenile arthritis.

Contra-indications, Precautions, etc: See Indometacin.

Advice to patients: See Label 21 in Appendix 6.

Nursing considerations: •Give with food or milk to minimize GI upset.
•Teach patient the symptoms of GI bleeding and encourage him to report such to the doctor.
•Co-administration with alcohol, aspirin, or steroids may increase the risk of GI bleeding.
•Periodic eye & ear examinations may be required for patients on long-term therapy.
•Advise patient to avoid driving or any hazardous activities if dizziness, drowsiness occurs.

Dose: By mouth, *Adult*, 0.5-1.0 g daily in 2 divided doses. *Acute musculoskeletal disorders and dysmenorrhoea*, initially 500 mg, then 250 mg 6-8 hourly as required; up to a max. daily dose of 1250 mg after the first day.*Acute gout*, initially 750 mg, then 250 mg 8 hourly until attack is over. *Elderly*: Use lowest effective dose. *Child*, (over 5 years): *Juvenile arthritis*, 5 mg/kg b.wt. twice daily.

POM **Naproxen** *(EDL 2.4)*
Tablets, Naproxen 250 mg, 500 mg.

POM **APO-NAPROXEN®** *(Lahams)*
Tablet, Naproxen 500 mg; yellow, scored oblong tab. marked 'APO 500'.
500 mg - 100.

POM **HOPROXEN®** *(Hovid)*
Tablet, Naproxen 250 mg; yellow tab.
250 mg - 500.

POM **NAXEN®** *(Swipha)*
Tablets, Naproxen 250 mg, 500 mg.
250 mg - 20; 200.
500 mg - 20; 100.

NIMESULIDE

Pharmacology: Nimesulide is a nonsteriodal anti-inflammatory drug (NSAIDs) of the sulfonanilide class. It has anti-inflammatory activity similar to or greater than that of Indometacin, diclofenac, piroxicam and ibuprofen; the analgesic efficacy is similar to that of ibuprofen and less than that of Indometacin; the antipyretic effect is superior to that of Indometacin, ibuprofen, aspirin and paracetamol. It acts through a variety of mechanisms which includes selective cyclo-oxygenase 2 inhibition. Oral drug absorption is nearly complete and concomitant administration of food may decrease the rate, but not the extent, of absorption of nimesulide. It is extensively bound to plasma proteins, extensively metabolised and excreted mainly in the urine.

Indications: Treatment of a variety of painful inflammatory conditions including, osteoarthri tis, rheumatoid arthritis, oncology, post-operative trauma, sports injuries, ENT disorders, dental surgery, bursitis/tendintis, thrombophlebitis, upper airways inflammation and gynaecological disorders.

Contra-indications: Active peptic ulcer disease, moderate to sever hepatic impairment, severe renal failure; pregnancy, breast-feeding.

Precautions: Renal impairment, cirrhosis of liver, CHF, renovascular disease or those who are volume or salt depleted. Periodic liver function tests are required for prolonged therapy

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(discontinue drug immediately if liver test worsens).

Adverse effects: GI disturbances namely epigastralgia, heartburns, nausea, diarrhoea and vomiting; dermatological reactions including rash and pruritus; CNS effects such as dizziness, somnolence and headache. Occasionally, excessive perspiration, flushing, hyperexcitability and sleep disorders. Rarely, a rise in liver enzyme levels.

Dose: By mouth, Adult, 100 mg twice daily; increased if necessary to 200 mg twice daily.

POM **ASKANYM®** *(Diamond Remedies)*
Tablet, Nimesulide 100 mg; uncoated tab.
100 mg - 2 x 10.

POM **NILIDE®** *(Interpharma)*
Tablet, Nimesulide 100 mg; f-c tab.
100 mg - 10 x 10's (in blisters).

POM **NIMICA®** *(IPCA)*
Tablet, Nimesulide BP 100 mg.
100 mg - 10's.
Suspension, Nimesulide BP 50 mg per 5 ml.
Pack - 30 ml; 60 ml.

POM **NIMULID®** *(Panvij Biotec)*
Tablet, Nimesulide 100 mg; pale yellow coloured tab. marked 'NIMULID' on one side and 'LOGO' on the reverse.
100 mg - 2 x 10 (blister).

POM **NIPAN®** *(Pharmabox)*
Tablet, Nimesulide 100 mg; light yellow oblong tab.
100 mg - 20's; 100's.

POM **ONAXO®** *(Diamond Remedies)*
Tablet, Nimesulide 100 mg; uncoated tab.
100 mg - 12 x 20 (in blisters).

POM **SUGAM®** *(Jawa)*
Suspension, Nimesulide 50 mg per 5 ml.
Pack - 60 ml x 20's.

PIROXICAM

Indications: Rheumatoid arthritis, juvenile rheumatoid arthritis, osteoarthritis (arthrosis, degenerative joint disease), ankylosing spondylitis, acute musculoskeletal disorders including tendinitis, sprains and low back pain; acute gout, post–operative pain and post-traumatic pain; primary dysmenorrhoea in patients 12 years and above; fever and pain associated with acute upper respiratory tract inflammation.

Contra-indications, Precautions, etc: See Indometacin.

Advice to patients: See Label 21 in Appendix 6.

Nursing considerations: •Administer with food to decrease GIT symptoms.
•Teach patient to notify the physician of blurred vision or ringing in the ear; may indicate toxicity.
•Tell patient to avoid driving or other hazardous activities if dizziness and drowsiness occur.
•Instruct patient about the signs of GI bleeding.
•Advise patient to avoid other medications namely aspirin, other NSAIDs, alcohol, unless prescribed.

Dose: By mouth, initially 20 mg daily as a single dose; maintainance dose, 10-30 mg daily as single or divided doses. See lit. for other indications and use in children.

POM **Piroxicam** *(EDL 2.4)*
Capsules or tablets, Piroxicam 10 mg, 20 mg.
Gel, Piroxicam 0.5%.
Injection, Piroxicam 10 mg per ml.

POM **APO-PIROXICAM®** *(Lahams)*
Capsule, Piroxicam 20 mg; maroon cap. marked 'APO 20'.
20 mg - 100; 500.

POM **ARTRITE®** *(Strides Vital)*
Capsule, Piroxicam 20 mg; red cap. marked 'ARTRITE'.
20 mg - 10 x 10's.

POM **CICAM®** *(Justeen)*
Capsule, Piroxicam BP 20 mg.
Pack - 10 x 10's.

POM **FELDENE®** *(Neimeth)*
Capsules, Piroxicam 10 mg, maroon/blue cap.; 20 mg, maroon cap. Both marked 'PFIZER' and 'FEL 10' or 'FEL 20'.
10 mg - 20; 100.
20 mg - 10; 50.
Tablet (Dispersible), Piroxicam 20 mg, white oblong tab. marked 'PFIZER' and 'FEL 20'.
20 mg - 10; 50.
Injection, Piroxicam 20 mg per ml; in 1 ml amp.
Pack - 10; 50.
Gel, Piroxicam 0.5%; clear pale yellow gel in tube.
Pack - 25 g; 50 g.

Indications: Osteoarthritis (arthrosis, degenerative joint disease), post traumatic or acute musculoskeletal disorders including tendonitis, tenosynovitis, periathritis, sprains, strains and low back pain.

Dose: Usually about 1 g gel (i.e., 5 mg

piroxicam) to be applied to the affected site 3-4 times daily.

Note: No occlusive dressing should be employed. Rub in the gel leaving no residue on the skin. Do not apply to the eyes, mucosa or to open skin lesion. Safety in children not yet established.

POM **FELOXIN**® *(Diamond Remedies)*
Capsule, Piroxicam 20 mg; bright red cap. marked with brand name and strenght.
20 mg - 10 x 10.

POM **FELVIN**® *(Greenlife)*
Capsule, Piroxicam 20 mg.
20 mg - 10 x 10 (blister).

POM **FELXICAM**® *(Hovid)*
Capsule, Piroxicam 20 mg.
20 mg - 100; 1000; 10 x 10 (blister).

POM **GEVICAM**® *(Geneith)*
Capsule, Piroxicam 20 mg.
20 mg – 10's (in blister)

POM **PIRO**® *(Titan)*
Capsule, Piroxicam 20 mg
20 mg - 10 x 10.

POM **PIXICAM**® *(Fill Pharma)*
Capsule, Piroxicam 20 mg.
20 mg - 10 x 10's (in blister).

POM **PROXISAM**® *(Sam)*
Capsule, Piroxicam 20 mg
20 mg - 10 x 10.

POM **REUMADENE**® *(L.B.S.)*
Capsule, Piroxicam 20 mg.

POM **RICAM**® *(GoldMoore)*
Capsule, Piroxicam BP 20 mg.
Pack - 10 x 10's; 1 x 10's (in blister).

POM **ROXIDEN**® *(Fill Pharma)*
Capsule, Piroxicam BP 20 mg.
Dose: *Acute Musculoskeletal disorders*, 40 mg daily for 2 days followed by 20 mg daily for 1 to 2 weeks.
Acute Gout, 40 mg daily for 5 to 7 days.
Rheumatic Disorders, 20 mg daily; main tenance 10-30 mg.
For *Juvenile Arthritis*, Children over 6 years (weight less than 15 kg): 5 mg daily; 16 to 25 kg: 10 mg daily; 25 to 45 kg: 15 mg daily; above 46 kg: 20 mg daily.

SULINDAC

Indications: Osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, acute gouty arthritis, peri-articular disorders such as bursitis, tendinitis, and tenosynovitis.
Contra-indications: Allergy to sulindac; acute asthmatic attacks, urticaria or rhinitis precipitated by aspirin or other NSAIDs; active GI bleeding; active peptic ulcer; children; pregnant or lactating women.
Precautions: History of G.I. haemorrhage or ulcers; impaired renal function (reduce dose); liver dysfunction; discontinue treatment and conduct liver function tests if unexplained fever, rash or other dermatological reactions, or constitutional symptoms occur.
Adverse effects: Gastro-intestinal (GI pain, dyspepsia); dermatological (rash, pruritus); CNS (dizziness, nervousness); special senses (tinnitus); oedema.
Advice to patients: See label 21 in Appendix 6.
Nursing considerations: •Administer with food or milk to minimise GI symptoms; best taken on empty stomach to enhance absorption.
•Advise patient to inform dentist or surgeon because of prolonged bleeding.
•Avoid co-administration with aspirin and alcohol.
•Tell patient to avoid hazardous activities such as driving, if dizziness or drowsiness occurs.
•Instruct patient to report to the doctor if visual or hearing disturbances occur; may indicate toxicity.
Dose: By mouth, usually 400 mg daily in 2 divided doses; to be adjusted according to the severity of the disease and response but not exceeding 400 mg daily.
Acute gouty arthritis, usually for 7 days.
Peri-articular disorders, usually for 7 to 10 days.Child, avoid use in children.
Elderly, same as for adult dose.

POM **CLINORIL**® *(Bolax/BPP)*
Tablets, Sulindac 100 mg, 200 mg; both are brilliant yellow, biconvex shaped, scored, hexagonal tabs marked 'MSD 943' and 'MSD 942' respectively.
100 mg – 100.
200 mg – 100; 500.

2.1.2 Disease-modifying antirheumatic drugs (DMARDs)

The process of cartilage and bone destruction which occurs in rheumatoid arthritis may be reduced by the use of a diverse group of drugs known as DMARDs (disease-modifying antirheumatic drugs). DMARDs include antimalarials

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(chloroquine, hydroxychloroquine), penicillamine, sulfasalazine, immunosuppressants (azathioprine, cyclophosphamide, methotrexate) and gold compounds.

Treatment should be started early in the course of the disease, before joint damage starts. Treatment is usually initiated with a NSAID when the diagnosis is uncertain and the disease course unpredictable. However, when the diagnosis, progression and severity of rheumatic disease have been confirmed, a DMARD should be introduced.

DMARDs do not produce an immediate improvement but require 4–6 months of treatment for a full response. Their long-term use is limited by toxicity and loss of efficacy. If one drug does not lead to objective benefit within 6 months, it should be discontinued and another DMARD substituted. Adverse reactions with DMARDs occur frequently and may be life threatening; careful monitoring is needed to avoid severe toxicity. Blood disorders (bone marrow suppression) can occur during treatment with many DMARDs; blood counts should be carried out before and during treatment, and patients should be advised to report without delay any unexplained symptom such as bleeding, bruising, purpura, infection, sore throat or fever. It has been suggested that combinations of DMARDs may be more effective than single drugs but increased toxicity may be a problem; whether used alone or in combination, they should be prescribed only by specialists to ensure that they are used safely and to best advantage.

The antimalarial **chloroquine** is less effective than most other DMARDs, but as it is generally better tolerated it may be preferred in the treatment of mild rheumatoid arthritis. Chloroquine should not be used for psoriatic arthritis. Because long-term therapy can result in retinopathy ophthalmological examinations should be conducted before and during treatment.

Sulfasalazine has a beneficial anti-inflammatory effect and is considered by some rheumatologists to be a first-line DMARD, but it is poorly tolerated by about 25% of patients. Adverse reactions include blood disorders (bone marrow suppression), hepatotoxicity, skin reactions and gastrointestinal disturbances.

Methotrexate, an immunosuppressant, is considered to be a first-line DMARD; at the low doses used for rheumatoid arthritis it is well tolerated but there remains the risk of blood disorders (bone marrow suppression) and of hepatic and pulmonary toxicity. Other immunosuppressant drugs, including **azathioprine**, are generally reserved for use in patients with severe disease who have failed to respond to other DMARDs, especially in those with extra-cellular manifestations such as vasculitis. Immunosuppressants are used in psoriatic arthritis. Adverse reactions include blood disorders, alopecia, nausea and vomiting.

Penicillamine is not a first-line drug and its use is limited by a significant incidence of adverse effects including blood disorders (bone marrow suppression), proteinuria and rash.

Corticosteroids (section 10.3) are potent anti-inflammatory drugs but their place in the treatment of rheumatoid arthritis remains controversial. Their usefulness is limited by adverse effects and their use should be controlled by specialists. Corticosteroids are usually reserved for use in patients with severe disease which has failed to respond to other antirheumatic drugs, or where there are severe extra-articular effects such as vasculitis. Corticosteroids are also used to control disease activity during initial therapy with DMARDs. Although corticosteroids are associated with bone loss this appears to be dose-related; recent studies have suggested that a low dose of a corticosteroid started during the first two years of moderate to severe rheumatoid arthritis may reduce the rate of joint destruction. The smallest effective dose should be used, such as oral prednisolone 7.5 mg daily for 2–4 years only, and at the end of treatment the dose should be tapered off slowly to avoid possible long term adverse effects. Relatively high doses of a corticosteroid, with cyclophosphamide, may be needed to control vasculitis.

AZATHIOPRINE

Azathioprine is a complementary drug for rheumatoid arthritis.

Indications: Rheumatoid arthritis in cases that have failed to respond to chloroquine or penicillamine; psoriatic arthritis; transplant rejection (section 12.2); inflammatory bowel disease (section 4.7)

Contra-indications: Hypersensitivity to

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azathioprine or mercaptopurine.

Precautions: Monitor throughout treatment including blood counts; hepatic impairment (Appendix 5); renal impairment (Appendix 4); elderly (reduce dose); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

BONE MARROW SUPPRESSION: PATIENTS SHOULD BE WARNED TO REPORT IMMEDIATELY ANY SIGNS OR SYMPTOMS OF BONE MARROW SUPPRESSION, FOR EXAMPLE UNEXPLAINED BRUISING OR BLEEDING, PURPURA, INFECTION, SORE THROAT.

Adverse effects: Hypersensitivity reactions requiring immediate and permanent withdrawal include malaise, dizziness, vomiting, diarrhoea, fever, rigors, myalgia, arthralgia, rash, hypotension and interstitial nephritis; dose-related bone marrow suppression; liver impairment, cholestatic jaundice; hair loss and increased suceptibility to infections and colitis in patients also receiving corticosteroids; nausea; rarely pancreatitis and pneumonitis. hepatic veno-occlusive disease; also herpes zoster infection.

Dose: Administered on expert advice.

Rheumatoid arthritis, by mouth, initially, 1.5–2.5 mg/kg daily in divided doses, adjusted according to response; maintenance 1–3 mg/kg daily; consider withdrawal if no improvement within 3 months.

POM **Azathioprine** *(WMF 2.4)*
Tablet, Azathioprine 50 mg.

CHLOROQUINE SALTS

Indications: Rheumatoid arthritis (including juvenile arthritis); malaria (section 9.4.1).

Contra-indications: Psoriatic arthritis.

Precautions: Monitor visual acuity throughout treatment; warn patient to report immediately any unexplained visual disturbances; hepatic impairment; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); neurological disorders including epilepsy; severe gastrointestinal disorders; G6PD deficiency; elderly; may exacerbate psoriasis and aggravate myasthenia gravis; porphyria; **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances, headache, skin reactions (rash, pruritus); less frequently ECG changes, convulsions, visual changes, retinal damage, keratopathy, ototoxicity, hair depigmentation, alopecia, discoloration of skin, nails and mucous membranes; rarely blood disorders (including thrombocytopenia, agranulocytosis, aplastic anaemia); mental changes (including emotional disturbances, psychosis), myopathy (including cardiomyopathy and neuromyopathy), acute generalized exanthematous pustulosis, exfoliative dermatitis, erythema multiforme (Stevens-Johnson syndrome) and hepatic damage; **important**: arrhythmias and convulsions in overdosage.

Dose: Administered on expert advice.

NOTE: ALL DOSES IN TERMS OF CHLOROQUINE BASE.

Rheumatoid arthritis, by mouth , ADULT 150 mg daily; maximum 2.5 mg/kg daily; CHILD up to 3 mg/kg daily.

NOTE: TO AVOID EXCESSIVE DOSAGE IN OBESE PATIENTS THE DOSE OF CHLOROQUINE SHOULD BE CALCULATED ON THE BASIS OF LEAN BODY WEIGHT.

POM **Chloroquine** *(WMF 2.4)*
Tablets, Chloroquine sulfate 200 mg; Chloroquine phosphate 250 mg.

NOTE: CHLOROQUINE BASE 150 MG IS APPROXIMATELY EQUIVALENT TO CHLOROQUINE SULFATE 200 MG OR CHLOROQUINE PHOSPHATE 250 MG.

See Section 9.4.1 for the proprietary preparations of Chloroquine.

METHOTREXATE

Methotrexate is a complementary drug for rheumatoid arthritis.

Indications: Rheumatoid arthritis which has failed to respond to penicillamine or chloroquine; malignant disease (section 12.1).

Contra-indications: Pregnancy and breastfeeding (Appendices 2 and 3); immunodeficiency syndromes; significant pleural effusion or ascites.

Precautions: Monitor throughout treatment including blood counts and hepatic and renal function tests; renal and hepatic impairment (avoid if severe, see also Appendices 4 and 5); reduce dose or withdraw if acute infection develops; for woman or man, contraception during and for at least 6 months after treatment; peptic ulceration, ulcerative colitis, diarrhoea, ulcerative stomatitis; advise patient to avoid self-medication with salicylates or other NSAIDs; warn patient with rheumatoid arthritis to report cough or dyspnoea; **interactions**: Appendix 1.

BONE MARROW SUPPRESSION: PATIENTS SHOULD BE

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WARNED TO REPORT IMMEDIATELY ANY SIGNS OR SYMPTOMS OF BONE MARROW SUPPRESSION, FOR EXAMPLE UNEXPLAINED BRUISING OR BLEEDING, PURPURA, INFECTION, SORE THROAT.

Adverse effects: Blood disorders (bone marrow suppression), liver damage, pulmonary toxicity; gastrointestinal disturbances—if stomatitis and diarrhoea occur, stop treatment; renal failure, skin reactions, alopecia, osteoporosis, arthralgia, myalgia, ocular irritation, precipitation of diabetes.

Dose: Administered on expert advice.

Rheumatoid arthritis, by mouth, ADULT 7.5 mg once weekly (as a single dose or divided into 3 doses of 2.5 mg given at intervals of 12 hours), adjusted according to response; maximum total dose of 15 mg (occasionally 20 mg) once weekly.

IMPORTANT: THE DOSES ARE **WEEKLY** DOSES AND CARE IS REQUIRED TO ENSURE THAT THE CORRECT DOSE IS PRESCRIBED AND DISPENSED.

POM **Methotrexate** *(WMF 2.4)*
Tablet, Methotrexate 2.5 mg.

PENICILLAMINE

Penicillamine is a complementary drug for rheumatoid arthritis.

Indications: Severe rheumatoid arthritis; copper and lead poisoning (section 19.2.3).

Contra-indications: Hypersensitivity; lupus erythematosus.

Precautions: Monitor throughout treatment including blood counts and urine tests; renal impairment (Appendix 4); pregnancy (Appendix 2); avoid concurrent gold, chloroquine or immunosuppressive treatment; avoid oral iron within 2 hours of a dose; **interactions**: Appendix 1.

BONE MARROW SUPPRESSION: PATIENTS SHOULD BE WARNED TO REPORT IMMEDIATELY ANY SIGNS OR SYMPTOMS OF BONE MARROW SUPPRESSION, FOR EXAMPLE UNEXPLAINED BRUISING OR BLEEDING, PURPURA, INFECTION, SORE THROAT.

Adverse effects: Initially nausea (less of a problem if taken before food or on retiring, and if initial dose is only gradually increased), anorexia, fever; taste loss (mineral supplements not recommended); blood disorders including thrombocytopenia, neutropenia, agranulocytosis and aplastic anaemia; proteinuria, rarely haematuria (withdraw immediately); haemolytic anaemia, nephrotic syndrome, lupus erythematosus-like syndrome, myasthenia-like syndrome, polymyositis (rarely with cardiac involvement), dermatomyositis, mouth ulcers, stomatitis, alopecia, bronchiolitis and pneumonitis, pemphigus, glomerulonephritis (Goodpasture syndrome) and erythema multiforme (Stevens-Johnson syndrome) also reported; male and female breast enlargement reported; rash (early rash disappears on withdrawing treatment—reintroduce at lower dose and increase gradually; late rash is more resistant—either reduce dose or withdraw treatment).

Dose: Administered on expert advice.

Rheumatoid arthritis, by mouth, ADULT initially 125–250 mg daily before food for 1 month, increased by similar amounts at intervals of not less than 4 weeks to usual maintenance of 500–750 mg daily in divided doses; maximum 1.5 g daily; ELDERLY initially up to 125 mg daily before food for 1 month increased at intervals of not less than 4 weeks; maximum 1 g daily; CHILD 8–12 years initially 2.5–5 mg/kg daily, gradually increased to usual maintenance of 15–20 mg/kg daily at intervals of 4 weeks over a period of 3–6 months.

POM **Penicillamine** *(WMF 2.4)*
Capsules, Penicillamine 125 mg, 250 mg [125-mg strength not included on WHO Model List].
Tablets, Penicillamine 125 mg, 250 mg [125-mg strength not included on WHO Model List].

SULFASALAZINE

Sulfasalazine is a complementary drug for rheumatoid arthritis.

Indications: Severe rheumatoid arthritis; ulcerative colitis and Crohn disease (section 4.7).

Contra-indications: Hypersensitivity to salicylates and sulfonamides; severe renal impairment; child under 2 years; porphyria.

Precautions: Monitor during first 3 months of treatment including blood counts and hepatic and renal function tests; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); history of allergy; G6PD deficiency; slow acetylator status; **interactions**: Appendix 1.

BONE MARROW SUPPRESSION: PATIENTS SHOULD BE WARNED TO REPORT IMMEDIATELY ANY SIGNS OR

SYMPTOMS OF BONE MARROW SUPPRESSION, FOR EXAMPLE UNEXPLAINED BRUISING OR BLEEDING, PURPURA, INFECTION, SORE THROAT.

Adverse effects: Nausea, diarrhoea, headache, loss of appetite; fever; blood disorders (including Heinz body anaemia, megaloblastic anaemia, leukopenia, neutropenia, thrombocytopenia); hypersensitivity reactions (including rash, urticaria, erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, epidermal necrolysis, pruritus, photosensitization, anaphylaxis, serum sickness, interstitial nephritis, lupus erythematosus-like syndrome); lung complications (including eosinophilia, fibrosing alveolitis); ocular complications (including periorbital oedema); stomatitis, parotitis; ataxia, aseptic meningitis, vertigo, tinnitus, alopecia, peripheral neuropathy, insomnia, depression, hallucinations; kidney reactions (including proteinuria, crystalluria, haematuria); oligospermia; rarely acute pancreatitis, hepatitis; urine may be coloured orange; some soft contact lenses may be stained.

Dose: Administered on expert advice.
Rheumatoid arthritis, by mouth as gastro-resistant tablets, ADULT initially 500 mg daily, increased by 500 mg at intervals of 1 week to a maximum of 2–3 g daily in divided doses.

POM **Sulfasalazine** *(WMF 2.4)*
Enteric-coated tablets (Gastro-resistant tablets), Sulfasalazine 500 mg.

2.1.3 Other antirheumatic drugs

HYDROXYMETHOXYPHENYL COMPOUND

(Standardised Ginger Extract)

Indications: Treatment of rheumatic and arthritic pain; may be used as an alternative or supplement to the NSAIDs.

Contra-indications: Hypersensitivity to ginger or other component of the drug; GI bleeding.

Precautions: Children below the age of 12 years; pregnancy, lactation.

Dose: By mouth, Adult, 2 capsules daily; one in the morning and one in the evening. To be taken with food.

POM **ZINAXIN®** *(Swipha)*
Capsule, HMP-33 Ginger extract 255 mg Pack - 30.

CHONDROITIN plus GLUCOSAMINE

Pharmacology: Glucosamine, an amino monosaccharide, is a component of almost all human connective tissues. It is naturally produced in the body by the addition of amino group to glucose, this molecule is subsequently acetylated to acetyl glucosamine. Repeating units of acetylglucosamine composes Hyaluronan, Keratan and Heparan. Hence, glucosamine is used in the body to synthesize Glycosamino-glycans (GAGs) and glyco-proteins (Proteoglycans) which play an important role in the maintenance and repair of cartilage. The 2 active forms of chondroitin are Chondroitin-4-sulphate and chondroitin-6-sulphate. Chondroitin is one of the predominant GAGs. It is polymer of the repeating disaccharide unit of galaclosamine sulphate and glucuronic acid. Chondroitin inhibits the enzymes that breakdown proteoglycans and helps in maintaining the basic structure of cartilage. Arthocare (Glucosamine/Chondroitin) is chondro-protective agent which aids cartilage production and repair and it also aids synthesis of Hyaluronic acid.

Chondroprotective agents including glucosamine and chondroitin protect and restore joint cartilage by: Supporting and enhancing anabolic chondrocytes synthesis; Supporting and enhancing the synthesis of synovial fluid which is required to lubricate the joint; Inhibiting free radical enzymes and autoimmune processes that degrade joint cartilage; Removing blockages in the blood vessels leading to the joint.

Analgesic/Anti-inflammatory properties - Glucosamine possesses direct anti-inflammatory effect, which is not due to inhibition of Cyclo-oxygenase but as a result of: Stabilization of cell membranes; Inhibition of Lysosomal enzymes; Reduced generation of super oxide radicals by macrophages. Glucosamine sulphate controls pain better and longer (though initially slower) than Ibuprofen. Chondroitin reduces Phospholipase A_2 concentrations causing diminished formation of pro-inflammatory Prostaglandins (PGS_2) and Leukotriene (LTB_4). It increases Hyaluronate concentration thus enhancing the synovial fluid and also the viscosity of the latter which are determining factors for producing pain relief.

Indications: *General - Anti-arthritic.*

Joint - Since Arthocare stimulates biosynthesis of cartilage and joint substances such as Hyaluronic acid, it is a complete chondro-protective of choice in osteoarthritis. It is also indicated for a number of joint related ailments

which include: Rheumatoid arthritis, Fractures, Otosclerosis, Low backache, Ankylosing spondylitis, Arthritis due to sport injury/active lifestyle.

Eyes - For Uveitis, that is an inflammatory disease of the iris and focusing muscle. It is useful also in preventing changes in the vitreous humour (substance within the eye) and thus protecting the retina from release.

Contra-indications: Hypersensitivity to Glucosamine and Chondroitin sulphate.

Precautions: Allergy to shellfish.

Pregnancy/Lactation - Use of Arthocare in pregancy should be avoided in the 1st trimester of pregancy. However, there is no evidence of fetal toxicity or teratogenicity with the use of Arthocare.

Impaired renal and hepatic function - Dosage adjustment in patients with impaired renal or liver function is not required.

Adverse effects: Arthocare is a true chondroprotective, hence it carries little or no clinically significant side effects. Only 3.48% of patients can complain of gastro-intestinal disturbances. About 2% will complain of diarrhea, nausea and heartburn. Arthocare is thus well tolerated.

Dose: Dosage requirement are usually based on bodyweights: Up to 60 kg - 2 caps twice a day; Above 60 kg - 3 caps twice a day. To be taken after food.

Prophylactic use: 2 capsules once or twice daily after food depending upon the severity of the disease process. This is important in preventing athritis due to sport injury.

Note: It requires 1-2 weeks for the effects of Arthocare to appear. Once the desired effects have been achieved, the dosage can be reduced. Arthocare should be used for a mininium of 2-4 weeks to experience optimal results. It takes around 8 weeks to 6 months to repair damaged cartilage.

Once the therapeutic effects are achieved, they persist for a prolonged time. This allows for cyclic supplementation with Arthocare. The longer the Arthocare is taken, the more outstanding and effective the results.

POM **ARTHOCARE**® *(Fidson)*

Capsule, Chondroitin Sulphate 200 mg, Glucosamine HCl 250 mg.

SODIUM HYALURONATE

Pharmacology: Synovial fluid, which is visco-elastic owing to its contents of hyaluronic acid, is present in all synovial joints, especially in the large weight joints, where it provides a normal, painless movement owing to its synovial and shock-absorbing properties. It is responsible for supplying nourishment to the joint cartilage. In degenerative joint diseases like osteoarthritis, the visco-elasticity of the joint synovium is considerably impaired, which reduces its shock-absorbing effect. The mechanical load of joint and disintegration of joint cartilage is so increased that it leads to pain and restricted movement at the affected joint. Sodium hyaluronate is injected intra-articularly to supplement natural hyaluronic acid in the synovial fluid. These injections may reduce pain over 1–6 months but they are associated with short-term increase in knee inflammation.

Indications: Pain and restricted movement in degenerative and traumatic changes of knee joints and other synovial joints.

Contra-indications: Hypersensitivity to the drug.

Precautions: Avoid injection into blood vessels and surrounding tissue. Not recommended for use in children, pregnancy and breastfeeding or in patients with inflammatory joint diseases like rheumatoid arthritis.

Adverse effects: Local side effects like pain, heat sensation, reddening and swelling can occur at the treated joint. Placing an ice pack on the treated joint for 5 to 10 minutes would reduce the occurrence of such side effects

Dosage & Administration: By intra-articular injection, 20 mg once a week; up to 3 to 5 injections into the affected joint. Several joints can be treated simultaneously. Depending on the degree of severity of the joint disease, the effect of a treatment with 5 injections can sustain for more than 6 months. Repeated treatment cycles may be possible depending on the requirement.

Note: In case of joint effusion, an aspiration of effusion, resting of the joint as well as placing an ice pack and/or the intra-articular administration of corticosteroids is advised. 2-3 days thereafter, the treatment with Sodium hyaluronate 20 mg is started.

As long as the sterile pack is not opened, the contents and the surface of the prefilled syringe are sterile. The prefilled syringe is taken out from the sterile pack, the cap is removed from Leurlock connection, a suitable canula (e.g. 19 or 21 G) is fixed and this is locked by a slight rotation. Before injection, the air bubble is removed from the injection.

POM **SYNJECT**® *(Fidson)*

Injection, Sodium hyaluronate 20 mg per 2 ml;

a visco-elastic solution for injection into the knee joint gap sterilized by autoclaving.
Pack - 1 prefilled syringe in sterile pack.

2.2 Drugs used in gout

2.2.1 Acute gout
2.2.2 Chronic gout

Gout is a familial metabolic disease characterized by recurrent episodes of acute arthritis due to deposits of monosodium urate in joint and cartilage. Formation of uric acid calculi in the kidneys may also occur. Gout is associated with high serum levels of uric acid, a poor soluble substance that is the major end product of purine metabolism.
Treatment of gout and hyperuricemia consists of a two–step approach. The first step is to terminate the acute attack and resolve the pain. Once the acute attack is resolved, the goal is to gradually reduce the serum uric acid concentration.

2.2.1 Acute gout

Acute attacks of gout are usually treated with high doses of a **NSAID** such as indometacin (150–200 mg daily in divided doses); ibuprofen has weaker anti-inflammatory properties than other NSAIDs and is therefore less suitable for treatment of gout. Salicylates, including acetylsalicylic acid are also not suitable because they may increase plasma-urate concentrations. **Colchicine** is an alternative for those patients in whom NSAIDs are contraindicated. Its use is limited by toxicity with high doses. It does not induce fluid retention and can therefore be given to patients with heart failure; it can also be given to patients receiving anticoagulants.

COLCHICINE

Indications: Acute gout; short-term prophylaxis during initial therapy with allopurinol.
Contra-indications: Pregnancy (Appendix 2).
Precautions: Elderly; gastrointestinal disease; cardiac impairment; hepatic impairment; renal impairment (Appendix 4); breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Nausea, vomiting, abdominal pain; excessive doses may cause severe diarrhoea, gastrointestinal haemorrhage, rash, renal and hepatic damage; rarely peripheral neuritis, myopathy, alopecia, inhibition of spermatogenesis; with prolonged treatment, blood disorders.
Nursing considerations: •Administer on empty stomach to enhance absorption; but for maintenance therapy, give with meals to reduce GI effects.
•Monitor fluid I&O; teach patient to increase fluid intake to about 3-4 litres daily.
•Tell patient to avoid alcohol and OTC preparations containing alcohol.
•Discontinue if nausea or vomiting occurs; if used for acute attack, discontinue as soon as pain resolves or if nausea, vomiting or diarrhoea occurs.
Dose: *Acute gout*, by mouth, adult 0.5–1 mg initially, followed by 500 micrograms every 2–3 hours until relief of pain is obtained, or vomiting or diarrhoea occurs; maximum total dose 6 mg; the course should not be repeated within 3 days
Prevention of gout attacks during initial treatment with allopurinol, adult 500 micrograms 2–3 times daily continuing for at least 1 month after hyperuricaemia has been corrected.

POM **Colchicine** *(WMF 2.3.1)*
Tablet, Colchicine 500 micrograms.

POM **Colchicine** *(EDL 2.4)*
Tablet, Colchicine 0.5 mg.

2.2.2 Chronic gout

For long-term control of gout in patients who have frequent attacks, the xanthine oxidase inhibitor **allopurinol** may be used to reduce production of uric acid. It should not be used to treat an acute attack since it may prolong it indefinitely. Treatment for chronic gout should not be started until after an acute attack has completely subsided, usually 2–3 weeks. The initiation of allopurinol treatment may precipitate an acute attack therefore colchicine or a suitable NSAID should be used as a prophylactic and continued for at least one month after the hyperuricaemia has been corrected. If an acute attack develops during treatment for chronic gout, then allopurinol should continue at the same dosage and the acute attack should be treated in its own right. Treatment for chronic gout must be continued indefinitely to prevent further attacks of gout.

ALLOPURINOL

RETURN

Indications: Prophylaxis of gout; prophylaxis of hyperuricaemia associated with cancer chemotherapy.

Contra-indications: Acute gout; if an acute attack occurs while receiving allopurinol, continue prophylaxis and treat attack separately.

Precautions: Ensure adequate fluid intake of 2–3 litres daily; pregnancy and breastfeeding (Appendices 2 and 3); renal and hepatic impairment (Appendices 4 and 5); withdraw treatment if rash occurs, reintroduce if rash is mild but discontinue immediately if it recurs; **interactions**: Appendix 1.

Adverse effects: Rash (see Precautions above), hypersensitivity reactions occur rarely and include fever, lymphadenopathy, arthralgia, eosinophilia, erythema multiforme (Stevens-Johnson syndrome) or toxic epidermal necrolysis, vasculitis, hepatitis, renal impairment and, very rarely, seizures; gastrointestinal disorders; rarely malaise, headache, vertigo, drowsiness, visual and taste disturbance, hypertension, alopecia, hepatotoxicity, paraesthesia, neuropathy, gynaecomastia, blood disorders (including leukopenia, thrombocytopenia, haemolytic anaemia and aplastic anaemia).

Advice to patients: See Labels 18, 21 and 27 in Appendix 6.

Nursing considerations: •Administer after meals with plenty of fluid.

•Patient should increase fluid intake to about 3 - 4 litres daily.

•Discontinue the drug and contact physician at first sign of rash, painful urination, blood in urine, irritation of the eyes, or swelling of the lips or mouth.

•Teach patient to avoid hazardous activities, if drowsiness occurs; alcohol decreases effectiveness of the drug.

•Colchicine or NSAID (not aspirin or salicylates) may be prescribed to prevent acute gouty attacks which may occur in first 6 weeks of therapy.

Dose: *Prophylaxis of gout*, by mouth, adult initially 100 mg daily as a single dose, preferably after food, then adjusted according to plasma or urinary uric acid concentration; usual maintenance dose in mild conditions 100–200 mg daily, in moderately severe conditions 300–600 mg daily, in severe conditions 700–900 mg daily; doses over 300 mg daily given in divided doses.

NOTE: INITIATE 2–3 WEEKS AFTER ACUTE ATTACK HAS SUBSIDED AND ADMINISTER COLCHICINE OR A SUITABLE NSAID (NOT IBUPROFEN OR A SALICYLATE) FROM THE START OF ALLOPURINOL TREATMENT AND CONTINUE FOR AT LEAST 1 MONTH AFTER HYPERURICAEMIA CORRECTED.

Prophylaxis of hyperuricaemia, by mouth, adult maintenance doses as for acute gout, adjusted according to response, started 24 hours before cancer treatment and continued for 7–10 days afterwards; child under 15 years 10–20 mg/kg daily (maximum 400 mg daily).

POM **Allopurinol** *(WMF 2.3.2)*
Tablets, Allopurinol 100 mg.

POM **Allopurinol** *(EDL 2.4)*
Tablet, Allopurinol 100 mg.

POM **Allopurinol** *(Dizpharm)*
Tablet,, Allopurinol 100 mg.
100 mg - 100.

POM **ZYLORIC**® *(GSK)*
Tablet, Allopurinol 100 mg; white tab. marked 'ZYLORIC 100' and 'Coded U4A'.
100 mg - 50.

PROBENECID

Therapeutic category: Uricosuric Agent.

Indications:Gout prophylaxis, hyperuricaemia; prolongation of beta-lactam effect (i.e., serum levels)

Contra-indications: Renal uric acid calculi, blood dyscrasia; initiation of therapy during acute attack; children under 2 years.

Precautions: History of peptic ulceration, renal impairment, pregnancy; ensure adequate fluid intake.

Adverse effects: GI upset, sore gums, dizziness, headache, skin rashes, urinary frequency.

Advice to patients: See Labels 12, 21 and 27 in Appendix 6.

Nursing considerations: •Administer with food, milk or antacid to minimize GI distress.

•Encourage patient to drink plenty of fluids to reduce the risk of uric acid stones.

•Do not initiate therapy until acute attack subsides; it has no analgesic or anti-inflammatory action and therefore of no value in acute attack.

•Tell patient with gout to avoid alcohol and aspirin or other salicylates because they increase urate level and may precipitate gout respectively. Paracetamol may be used for pain.

•The frequency and severity of acute attacks may increase during the first 6 -12 months of therapy; Colchicine or another anti-inflammatory agent may be prescribed during first 3 - 6 months of therapy to prevent such attacks.

•Provide low purine diet, restricting liver, kidneys, sardines, peas.

•Probenecid is preferred to Sulphinpyrazone becuase it has lower incidence of GI and haematological adverse reactions.

Dose: By mouth, Adult, *Hyperuricaemia with gout*, initially 250 mg twice daily; increased after a week to 500 mg twice daily; then, up to a max. 2-3 g daily in 2-4 divided doses.
Prolong penicillin serum levels, 500 mg 4 times daily.
Gonorrhoea, 1 g 30 minutes before Penicillin, Ampicillin or Amoxicillin.

POM **Probenecid** *(EDL 2.4)*
Tablet, Probenecid 500 mg.
Injection, Probenecid 100 mg per ml.

POM **BENEMID®** *(Bolax/BPP)*
Tablet, Probenecid 500 mg; white scored tab. marked 'MSD 501'.

2.3 Skeletal muscle relaxants (antispasmodics)

Drugs that affect skeletal muscle function fall into 2 major therapeutic groups:

(a) Neuromuscular blockers which are used during surgical procedures and in intensive care units to cause paralysis (see section 3.3).
(b) Spasmolytics which are used to reduce spasticity in a variety of neurological conditions.

Members of the first group, as their name implies, interfere with transmission at the neuromuscular end plate and are not CNS–active drugs. Because they are used primarily as an adjunct to general anaesthesia, they are discussed under anaesthetic drugs in chapter 3, section 3.3.

Drugs in the second group have traditionally been called "centrally acting muscle relaxants but dantrolene, a member of the group, has no central effects.

Antispasmodic drugs

Spasticity is characterized by an increase in tonic stretch reflexes and flexor muscle spasms together with muscle weakness. It is often associated with cerebral palsy, multiple sclerosis, and stroke.

These conditions often involve abnormal function of the bowel and bladder, as well as skeletal muscle. This section deals with skeletal muscle spasticity only while chapter 4, section 4.2, deals with bowel spasms.

Drug therapy may ameliorate some of the symptoms of spasticity by modifying the stretch reflex arc or by interfering directly with skeletal muscle excitation - contraction coupling. The major disadvantage of treatment with these drug is that reduction in muscle tone can cause a loss of splinting action of the spastic leg and truck muscles and sometimes lead to an increase in disability.

Diazepam can be used in patients with muscle spasm of almost any origin, including local muscle trauma. However, it produces sedation in most patients at the doses required to significantly reduce muscle tone. Other benzodiazepines can be used. Muscle-relaxant doses of benzodiazepines are similar to anxiolytic doses (see section 1.1).

Orphenadrine, a congener of diphenhydramine, is an anticholinergic agent with weak antihistaminic, anaesthetic, and skeletal muscle-relaxant properties.

Tizanidine is a centrally acting skeletal muscle relaxant; its major site of action is in the spinal cord. It preferentially inhibits polysynaptic mechanisms responsible for excessive muscle tones, mainly by reducing the release of excitatory amino acids from interneurones. The drug does not affect neuromuscular transmission.

Other skeletal antispasticity drugs include **Dantrolene** (which acts directly on skeletal muscle and produces fewer central adverse effects) and **Baclofen** (which inhibits transmission at spinal level and also depresses the CNS).

Quinine salts are also effective in reducing the frequency of nocturnal leg cramps by about 25% in ambulatory patients. Requires close patient monitoring during the early stages for adverse effects as well as for benefit. Quinine is very toxic in overdosage and accidental fatalities have occurred in children.

METHOCARBAMOL

Therapeutic category: Skeletal Muscle Relaxant.

Indications: Symptomatic relief of muscular spasm.

Contra-indications: Coma or pre-coma, brain damage, epilepsy, myasthenia gravis, glaucoma, tachycardia.

Precautions: May cause drowsiness, avoid extravasation, history of seizures.

Adverse effects: Drowsiness, skin rash, urticaria, angioneurotic oedema, lightheadness, allergic reactions.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: •Give with food or milk to minimize GI distress.
•Give I.M. deeply and slowly, only in upper outer quad-

rant of buttocks; max. of 5ml in each buttock.
•Give I.V. slowly to avoid fainting; observe injection site for irritation and phlebitis. Monitor closely for extravasation.
•Parenteral dose may cause orthostatic hypotension; keep patient supine for 15 minutes after injection and let him get up slowly. Supervise ambulation.
•May cause drowsiness, impair judgement or coordination. Advise patient to avoid alcohol and hazardous activities.
•Inform patient that drug may turn urine brown, black or green.
•Tell patient to notify physician of rash, itching, or nasal congestion.

Dose: By mouth, Adult, 1.5 g 4 times daily.
Elderly: 750 mg 4 times daily or less.
By slow I.V. Injection or infusion (max. 3 ml per minute), Adult, 10–30 ml depending on the severity and patient's response; not exceeding 3 ml per day. Not to be administered for more than 3 consecutive days.
Elderly: Half the max. adult dose or less.
Child: Not recommended.

POM **Methocarbamol** *(EDL 2.5)*
Tablet, Methocarbamol 750 mg.

POM **ROBAXIN®** *(Wyeth/Delpitano)*
Tablet, Methocarbamol 750 mg; white scored oblong tab. marked 'AHR'.
750 mg - 100.
Injection, Methocarbamol 100 mg per ml in aqueous macrogol 300; in 10 ml amp.
Pack - 10 ml x 5.

ORPHENADRINE

Therapeutic category: Skeletal Muscle Relaxant; Anticholinergic Agent.
Indications: Pain due to spasm of voluntary muscle in injury, strains, sprains.
Contra-indications: Glaucoma, urinary retention, myasthenia gravis, breast-feeding.
Precautions: Tachycardia, pregnancy, elderly.
Adverse effects: Dry mouth, nausea, blurred vision, dizziness, confusion, tremor.
Nursing considerations: •Administer whole, do not crush sustained release product.
•Administer I.V. injection over 5 minutes with patient in the supine position; wait for 5-10 minutes before helping patient to a sitting position (this is due to bradycardia associated with I.V. injection which usually disappears in 2 minutes).
•May cause drowsiness, impair judgement or coordination. Advise patient to avoid alcohol and hazardous activities.
•Raise bed rails, institute safety measures, assist with ambulation.
•Instruct patient to notify physician if urinary hesitancy or retention occurs. Patient should void before taking the drug.
•Give patient cool drinks or chewng gum to relieve dry mouth.

Dose: By mouth, 150-300 mg daily in divided doses; up to 400 mg daily if necessary.
In Emergency, by I.M. or slow I.V. injection, 60 mg repeated 12 hourly if necessary.
Not recommended for children.

POM **Orphenadrine** *(EDL 2.4)*
Tablet, Orphenadrine citrate 100 mg.
Injection, Orphenadrine Citrate 30 mg per ml; in 1 ml amp.

With Paracetamol
POM **HORGESIC®** *(Hovid)*
Tablet, Orphenadrine citrate 35 mg, paracetamol 450 mg.
Pack - 1000.

POM **MYOGESIC®** *(Supreme)*
Tablet, Orphenadrine, paracetamol.
Pack - 20.

TIZANIDINE

Indications: Painful muscle spasms associated with static and functional disorders of the spine and following surgery; spasticity due to neurological disorders such as chronic myelopathy, cerebro-vascular accidents.
Precautions: Impaired kidney or liver function; road users and operators of machineries; pregnancy, breast-feeding, children.
Adverse effects: Drowsiness, fatigue, dizziness, dry mouth, nausea, slight reduction in blood pressure; in high doses, muscle weakness, insomnia, hypotension, bradycardia.
Dose: *Painful muscle spasms*, by mouth, 2-4 mg 3 times daily; increased to 2-4 mg 4 times daily in severe cases.
Spasticity due to neurological disorders, by mouth, initially 6 mg in 3 divided doses; increased stepwise at half-weekly or weekly intervals by 2-4 mg up to an optimal daily dose of 12-24 mg in 3–4 doses; max. 36 mg daily.

POM **SIRDALUD®** *(Novartis)*
Tablets, Tizanidine HCl 2 mg, 6 mg (all scored tabs); 4 mg (cross-scored tab.).

2.4 Muscle relaxants (peripherally acting) and cholinesterase inhibitors

2.4.1 Muscle relaxants
2.4.2 Cholinesterase inhibitors

2.4.1 Muscle relaxants

Muscle relaxants used in surgery include **suxamethonium**, **alcuronium**, and **vecuronium**; for further details see section 3.3.1.

2.4.2 Cholinesterase inhibitors

MYASTHENIA GRAVIS

Cholinesterase inhibitors, such as **neostigmine** and **pyridostigmine**, are used in the symptomatic treatment of myasthenia gravis. They act by inhibiting acetylcholinesterase, thereby prolonging the action of acetylcholine, and thus enhancing neuromuscular transmission; this produces at least a partial improvement in most myasthenic patients but complete restoration of muscle strength is rare. Unless the patient has difficulty in swallowing, cholinesterase inhibitors are given by mouth. Pyridostigmine has a slower onset (usually within 30–60 minutes), but a longer duration of effect than neostigmine; it also tends to cause fewer muscarinic effects such as diarrhoea, abdominal cramps, and excess salivation, so is usually preferred. Doses should be carefully adjusted to avoid precipitating a cholinergic crisis due to overdosage; this must be differentiated from a myasthenic crisis due to disease progression, and consequent underdosage; the principal effect in both cases is increased muscle weakness.

In myasthenic crisis, if the patient has difficulty in breathing and in swallowing, the cholinesterase inhibitor must be given by intramuscular or subcutaneous injection; neostigmine is usually preferred. To reduce muscarinic effects, atropine (section 3.2) should also be given.

For the use of neostigmine in surgery, see section 3.3.

A corticosteroid such as **prednisolone** (section 10.3), is used for the treatment of myasthenia gravis; addition of **azathioprine** (section 12.2) may allow a dose reduction of both the corticosteroid and of the anticholinesterase.

NEOSTIGMINE

Indications: Myasthenia gravis; reversal of non-depolarizing block, postoperative urinary retention (section 3.3).

Contra-indications: Recent intestinal or bladder surgery; mechanical intestinal or urinary tract obstruction; after suxamethonium; pneumonia; peritonitis.

Precautions: Asthma; urinary tract infections; cardiovascular disease including arrhythmias (especially bradycardia, vagotonia, recent myocardial infarction or atrioventricular block); hyperthyroidism; hypotension; peptic ulcer; epilepsy; parkinsonism; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Increased salivation, nausea and vomiting, abdominal cramps, diarrhoea; signs of overdosage include bronchoconstriction, increased bronchial secretions, lacrimation, excessive sweating, involuntary defecation and micturition, miosis, nystagmus, bradycardia, heart block, arrhythmias, hypotension, agitation, excessive dreaming, weakness eventually leading to fasciculation and paralysis; thrombophlebitis reported; rash associated with bromide salt.

Advice to patients: Notify physician if nausea, vomiting, muscle weakness, severe abdominal pain, or difficulty in breathing occurs.

Nursing considerations: •Administer with food or milk if GI upset occurs (absorption is better on an empty stomach).

•Observe patient for bronchospasm, hypotension, respiratory depression, headache, dizziness and convulsions (discontinue therapy and inform the doctor if these occur).

•Monitor patient's VS, respiration.

•Evaluate patient's therapeutic response namely increased muscle strength, hand grasp, improved gait.

•Aropine sulphate and adrenaline should be ready for hypersensitivity reactions.

Dose: *Myasthenia gravis*, by mouth as neostigmine bromide, ADULT initially 15–30 mg at suitable intervals throughout the day, gradually increased until desired response obtained, total daily dose within range 75–300 mg, taken at appropriate intervals when maximum strength required, but doses above 180 mg daily not usually tolerated; CHILD up to 6 years, initially 7.5 mg, 6–12 years, initially 15 mg, total daily dose usually 15–90 mg in divided doses at appropriate intervals.

Myasthenia gravis, by subcutaneous or intramuscular injection as neostigmine metilsulfate, ADULT

0.5–2.5 mg as required, total daily dose 5–20 mg; NEONATE 50–250 micrograms 30 minutes before feeds (not usually required beyond 8 weeks of age); CHILD 200–500 micrograms as required.

POM **Neostigmine** *(WMF 20.2)*
Tablet, Neostigmine bromide 15 mg.
Injection (Solution for injection), Neostigmine metilsulfate 500 micrograms/ml, in 1-ml ampoule; 2.5 mg/ml, in 1-ml ampoule.

POM **Neostigmine** *(EDL 9.2)*
Tablet, Neostigmine bromide 15 mg.

PYRIDOSTIGMINE

Pyridostigmine bromide is a complementary cholinesterase inhibitor.

Indications: Myasthenia gravis.

Contraindications: Recent intestinal or bladder surgery; mechanical intestinal or urinary tract obstruction; after suxamethonium; pneumonia; peritonitis.

Precautions: Asthma; urinary tract infection; cardiovascular disease including arrhythmias (especially bradycardia or atrioventricular block); hyperthyroidism; hypotension; peptic ulcer; epilepsy; parkinsonism; avoid intravenous injection; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Muscarinic effects generally weaker than with neostigmine: increased salivation, nausea and vomiting, abdominal cramps, diarrhoea; signs of overdosage include bronchoconstriction, increased bronchial secretions, lacrimation, excessive sweating, involuntary defecation and micturition, miosis, nystagmus, bradycardia, heart block, arrhythmias, hypotension, agitation, excessive dreaming, weakness eventually leading to fasciculation and paralysis; thrombophlebitis; rash associated with bromide salt.

Nursing considerations: •Give on an empty stomach for better absorption.
•Observe patient for bronchospasm, hypotension, respiratory depression, headache, dizziness and convulsions (discontinue therapy and inform the doctor if these occur).
•Monitor patient's VS, respiration.
•Evaluate patient's therapeutic response namely increased muscle strength, hand grasp, improved gait.

Dose: *Myasthenia gravis*, by mouth, ADULT initially 30–120 mg at suitable intervals throughout the day, gradually increased until desired response obtained; total daily dose within range 0.3–1.2 g, taken at appropriate intervals when maximum strength required, but doses above 450 mg daily not usually advisable in order to avoid acetylcholine receptor downregulation; CHILD up to 6 years initially 30 mg, 6–12 years initially 60 mg; total daily dose usually 30–360 mg in divided doses at appropriate intervals.
Myasthenia gravis, by intramuscular injection, ADULT 2 mg every 2–3 hours; neonate 50–150 micrograms before feeds (but neostigmine usually preferred); CHILD, total daily dose 1–12 mg given in divided doses at appropriate intervals.

POM **Pyridostigmine** *(WMF 20.2)*
Tablets, Pyridostigmine bromide 60 mg.
Injection (Solution for injection), Pyridostigmine bromide 1 mg/ml, 1-ml. ampoule.

POM **Pyridostigmine** *(EDL 9.2)*
Tablet, Pyridostigmine bromide 60 mg.

2.5 Topical antirheumatic drugs

METHYL SALICYLATE

Therapeutic category: Counter irritant

Indications: Relief of pain, swelling, stiffness associated with rheumatism and other musculo-skeletal disorders.

Precautions: Avoid contact with eyes, mucous membranes, broken or irritated skin.

Administration: Apply generously and gently massage 3-4 times daily.

OTC **Methyl Salicylate** (*EDL 14.2)*
Ointment, Liniment or Embroication

OTC **Methylsalicylate** *(Leady)*
Ointment, Methylsalicylate 50%.

OTC **SLOANS LINIMENT®** (*NGC)*
Liniment, Methylsalicylate 25%

OTC **Methyl Salicylate Compound** (*EDL 14.2)*
Ointment, Liniment, Embrocation or Inhalation, Various Formulations of the approved active ingredients and strengths as specified in the EDL.

OTC **BAM-BAM**® *(Jawa)*
Ointment, Methyl salicylate 5%, menthol 5.5%, pine oil 0.5%, oleoresin capsicum 0.3%, eucalyptus oil 3%, camphor 11%.
Pack - 4 g (in metal tin); 25 g (in bottle).
Dose: Apply on the affected parts 2 times daily.

OTC **BCN BALM**® (*BCN*)
(Menthol and Wintergreen Embrocation)
Ointment, Menthol 2.4%, eucalyptol 2%, cajuput oil 0.5%, eucalyptus oil 1.5%, methylsalicylate 14.2%.
Pack - 25 g.

OTC **BENGAY**® (*Pfizer/Neimeth)*
Ointment, Methylsalicylate 15%, menthol 10%; greaseless and stainless.
Pack -35 g; 85 g (in tubes).
Dose: Apply generously and gently massage the affected parts 3-4 times daily.

POM **BONERVE**® *(Vitabiotics)*
Liniment, Methyl salicylate 4% v/v, Methyl nicotinate 0.3% w/v, Camphor 5% w/v, Eucalyptus oil 2.5% v/v, Lemon grass oil 2.5% v/v.
Pack - 60 ml

OTC **HEATOL**® (*P.Z.)*
Ointment, Camphor synthetic 26%, peppermint oil 13%, cajaput oil 10%, menthol crystals 8%, clove oil 5%.
Pack - 4 g; 25 g.
Administration: Apply directly and rub in gently to the affected parts 2-4 times daily.

OTC **HOUSEHOLD EMBROCATION**® (*BCN)*
Liniment, Oleic acid 8.5%, ammonia solution (dilute) 4.5%, ammonium chloride 1.25%, turpentine oil 25%.
Pack - 4000 ml.

OTC **MEDIX VAPO-RUB**® (*Morison)*
Ointment, Menthol, eucalyptus oil, turpentine oil, tinc. capsicum.

OTC **Moko Nerve Liniment** *(New Healthway)*
Emulsion, Ammonium chloride 1.88 g, ammonium bicarbonate 3.75 g, ammonium solution 2.6 ml, turpentine oil 12.5 g.
Pack – 200 ml

OTC **NERVE & BONE**® (*BCN)*
Liniment, Technical turpentine oil 12.5%, oleic acid 2.5%, ammonium bicarbonate 3.75%, ammonium chloride 1.875%, strong ammonia solution 2.5%.
Pack - 110 ml.

OTC **NEUROGESIC**® *(Drugfield)*
Ointment, Methylsalicylate, menthol; greaseless ointment.
Pack - 35 mg.

OTC **NOWW-NOWW** ®*(Jawa)*
Ointment, Methyl salicylate 20%, menthol 10%, oleoresin capsicum 1.5%, camphor oil 5%.
Pack - 25 g tube.
Dose: Apply on the affected parts 2 times daily.

OTC **ROBB**® *(P.Z.)*
Ointment, Camphor synthetic 11%, menthol crystals 5.5%, methyl salicylate 4%, eucalyptus oil 1%, pumilio pine oil 0.5%.
Pack - 4 g; 25 g.
Liniment, same as for ointment
Pack - 100 ml.
Administration: Apply to the chest or other affected parts of the body 2-4 times daily.

OTC **SKENO BALM**® (*Leady)*
Ointment, Methylsalicylate 9.7%, menthol 4.9%, eucalyptus oil 4.0%, camphor 5.5%; whitish thick ointment with sharp odour of menthol.
Pack - 4 g; 25 g.

OTC **SKENO HEAT RUB**® *(Leady)*
Ointment, Methylsalicylate 15%, menthol 10%.

OTC **SPRANE**® *(Fidson)*
Ointment, Methylsalicylate, capsaicin, menthol.
Pack - 20 g (in tube).
Pharmacology: Sprane contains Methyl Salicylate, a topical analgesic and anti-inflammatory agent for the relief of pain associated with musculoskeletal discomfort. Capsacin is a counter-irritant used also as a topical analgesic in painful conditions. Topical application of capsacin produces a counter-irritant effect, attributed to its ability to deplete the neuropeptide substance P (pain causing substance) from local sensory C-type nerve fibres, and is therefore useful in a range of painful conditions. Menthol results in dilatation of blood vessels in the affected area causing a soothing effect followed by analgesic action.
Indications: Inflammation, pain, sprain of muscles and joints; Arthritis, rheumatism and related diseases.
Contra-indications: Do not use in patients

with Aspirin or Salicylate idiosyncrasy.
Precautions: Do not use excessive amounts. Do not apply to eyes or broken skin.
Adverse effects: Excessive irritation and tinnitus may occur. Due to percutaneous absorption into bloodstream, nausea or vomiting may occur if excessive or extreme dosage is applied.
Dosage and Administration:

Gently massage thin film of Sprane in thin applications into affected painful and surrounding areas. The number of thin applications applied determines the intensity of action. Apply to affected region 3 to 4 times daily.

OTC **VILICIN**® (*Daily Need)*

Ointment, Methylsalicylate, menthol.
Pack - 25 g.

EUCALYPTUS OIL

Indications: For the relief of sprains, lumbago and rheumatism.
Administration: Rub the oil into the affected parts and repeat until the pain disappears.

OTC **BELL'S SILVERBIRD EUCALYPTUS OIL**® *(De-Sears)*
Liquid, Eucalyptus oil BP; a colourless or pale yellow oil with a characteristic aromatic camphoraceous odour.
Pack - 30 ml.

3. Drugs used in anaesthesia

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3.1 General anaesthetics and oxygen
3.1.1 Intravenous agents
3.1.2 Volatile inhalational agents
3.1.3 Inhalational gases
3.2 Preoperative medication and sedation
3.3 Muscle relaxants and cholinesterase inhibitors
3.3.1 Muscle relaxants
3.3.2 Cholinesterase inhibitors
3.4 Local anaesthetics
3.5 Analgesics and opioid antagonists
3.6 Blood substitutes and solutions for correcting fluid imbalance

This section describes drugs used in anaesthesia. The reader is referred to WHO. *Model Prescribing Information. Drugs used in Anaesthesia*. Geneva: WHO; 1989 for more detailed information.

To produce a state of prolonged full surgical anaesthesia reliably and safely, a variety of drugs is needed. Special precautions and close monitoring of the patient are required. These drugs may be fatal if used inappropriately and should be used by non–specialized personnel only as a last resort. Irrespective of whether a general or conduction (regional or local) anaesthetic technique is used, it is essential that facilities for intubation and mechanically assisted ventilation are available. A full preoperative assessment is required including, if necessary, appropriate fluid replacement.

Anaesthesia may be induced with an intravenous barbiturate, parenteral ketamine, or a volatile agent. Maintenance is with inhalational agents often supplemented by other drugs given intravenously. Specific drugs may be used to produce muscle relaxation. Various drugs may be needed to modify normal physiological functions or otherwise to maintain the patient in a satisfactory condition during surgery.

LONG-TERM MEDICATION

The risk of stopping long-term medication before surgery may be greater than the risk of continuing it. It is essential that the anaesthetist is told of all drugs that the patient is (or has been) taking; for further advice see section 6.2 (drugs affecting coagulation), section 10.3 (corticosteroids), section 11.3.1 (hormonal contraceptives), and section 10.1 (diabetic patients).

Nursing Considerations:- General/Local Anaesthetics

•Monitor VS q10min during IV administration, q30min after IM dose.
•Give anticholinergic preoperatively to decrease secretions.
•Provide quiet environment for recovery to decrease psychotic symptoms.
•Evaluate therapeutic response viz maintenance of anaesthesia, decreased pain.

3.1 General anaesthetics and oxygen

3.1.1 Intravenous agents
3.1.2 Volatile inhalational agents
3.1.3 Inhalational gases

3.1.1 Intravenous agents

Intravenous anaesthetics may be used alone to produce anaesthesia for short surgical procedures but are more commonly used for induction only. They can produce apnoea and hypotension and thus facilities for adequate resuscitation must be available. They are contraindicated if the anaesthetist is not confident of being able to maintain an airway. Before intubation is attempted, a muscle relaxant must be given. Individual requirements vary considerably; lesser dosage is indicated in the elderly, debilitated or hypovolaemic patients.

Intravenous induction using **thiopental** is rapid and excitement does not usually occur. Anaesthesia persists for about 4–7 minutes; large or repeated doses severely depress respiration and delay recovery.

Anaesthesia with **ketamine** persists for up to 15 minutes after a single intravenous

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injection and is characterized by profound analgesia. It may be used as the sole agent for diagnostic and minor surgical interventions. Subanaesthetic concentrations of ketamine may be used to provide analgesia for painful procedures of short duration such as the dressing of burns, radiotherapeutic procedures, marrow sampling and minor orthopaedic procedures. Recovery from ketamine anaesthesia is associated with a high incidence of hallucinations and other emergence reactions. Ketamine is of particular value in children, in whom hallucinations are believed to be less significant.

THIOPENTAL SODIUM

Thiopental is a representative intravenous anaesthetic. Various drugs can serve as alternatives.

Synonym: Thiopentone Sodium.

Therapeutic category: Anticonvulsant; Barbiturate; General Anaesthetic; Sedative.

Indications: Induction of anaesthesia prior to administration of inhalational anaesthetic; anaesthesia of short duration.

Contra-indications: Inability to maintain airway; hypersensitivity to barbiturates; cardiovascular disease; dyspnoea or obstructive respiratory disease; porphyria.

recautions: Local extravasation can result in extensive tissue necrosis and sloughing; intra-arterial injection causes intense pain and may result in arteriospasm; hepatic impairment (Appendix 5); pregnancy (Appendix 2); **interactions**: Appendix 1.

SKILLED TASKS: WARN PATIENT NOT TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING, FOR 24 HOURS AND ALSO TO AVOID ALCOHOL FOR 24 HOURS.

Adverse effects: Rapid injection may result in severe hypotension and hiccup; cough, laryngeal spasm, allergic reactions.

Nursing considerations: •Test dose may be given to assess patient's reaction to drug.

•Monitor vital signs every 3-5 minutes during I.V. administration.

•Make emergency resuscitative equipment and oxygen available; maintain airway.

•Avoid extravasation as necrosis may occur.

•Monitor for respiratory distress; in general anaesthesia, atropine sulphate may be given as premedication to prevent laryngeal spasm.

•Place patient in Sim's position if vomiting, to prevent from aspirating vomitus.

Dose: *Induction*, by intravenous injection as a 2.5% (25 mg/ml) solution over 10–15 seconds, Adult 100–150 mg (reduced in elderly or debilitated patients), followed by a further 100–150 mg if necessary according to response after 60 seconds; or up to 4 mg/kg; Child 2–7 mg/kg repeated if necessary according to response after 60 seconds.

RECONSTITUTION: SOLUTIONS CONTAINING 25 MG/ML SHOULD BE FRESHLY PREPARED BY MIXING 20 ML OF WATER FOR INJECTIONS WITH THE CONTENTS OF THE 0.5-G AMPOULE OR 40 ML WITH THE 1-G AMPOULE. ANY SOLUTION MADE UP OVER 24 HOURS PREVIOUSLY OR IN WHICH CLOUDINESS, PRECIPITATION OR CRYSTALLIZATION IS EVIDENT SHOULD BE DISCARDED.

POM **Thiopental sodium** *(WMF 3.1.1)*
Injection (Powder for solution for injection), Thiopental sodium, 0.5-g and 1-g ampoules.

POM **Thiopentone Sodium** *(EDL 3.1.1)*
Injections, Thiopentone sodium. 0.5 g, 1.0 g, 2.5 g in amps.

KETAMINE

Indications: Induction and maintenance of anaesthesia; analgesia for painful procedures of short duration.

Contra-indications: Thyrotoxicosis; hypertension (including pre-eclampsia); history of cerebrovascular accident, cerebral trauma, intracerebral mass or haemorrhage or other cause of raised intracranial pressure; eye injury and increased intraocular pressure; psychiatric disorders, particularly hallucinations.

Precautions: Supplementary analgesia often required in surgical procedures involving visceral pain pathways (morphine may be used but addition of nitrous oxide will often suffice); during recovery, patient must remain undisturbed but under observation; pregnancy (Appendix 2); **interactions**: Appendix 1

SKILLED TASKS: WARN PATIENT NOT TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY OR DRIVING, FOR 24 HOURS AND ALSO TO AVOID ALCOHOL FOR 24 HOURS.

Adverse effects: Hallucinations and other emergence reactions during recovery possibly accompanied by irrational behaviour (effects rarely persist for more than few hours but can recur at any time within 24 hours); transient elevation of pulse rate and blood pressure common, arrhythmias have occurred; hypotension and bradycardia occasionally reported.

Nursing considerations: •Administer I.V. for over 1 minute; inject the dose directly into vein or into I.V. infusion containing free flowing compatible so-

lution.
•Monitor vital signs before, during and after anaesthesia.
•Because of rapid induction, patient should be physically supported during administration.
•Maintain clear airway and keep resuscitation equipment ready for use.
•Start supportive respiration if respiratory depression occurs, using mechanical support if possible rather than administering analeptics.
•Provide a quiet environment and ensure that patient is not disturbed during recovery phase to reduce emergent reactions.
•Patient may become excited and suffer from hallucination when recovering from anaesthesia; diazepam may be prescribed.
•Ketamine is a potent hallucinogen that can readily produce dissociative anaesthesia (i.e., patient feels detached from environment). The dissociative effect and hallucinatory side effects have resulted in the abuse of this drug.

Dose: *Induction*, by intramuscular injection, Adult and Child 6.5–13 mg/kg (10 mg/kg usually produces 12–25 minutes of anaesthesia).
Induction, by intravenous injection over at least 1 minute, Adult and Child 1–4.5 mg/kg (2 mg/kg usually produces 5–10 minutes of anaesthesia).
Induction, by intravenous infusion of a solution containing 1 mg/ml, Adult and Child total induction dose 0.5–2 mg/kg; maintenance (using microdrip infusion), 10–45 micrograms/kg/minute, rate adjusted according to response.
Analgesia, by intramuscular injection, Adult and Child initially 4 mg/kg.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Ketamine** *(WMF 3.1.1)*
Injection (Solution for injection), Ketamine (as HCl) 50 mg/ml; in 10-ml vial.

POM **Ketamine** *(EDL 1.1)*
Injection, Ketamine HCl 10 mg per ml in 20 ml vial; 50 mg per ml in 10 ml vial; 100 mg per ml in 5 ml vial.

PROPOFOL

Therapeutic category: General Anaesthetic; Sedative.
Indications: Induction and maintenance of general anaesthesia; sedation of ventilated adult patient receiving intensive care.
Contra-indications: Hypersensitivity to Propofol or Propofol's emulsion which contains soybean oil, egg lecithin, and glycerol.
Precautions: Monitor for signs of hypotension, airway obstruction and oxygen desaturation, disorders of fat metabolism (1ml preparation contains 0.1g fat); cardiac, respiratory, renal or hepatic impairment; avoid in pregnancy and obstetric anaesthesia; breast-feeding (safety to neonate not established); epilepsy (convulsion may occur); bradycardia; contains no antimicrobial preservative and should be used within 6 hours of opening and dilution (dilution should be done aseptically); elderly.
Adverse effects: Hypotension, transient apnoea; post-operative fever, nausea, vomiting and headache, rarely convulsion, anaphylaxis, discolouration of urine, pain on injection, thrombosis and phlebitis; sexual disinhibition on recovery from anaesthesia; pulmonary oedema.
Nursing considerations: •Drug should be administered only by persons who are familiar with airway management and the administration of I.V. anaesthetics.
•Do not mix with other drugs or blood products; may be diluted only with D_5W before infusion (avoid dilution below 2 mg/ml); give over 3-5 min. Use only glass containers for mixing, not stable in plastic.
•Tubing and any unused portions of propofol vials should be discarded after 12 hours.
•Observe closely for signs of significant hypotension or bradycardia; may be treated with increased rate of fluid administration, pressor agents, elevation of lower extremeties, or atropine.
•Apnoea may occur during induction and will require ventilatory support if it persists for longer than 60 seconds.
•Avoid abrupt discontinuation if infusion prior to weaning or daily wake up assessments; it can cause rapid awakening, anxiety, agitation, and resistance to mechanical ventilation.

Dose: *Induction*, by i.v. injection, healthy Adult, 1.5-2.5 mg/kg at a rate of 2-4 ml every 20 seconds; adjust dose according to response. Child (3-8 years): usually about 2.5mg/kg.
Maintenance, by i.v. infusion, Adult, usually 4-12 mg/kg/h; adjust dose to maintain depth of anaesthesia required. Child (3-8 years):usually 9-15 mg/kg/h
Sedation during intensive care, by i.v. infusion, Adult, usually 0.3-4 mg/kg/h; adjust dose according to depth of sedation required.

Note: Not recommended for ICU sedation in children of all ages and for anaesthesia in children below 3 years.

POM **DIPRIVAN®** *(Reals)*
Injection (emulsion), Propofol 10 mg per ml.

One of the volatile anaesthetics, ether, halothane (with or without nitrous oxide), must be used for induction when intravenous agents are contraindicated and particularly when intubation is likely to be difficult.

Full muscle relaxation is achieved in deep anaesthesia with **ether**. Excess bronchial and salivary secretion can be avoided by premedication with atropine. Laryngeal spasm may occur during induction and intubation. Localized capillary bleeding can be troublesome and postoperative nausea and vomiting are frequent; recovery time is slow particularly after prolonged administration.

If intubation is likely to be difficult, **halothane** is preferred. It does not augment salivary or bronchial secretions and the incidence of postoperative nausea and vomiting is low. Severe hepatitis, which may be fatal, sometimes occurs; it is more likely in patients who are repeatedly anaesthetized with halothane within a short period of time.

ETHER, Anaesthetic

DRUG SUBJECT TO INTERNATIONAL CONTROL UNDER THE UNITED NATIONS CONVENTION AGAINST ILLICIT TRAFFIC IN NARCOTIC DRUGS AND PSYCHOTROPIC SUBSTANCES (1988).

Indications: Induction and maintenance of anaesthesia (administered from many types of vaporizers).

Contra-indications: Severe liver disease; diabetes mellitus; impaired kidney function; raised cerebrospinal fluid pressure.

Precautions: Risk of potentially fatal convulsions in febrile patients; pregnancy (Appendix 2); **interactions**: Appendix 1.

FIRE HAZARD: DIATHERMY MUST NOT BE USED WHEN ETHER/OXYGEN MIXTURES IN USE AND OPERATING THEATRE AND ITS EQUIPMENT SHOULD BE DESIGNED TO MINIMIZE RISK OF STATIC DISCHARGE, PARTICULARLY IN HOT, DRY CLIMATES.

Adverse effects: Transient postoperative effects include impairment of liver function and leukocytosis; nausea and vomiting; capillary bleeding.

Dose: *Induction*, Adult and Child, up to 15% in inspired gases.
Maintenance of light anaesthesia, Adult and Child 3–5% in air (with or without muscle relaxants); up to 10% for deep anaesthesia.

POM **Ether, anaesthetic** *(WMF 3.1.2)*
Volatile liquid

POM **Anaesthetic Ether** *(EDL 1.1)*
Inhalation, Anaesthetic ether 500 ml; liquid in bottle.

HALOTHANE

Indications: Induction and maintenance of anaesthesia.

Contra-indications: History of unexplained jaundice or pyrexia following previous exposure to halothane; family history of malignant hyperthermia; raised cerebrospinal fluid pressure; porphyria.

Precautions: Anaesthetic history should be carefully taken to determine previous exposure and previous reactions to halothane (at least 3 months should be allowed to elapse between each re-exposure); avoid for dental procedures in patients under 18 years unless treated in hospital (high risk of arrhythmias); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Arrhythmias; bradycardia; respiratory depression; hepatic damage.

Dose: *Induction*, using specifically calibrated vaporizer, gradually increase inspired gas concentration to 2–4% (ADULT) or 1.5–2% (CHILD) in oxygen or nitrous oxide–oxygen.
Maintenance, ADULT and CHILD 0.5–2%.

POM **Halothane** *(WMF 3.1.2)*
Volatile liquid

POM **Halothane** *(EDL 1.1)*
Inhalation, Halothane 250 ml; liquid in bottle.

POM **FLUOTHANE®** *(Reals)*
Halothane 0.01% w/w, Colourless volatile liquid, non-explosive and non-flammable in the concentration usually used.
Pack - 250 ml.

3.1.3 Inhalational gases

Nitrous oxide is used for the maintenance of anaesthesia. It is too weak to be used alone, but it allows the dosage of other anaesthetic agents to be reduced. It has a strong analgesic action.

Oxygen should be added routinely during anaesthesia with inhalational agents, even when air is used as the carrier gas, to

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protect against hypoxia.

Oxygen is also used in the management of anaphylaxis (section 8.1), myocardial infarction (section 5.6), and severe acute asthma (section 7.1).

IDENTIFICATION OF CYLINDERS FOR INHALATION GASES

AN ISO STANDARD (INTERNATIONAL STANDARD 32, GAS CYLINDERS FOR MEDICAL USE, 1977) REQUIRES THAT CYLINDERS CONTAINING NITROUS OXIDE SHOULD BEAR THE NAME OF THE CONTENTS IN LEGIBLE AND PERMANENT CHARACTERS AND, PREFERABLY, ALSO THE CHEMICAL SYMBOL N_2O. THE NECK, FROM THE VALVE TO THE SHOULDER, SHOULD BE COLOURED BLUE. CYLINDERS CONTAINING OXYGEN INTENDED FOR MEDICAL USE SHOULD BEAR THE NAME OF THE CONTENTS IN LEGIBLE AND PERMANENT CHARACTERS AND, PREFERABLY, ALSO THE CHEMICAL SYMBOL O_2 . THE NECK, FROM THE VALVE TO THE SHOULDER, SHOULD BE COLOURED WHITE. CYLINDERS CONTAINING NITROUS OXIDE AND OXYGEN MIXTURES SHOULD BE SIMILARLY LABELLED, AND THE NECK COLOURED WHITE AND BLUE.

NITROUS OXIDE

Indications: Maintenance of anaesthesia in combination with other anaesthetic agents (halothane, ether, or ketamine) and muscle relaxants; analgesia for obstetric practice, for emergency management of injuries, during postoperative physiotherapy and for refractory pain in terminal illness.

Contra-indications: Demonstrable collection of air in pleural, pericardial or peritoneal space; intestinal obstruction; occlusion of middle ear; arterial air embolism; decompression sickness; chronic obstructive airway disease, emphysema.

Precautions: Minimize exposure of staff; pregnancy (Appendix 2); **interactions**: Appendix 1.

Adverse effects: Nausea and vomiting; after prolonged administration megaloblastic anaemia, depressed white cell formation; peripheral neuropathy.

Dose: *Anaesthesia*, Adult and Child nitrous oxide mixed with 25–30% oxygen.
Analgesia, 50% nitrous oxide mixed with 50% oxygen.

POM **Nitrous oxide** *(WMF 3.1.3)*
Inhalation gas.

POM **Nitrous Oxide** *(EDL 1.1)*
Medicinal gas for inhalation.

OXYGEN

Indications: To maintain an adequate oxygen tension in inhalational anaesthesia

FIRE HAZARD: AVOID USE OF CAUTERY WHEN OXYGEN IS USED WITH ETHER; REDUCING VALVES ON OXYGEN CYLINDERS MUST NOT BE GREASED (RISK OF EXPLOSION).

Precautions: **Interactions**: Appendix 1.

Adverse effects: Concentrations greater than 80% have a toxic effect on the lungs leading to pulmonary congestion, exudation and atelectasis.

Dose: Concentration of oxygen in inspired anaesthetic gases should never be less than 21%.

POM **Oxygen** *(WMF 3.1.3)*
Inhalation gas.

POM **Oxygen** *(EDL 1.1)*
Adjunct in general anaesthesia.
Medicinal gas for inhalation.

3.2 Preoperative medication and sedation

Pre-anaesthetic medication is often advisable prior to both conduction and general anaesthetic procedures.

Sedatives improve the course of subsequent anaesthesia in apprehensive patients. **Diazepam** and promethazine are effective. Diazepam can be administered by mouth, by rectum, or by intravenous injection. **Promethazine**, which has antihistaminic and antiemetic properties as well as a sedative effect, is of particular value in children.

A potent analgesic such as **morphine** (section 3.5) should be administered preoperatively to patients in severe pain or for analgesia during and after surgery.

Anticholinergic (more correctly antimuscarinic) drugs such as atropine are also used before general anaesthetia. They inhibit excessive bronchial and salivary secretions induced, in particular, by ether and ketamine. Intramuscular administration is most effective, but oral administration is more convenient in children. Lower doses should be used in cardiovascular disease or hyperthyroidism.

ATROPINE

Therapeutic category: Anticholinergic Agent; Antidote, Organophosphate Poisoning.

Indications: To inhibit salivary secretions; to inhibit arrhythmias resulting from

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excessive vagal stimulation; to block the parasympathomimetic effects of anticholinesterases such as neostigmine; organophosphate poisoning (section 19.2.3); antispasmodic (section 4.2); mydriasis and cycloplegia (section 13.3)

Contra-indications: Angle-closure glaucoma; myasthenia gravis; paralytic ileus, pyloric stenosis; prostatic enlargement.

Precautions: Down syndrome, children, elderly; ulcerative colitis, diarrhoea; hyperthyroidism; heart failure, hypertension; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

DURATION OF ACTION: SINCE ATROPINE HAS A SHORTER DURATION OF ACTION THAN NEOSTIGMINE, LATE UNOPPOSED BRADYCARDIA MAY RESULT; CLOSE MONITORING OF THE PATIENT IS NECESSARY.

Adverse effects: Dry mouth; blurred vision, photophobia; flushing and dryness of skin, rash; difficulty in micturition; less commonly arrhythmias, tachycardia, palpitations; confusion (particularly in elderly); heat prostration and convulsions, especially in febrile children.

Advice to patients: Maintain good oral hygiene habits because lack of saliva may increase chance of cavities. Observe caution while driving or performing other tasks requiring alertness, as drug may cause drowsiness, dizziness, or blurred vision. Notify physician if rash, flushing, or eye pain occurs, or if difficulty in urinating, constipation, or sensitivity to light becomes severe or persists.

Nursing considerations: Relieve dry mouth with frequent sips of water, gum. hard candy.

Advise patient to avoid hazardous activities if drowsiness occurs; to report blurred vision, chest patient, allergic reactions, constiaption.

•Observe for tachycardia if patient has cardiac problems.

•Drug causes urine retention and urinary hesitancy; patient should void before receiving the drug.

Dose: *Premedication*, by intramuscular injection 30–60 minutes before induction, ADULT and Child 20 micrograms/kg; by intravenous injection immediately before induction, ADULT up to maximum 500 micrograms.

Inhibition of bradycardia, by intravenous injection, ADULT 0.4–1 mg, CHILD 10–30 micrograms/kg.

Reversal of neuromuscular block, by intravenous injection 2–3 minutes before anticholinesterase, ADULT 0.6–1.2 mg, CHILD 20 micrograms/kg.

POM **Atropine** *(WMF 1.3)*

Injection (Solution for injection), Atropine sulfate 600 micrograms/ml; in 1-ml ampoule.

POM **Atropine** *(EDL 1.2)*

Injection, Atropine sulphate 0.5 mg, 1 mg per ml; in 1ml amp.

DIAZEPAM

DRUG SUBJECT TO INTERNATIONAL CONTROL UNDER THE CONVENTION ON PSYCHOTROPIC SUBSTANCES (1971).

Diazepam is a representative benzodiazepine. Various drugs can serve as alternatives.

Indications: Premedication before major or minor surgery; sedation with amnesia for endoscopic procedures and surgery under local anaesthesia; in combination with pethidine [not included on WHO Model List], when anaesthetic not available, for emergency reduction of fractures; epilepsy (section 1.7); anxiety disorders (section 1.1.2).

Contra-indications: Central nervous system depression or coma; shock; respiratory depression; acute pulmonary insufficiency; sleep apnoea; acute alcohol intoxication; severe hepatic impairment; myasthenia gravis.

Precautions: Respiratory disease; muscle weakness; history of alcohol or drug abuse; marked personality disorder; elderly or debilitated patients (adverse effects more common in these groups); hepatic impairment (Appendix 5) or renal failure (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); porphyria; **interactions**: Appendix 1.

SKILLED TASKS: WARN PATIENT NOT TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING, FOR 24 HOURS.

Adverse effects: Central nervous system effects common and include drowsiness, sedation, confusion, amnesia, vertigo, and ataxia; hypotension, bradycardia, or cardiac arrest, particularly in elderly or severely ill patients; also paradoxical reactions, including irritability, excitability, hallucinations, sleep disturbances; pain and thromboembolism on intravenous injection.

Dose: *Premedication*, by mouth 2 hours before surgery, ADULT and CHILD over 12 years, 5–10 mg

Sedation, by slow intravenous injection immediately before procedure, ADULT and CHILD over

12 years, 200 micrograms/kg.

ADMINISTRATION: ABSORPTION FOLLOWING INTRAMUSCULAR INJECTION SLOW AND ERRATIC; ROUTE SHOULD ONLY BE USED IF ORAL OR INTRAVENOUS ADMINISTRATION NOT POSSIBLE.

SLOW INTRAVENOUS INJECTION INTO LARGE VEIN REDUCES RISK OF THROMBOPHLEBITIS.

RESUSCITATION EQUIPMENT MUST BE AVAILABLE.

POM **Diazepam** *(WMF 1.3)*
Tablets, Diazepam 2 mg, 5 mg.
Injection (Solution for injection), diazepam 5 mg/ml; in 2-ml ampoule.

POM **Diazepam** *(EDL 1.2)*
Injection, Diazepam 5 mg per ml; in 2 ml amp.

See under section 1.1.2 for the proprietary preparations of Diazepam.

MIDAZOLAM

Therapeutic category: Benzodiazepine anxiolytic.

Pharmacology: Midazolam is a new benzodiazepine available for I.V. use. It is given as water-soluble drug and does not damage veins on injection. It has an elimination half-life of 2 hours and no active metabolites. In comparison with diazepam, it has greater amnesic properties.

Indications: Premedication before induction of anaesthesia; basal sedation before diagnostic or surgical interventions under local anaesthesia; long-term sedation in intensive care units (ICU); induction and maintenance of anaesthesia; as an induction agent in inhalation anaesthesia or a sleep-inducing component in combined anaesthesia, including total intravenous anaesthesia; ataralgesia in combination with ketamine in children.

Contra-indications: Hypersensitivity to benzodiazepines; acute narrow-angle glaucoma.

Precautions: Elderly and debilitated patients; obstructive pulmonary disease, chronic renal failure or CHF, myasthenia gravis; first three months of pregnancy, premature infants and neonates, breast–feeding.

Adverse effects: Rarely respiratory depression, apnoea, respiratory arrest and/or cardiac arrest; anaphylactoid reactions and skin reactions in isolated cases.

Nursing considerations: •Give I.M. deep into a large muscle mass.
•Oxygen and resuscitation equipment should be ready for use during I.V. infusion.
•Rapid dosage has been associated with respiratory arrest, particularly in the elderly.
•Monitor I.V. infusion and avoid extravasation.
•Observe B.P., pulse, respiration and airway integrity.
•Provide assistance with ambulation, until drowsy period is over.
•Teach patient to avoid hazardous activities that require alertness or physical co-ordination.

Dose: *Premedication before an operation*, by intramuscular injection, Adult: 0.07-0.1 mg/kg b.wt., depending on the age and condition of the patient; usually about 5 mg.
Child: 0.15-0.20 mg/kg i.m.; by rectal route, 0.35-0.45 mg/kg.
Elderly and debilitated Patients, 0.025-0.05 mg/kg i.m.
Doses should be administered about 30 minutes before induction of anaesthesia (20-30 minutes by rectal route in children).
Basal sedation in diagnostic or surgical interventions under local anaesthesia, by intravenous injection, initially 2.5 mg 5-10 minutes before the operation; further doses of 1 mg may be given, upto a max. total dose of 5 mg.
Sedation in ICU, by intravenous injection, loading dose, 0.03-0.3 mg/kg; maintenance dose, 0.03-0.2 mg/kg per hour.
Induction and maintenance of anaesthesia, by intravenous injection, induction, 10-15 mg; maintenance, according to individual patient's needs.
Intravenous anaesthesia in combination with ketamine, by i.v. continuous infusion, 0.03-0.1 mg/kg per hour; with narcotics, 0.03-0.3 mg/kg per hour.
Ataralgesia in combination with ketamine, by intramuscular injection, child: 0.15-0.20 mg/kg.

POM **DORMICUM®** *(Swipha)*
Injection, Midazolam hydrochloride 5 mg per ml, in 1 ml and 3 ml amps; 5 mg per 5 ml, in 5 ml amp.; 50 mg per 10 ml, in 10 ml amp.

PROMETHAZINE

Indications: Premedication prior to surgery; antiemetic (section 4.5).

Contra-indications: Child under 1 year; impaired consciousness due to cerebral depressants or of other origin; porphyria.

Precautions: Prostatic hypertrophy, urinary retention; glaucoma; epilepsy; hepatic impairment (Appendix 5); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

SKILLED TASKS: WARN PATIENT NOT TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING, FOR 24 HOURS.

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Adverse effects: Drowsiness (rarely paradoxical stimulation in children); headache; anticholinergic effects such as dry mouth, blurred vision, urinary retention.

Dose: *Premedication*, by mouth 1 hour before surgery, CHILD over 1 year 0.5–1 mg/kg.
Premedication, by deep intramuscular injection 1 hour before surgery, ADULT 25 mg.

POM **Promethazine** *(WMF 1.3)*
Tablets, Promethazine HCl 10 mg, 25 mg
Elixir (Oral solution), Promethazine HCl 5 mg/5 ml.
Injection (Solution for injection), Promethazine HCl 25 mg/ml; in 2-ml ampoule.

POM **Promethazine** *(EDL 1.2)*
Elixir, Promethazine HCl 5 mg per 5 ml.

See under section 8.1 for the proprietary preparations of Promethazine.

3.3 Muscle relaxants and cholinesterase inhibitors

3.3.1 Muscle relaxants
3.3.2 Cholinesterase inhibitor

Muscle relaxants used in surgery are classified according to their mode of action as depolarizing or non–depolarizing neuromuscular blocking drugs. Their use allows abdominal surgery to be carried out under light anaesthesia. They should never be given until it is certain that general anaesthesia has been established and ventilation must be mechanically assisted until they have been completely inactivated.

Suxamethonium is the only widely used depolarizing muscle relaxant. It produces rapid, complete paralysis, which is very short-lasting in most patients and is of particular value for laryngoscopy and intubation. Should paralysis be prolonged, ventilation must be assisted until muscle function is fully restored. Suxamethonium normally produces a phase I (depolarizing) neuromuscular block. After high doses or prolonged use, the nature of the block changes to a phase II (non-depolarizing) block; this phase II block (also known as dual block) is associated with prolonged neuromuscular blockade and apnoea.

Alcuronium is a non-depolarizing muscle relaxant with a duration of action of about 30 minutes. Its effects may be rapidly reversed after surgery by the anticholinesterase neostigmine, provided atropine is given to prevent excessive autonomic activity. **Vecuronium**, a relatively new and expensive non-depolarizing muscle relaxant, has a shorter duration of action (20–30 minutes); it causes minimal adverse cardiovascular effects.

REVERSAL OF BLOCK.
Cholinesterase inhibitors, such as **neostigmine**, are used at the end of an operation to reverse the muscle paralysis produced by non-depolarizing blocking drugs, such as alcuronium and vecuronium. Neostigmine must not be used with depolarizing blocking drugs, such as suxamethonium, since neostigmine will prolong the muscle paralysis. Neostigmine is also used to treat postoperative non-obstructive urinary retention.

For use of cholinesterase inhibitors in myasthenia gravis, see section 20.2.

3.3.1 Muscle relaxants

ALCURONIUM

Alcuronium is a representative non-depolarizing muscle relaxant. Various drugs can serve as alternatives.

Indications: Muscle relaxation during surgery.

Contra-indications: Respiratory insufficiency or pulmonary disease; dehydrated or severely ill patients; myasthenia gravis or other neuromuscular disorders.

Precautions: Renal or hepatic impairment (see Appendices 4 and 5); possibly increase dose in patient with burns; electrolyte disturbances; possibly decrease dose in respiratory acidosis or hypokalemia; history of asthma; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Histamine release, causing allergic reactions, such as wheal and flare effects at site of injection, flushing, bronchospasm (anaphylactoid reactions reported); transient hypotension, slight increase in heart rate or decreased pulse rate.

Dose: *Muscle relaxation*, by intravenous

injection, ADULT initially 200–250 micrograms/kg, then 50 micrograms/kg as required for maintenance; CHILD initially 125–200 micrograms/kg, then 50 micrograms/kg for maintenance.

POM **Alcuronium** *(WMF 3.3)*
Injection (Solution for injection), Alcuronium chloride 5 mg/ml, 2-ml ampoule.

ATRACURIUM

Therapeutic category: Non-depolarising Neuromuscular Blocking Agent; Sekeletal Muscle Relaxant.
Pharmacology: Atracurium prevents acetylcholine from binding to the receptors on the muscle end plate, thus blocking depolarization. It is also a non–depolarizing blocker with a duration of action of 15 to 35 minutes. See notes above.
Indications: In anaesthesia to relax skeletal muscles during a wide range of surgical procedures and to facilitate controlled ventilation; for endotracheal intubation where subsequent maintenance of muscle relaxation is required; for maintenance of muscle relaxation during Caesarean section following intubation with a rapid-onset agent such as suxamethonium.
Contra-indications: Hypersensitivity to atracurium besylate.
Precautions: Should only be administered with adequate general anaesthesia and under the supervision of an anaesthetist with facilities for endotracheal intubation and artificial ventilation; myasthenia gravis, other neuromuscular diseases and severe electrolyte disorders; severe cardiovascular disease (administer slowly); should be flushed through the vein after injection and same applies to other agents co-administered through the same site; pregnancy.
Adverse effects: Skin flushing and transient hypotension due to histamine release; rarely bronchospasm and anaphylactoid reactions.
Advice to patients: May be difficult to talk because of head and neck muscle blockade (patient should be reassured).
Nursing considerations: •Assess vital signs of B.P., pulse, respiration and airway, until patient is fully recovered. Keep airway clear.
•Monitor recovery from neuromuscular blockade shown by hand grip, head lift and ability to cough.
•Avoid I.M. injection; causes too much tissue irritation.
Dose: Adult and children over 1 month, by i.v. injection, 0.3-0.6 mg/kg b.wt. produces adequate relaxation for about 15-35 min.
Endotracheal intubation, by i.v. injection, 0.5-0.6 mg/kg b.wt.
Long surgical procedures including cardiopulmonary bypass, initially by i.v. injection, 0.3-0.6 mg/kg b.wt.; then, by i.v. infusion, 0.3-0.6 mg/kg/hour.
Note: **Administration** - Give undiluted as a bolus injection; not for I.M. injection, too much tissue irritation; administration requires the use of infusion pump.

POM **Atracurium** *(EDL 1.3)*
Injection, Atracurium 10 mg per ml.

POM **TRACRIUM®** *(GSK)*
Injection, Atracurium besylate 10 mg per ml; clear, faintly yellow solution in 2.5 ml and 5 ml glass amps.

GALLAMINE

PHARMACOLOGY: Gallamine prevents acetylcholine from binding to the receptors on the muscle end plate, thus blocking depolarization. It is a non-depolarizing blocker like tubocurarine and pancuronium. See notes above.
Indication: Non-depolarising muscle relaxant of medium duration.
Contra-indication: Severe renal disease.
Precautions: Elderly, hepatic or pulmonary impairment, respiratory depression.
Adverse effects: Tachycardia.
Nursing considerations: See under Suxamethonium.
Dose: By I.V. injection, Adult, 80-120 mg, then 20-40 mg as required.
Child: 1.5 mg/kg
Neonate: 600 mg/kg.

POM **Gallamine** *(EDL 1.3)*
Injection, Gallamine triethiodide 40 mg per ml; in 2 ml amp.

PANCURONIUM

Therapeutic category: Non-depolarising Neuro-muscular Blocker; Skeletal Muscle Relaxant.
Indications: As an adjunct to general anaesthesia, to facilitate tracheal intubation and to provide skeletal muscle relaxation during surgery or mechanical ventilation.
Contra-indications: Hypersensitivity to pancuronium or any component; pre-existing tachycardia.
Precautions: Administration is I.V. only and should be done by experienced clinicians. Ventilation must be supported during

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neuromuscular blockade. Electrolyte imbalance alters blockade. Myasthenia gravis or other neuromuscular diseases; pre-existing pulmonary, hepatic or renal disease; elderly.

Adverse effects: Increased B.P. and pulse, tachycardia, hypertension, rash, itching, excessive salivation, muscle weakness, bronchospasm, hypersensitivity reaction, oedema.

Nursing considerations: See under Suxamethonium.

Dose: Adult and child (above 1 month), by I.V., initially 0.04-0.1 mg/kg; maintenance dose, 0.02-0.1 mg/kg/dose every 30 minutes to 3 hours as needed.

POM **Pancuronium** *(EDL 1.3)*

Injection, Pancuronium bromide 2 mg per ml; in 2 ml amp.

SUXAMETHONIUM

Synonym: Succinylcholine

Therapeutic category: Cholinergic Agent; Depolarising Neuromuscular Blocker; Skeletal Muscle Relaxant.

Indications: Brief muscular paralysis during endotracheal intubation, endoscopy and electroconvulsive therapy.

Contra-indications: Inability to maintain clear airway; personal or family history of malignant hyperthermia; neurological disease involving acute wasting of major muscle, prolonged immobilization (risk of hyperkalaemia); personal or family history of congenital myotonic disease; Duchenne muscular dystrophy; myasthenia gravis; glaucoma, ocular surgery; liver disease; burns; low plasma cholinesterase activity (including severe liver disease); hyperkalaemia.

Precautions: Digitalis toxicity or recent digitalization; cardiac, respiratory or neuromuscular disease; paraplegia, spinal cord inury, or severe trauma; severe sepsis (risk of hyperkalaemia); prolonged apnoea on repeated injection (infusion preferred for long surgical procedures); hepatic impairment (Appendix 5); renal impairment; pregnancy (Appendix 2); children; **interactions**: Appendix 1.

Adverse effects: Postoperative muscle pain, particularly in patients ambulant after operation, and more common in females; myoglobinuria; myoglobinaemia; prolonged apnoea; increased intra-ocular pressure; hyperkalaemia; bradycardia, hypotension, arrhythmias, particularly with halothane (however, with repeated doses tachycardia, hypertension); increased salivary, bronchial and gastric secretions; transient rise in intragastric pressure; hypersensitivity reactions including flushing, rash, urticaria, bronchospasm, and shock (more common in women, in history of allergy, or in asthmatics); rarely, malignant hyperthermia (often fatal).

Nursing considerations: •Monitor vital signs of B.P., pulse, respiration, until patient is fully recovered.

•Keep airway clear and make the emergency equipment available.

•Check strength of patient's hand grip as he recovers from anaesthesia; drug is given by slowl IV over 1-2 minutes only by qualified person, usually an anaesthesiologist, who will determine neuromuscular blockade.

•Provide reassurance if communication is difficult during recovery from neuromuscular blockade.

•Reassure him that post-operative stiffness is normal and will soon subside.

Dose: *Muscle relaxation*, by intramuscular injection, INFANT up to 4–5 mg/kg; CHILD up to 4 mg/kg; maximum 150 mg.

Muscle relaxation, by intravenous injection, ADULT and CHILD 1 mg/kg, followed if necessary by supplements of 0.5–1 mg/kg at 5–10 minute intervals; INFANT 2 mg/kg.

Muscle relaxation (prolonged procedures), by intravenous infusion, ADULT 2.5–4 mg/minute of solution containing 1–2 mg/ml; maximum 500 mg/hour; child reduce infusion rate according to body weight.

POM **Suxamethonium** *(WMF 3.3)*

Injection (Solution for injection), Suxamethonium chloride 50 mg/ml, 2-ml ampoule.

Injection (Powder for solution for injection), Suxamethonium chloride.

NOTE: POWDER FORMULATION RECOMMENDED; LIQUID REQUIRES REFRIGERATED STORAGE.

POM **Suxamethonium** *(EDL 1.3)*

Injection, Suxamethonium Chloride 50 mg per ml; in 2 ml amp.

TUBOCURARINE

Therapeutic category: Non-depolarising Neuro-muscular Blocker; Skeletal Muscle Relaxant.

Pharmacology: Tubocurarine prevents acetylcholine from binding to the receptors on the muscle end plate, thus blocking depolarization. See notes above.

Indications: Non-depolarising muscle relaxant of medium to long duration mainly indicated as an adjunct to anaesthesia to secure muscular relaxation in surgery and obstetrics.

Contra-indications: Respiratory insufficiency, renal or hepatic impairment, hypersensitivity to curare–like drugs, asthma.

Precautions: Myasthenia gravis or myasthenic syndrome; gross obesity, myopathy and after poliomyelitis (reduce dose); endocrine dysfunction; patients with family history of hyperpyrexia and drug reactions; hypokalaemia; pregnancy and lactation.

Adverse effects: Transient hypotension, profound muscle relaxation with prolonged apnoea, circulatory depression, ganglionic block, histamine release.

Nursing considerations: See under Suxamethonium.

Dose: By i.v. injection, initially 15-30 mg; may be maintained by supplementary doses of 5-10 mg. Initial doses may be reduced to 10-15 mg, according to the depth of muscle relaxation needed.

Child (above 1 year): Initially 300-500 mcg per kg, then 60-100 mcg per kg as required.

Premature infant and neonate, 200-250 mcg per kg, then 40-50 mcg per kg as required.

Elderly: Same initial doses as for adult but the maintenance doses should be reduced and intervals between them increased.

Note: **Administration** - May also be given I.M.; administer I.V. undiluted over 60-90 seconds and flush I.V. cannula with NS or D_5W.

POM **Tubocurarine** *(GSK)*

Injection, Tubocurarine chloride 10 mg per ml; clear colourless, or faintly coloured sterile solution.

VECURONIUM

Vecuronium is a complementary non-depolarizing muscle relaxant.

Indications: Muscle relaxation during surgery.

Contra-indications: Respiratory insufficiency or pulmonary disease; dehydrated or severely ill patients; myasthenia gravis or other neuromuscular disorders.

Precautions: Renal impairment (Appendix 4); hepatic impairment; possibly increase dose in patient with burns; electrolyte disturbances; possibly decrease dose in respiratory acidosis or hypokalemia; history of asthma; severe obesity (maintenance of adequate airway and ventilation support); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Minimal release of histamine (rarely hypersensitivity reactions including bronchospasm, hypotension, tachycardia, oedema, erythema, pruritus).

Dose: *Intubation*, by intravenous injection, ADULT and CHILD over 5 months, 80–100 micrograms/kg;

maintenance of relaxation 20–30 micrograms/kg; CHILD under 4 months, initially 10–20 micrograms/kg, followed by increments according to response.

Muscle relaxation, by intravenous infusion, ADULT , initial bolus 40–100 micrograms/kg then 0.8–1.4 micrograms/kg/minute.

POM **Vecuronium** *(WMF 3.3)*

Injection (Powder for solution for injection), Vecuronium chloride, 10-mg vial.

3.3.2 Cholinesterase inhibitors

NEOSTIGMINE

Therapeutic category: Cholinergic Agent; Antidote, Neuromuscular Blocking Agent; Diagnostic Agent, Myasthenia Gravis.

Indications: Counteract effect of non-depolarizing muscle relaxants administered during surgery; postoperative non-obstructive urinary retention; myasthenia gravis (section 2.4.2).

Contra-indications: Recent intestinal or bladder surgery; mechanical intestinal or urinary tract obstruction; after suxamethonium; pneumonia; peritonitis.

Precautions: Asthma; urinary tract infections; cardiovascular disease, including arrhythmias (especially bradycardia or atrioventricular block); vagotonia; hypotension; peptic ulcer; epilepsy; parkinsonism; hyperthyroidism; avoid before halothane administration has been stopped; maintain adequate ventilation (respiratory acidosis predisposes to arrhythmias); renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Increased salivation and bronchial secretions, nausea and vomiting, abdominal cramps, diarrhoea; allergic reactions, hypotension.

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Dose: *Reversal of non-depolarizing block*, by intravenous injection over 1 minute, ADULT 2.5 mg, followed if necessary by supplements of 500 micrograms to maximum total dose of 5 mg; CHILD 40 micrograms/kg (titrated using peripheral nerve stimulator).

NOTE: TO REDUCE MUSCARINIC EFFECTS ATROPINE SULFATE BY INTRAVENOUS INJECTION (ADULT 0.6–1.2 MG, CHILD 20 MICROGRAMS/KG) WITH OR BEFORE NEOSTIGMINE.

Postoperative urinary retention, by subcutaneous or intramuscular injection, ADULT 500 micrograms (catheterization required if urine not passed within 1 hour).

POM **Neostigmine** *(WMF 3.3)*
Injection (Solution for injection), Neostigmine metilsulfate 500 micrograms/ml, in 1-ml ampoule; 2.5 mg/ml, in 1-ml ampoule.

POM **Neostigmine** *(EDL 1.3)*
Injection, Neostigmine methylsulphate 2.5 mg per ml; in 1 ml amp.

POM **PROSTIGMIN®** *(Swipha)*
Injection, Neostigmine (as sulphate) 0.5 mg per ml.

3.4. Local anaesthetics

Drugs used for conduction anaesthesia (also termed local or regional anaesthesia) act by causing a reversible block to conduction along nerve fibres. Local anaesthetics are used very widely in dental practice, for brief and superficial interventions, for obstetric procedures, and for specialized techniques of regional anaesthesia calling for highly developed skills. Where patient cooperation is required the patient must be psychologically prepared to accept the proposed procedure. Facilities and equipment for resuscitation should be readily available at all times. Local anaesthetic injections should be given slowly in order to detect inadvertent intravascular injection.

LOCAL INFILTRATION
Many simple surgical procedures that neither involve the body cavities nor require muscle relaxation can be performed under local infiltration anaesthesia. Lower-segment caesarean section can also be performed under local infiltration anaesthesia. The local anaesthetic drug of choice is **lidocaine** 0.5% with or without epinephrine. No more than 4 mg/kg of plain lidocaine or 7 mg/kg of lidocaine with epinephrine should be administered on any one occasion. The addition of **epinephrine** (adrenaline) diminishes local blood flow, slows the rate of absorption of the local anaesthetic, and prolongs its effect. Care is necessary when using epinephrine for this purpose since, in excess, it may produce ischaemic necrosis. It should **not** be added to injections used in digits or appendages.

SURFACE ANAESTHESIA
Topical preparations of **lidocaine** are available and topical eye drop solutions of **tetracaine** (section 13.5) are used for local anaesthesia of the cornea and conjunctiva.

REGIONAL BLOCK
A regional nerve block can provide safe and effective anaesthesia but its execution requires considerable training and practice. Nevertheless, where the necessary skills are available, techniques such as axillary or ankle blocks can be invaluable. Either **lidocaine** 1% or **bupivacaine** 0.5% is suitable. Bupivacaine has the advantage of a longer duration of action.

SPINAL ANAESTHESIA
This is one of the most useful of all anaesthetic techniques and can be used widely for surgery of the abdomen and the lower limbs. It is a major procedure requiring considerable training and practice. Either **lidocaine** 5% in glucose or **bupivacaine** 0.5% in glucose can be used but the latter is often chosen because of its longer duration of action.

BUPIVACAINE

Bupivacaine is a representative local anaesthetic. Various drugs can serve as alternatives.

Indications: Infiltration anaesthesia; peripheral and sympathetic nerve block; spinal anaesthesia; postoperative pain relief.

Contra-indications: Adjacent skin infection, inflamed skin; concomitant anticoagulant therapy; severe anaemia or heart disease; spinal or epidural anaesthesia in dehydrated or hypovolaemic patient.

Precautions: Respiratory impairment; hepatic impairment (Appendix 5); epilepsy; porphyria; myasthenia gravis; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: With excessive dosage or following intravascular injection, light-headedness, dizziness, blurred vision, restlessness, tremors and, occasionally, convulsions rapidly followed by drowsiness, unconsciousness and respiratory failure; cardiovascular toxity includes hypotension, heart block and cardiac arrest; hypersensitivity and allergic reactions also occur; epidural anaesthesia occasionally complicated by urinary retention, faecal incontinence, headache, backache or loss of perineal sensation; transient paraesthesia and paraplegia very rare.

Advice to patient: Do not chew food in anaesthetised region to prevent traumatizing tongue, lip, or buccal mucosa.

Nursing considerations: •Monitor B.P., pulse, respiration during treatment; if used as local anaesthetic in labour, fetal heart rate should be monitored.

•For epidural block, test dose should be given to verify needle or catheter placement.

•Administration should be done only by experienced clinicians.

•Onset of anaesthesia depending on route of administration is within 4-10 minutes; duration of action is 1.5-8.5 hours.

•Check solution for particles.

•Keep resuscitative equipment and drugs available.

Dose: *Local infiltration*, using 0.25% solution, ADULT up to 150 mg (up to 60 ml).

Peripheral nerve block, using 0.5% solution, ADULT up to 150 mg (up to 30 ml).

Dental anaesthesia, using 0.5% solution, ADULT 9–18 mg (1.8–3.6 ml).

Lumbar epidural block in surgery, using 0.5% solution, ADULT 50–100 mg (10–20 ml).

Lumbar epidural block in labour, using 0.25–0.5% solution, ADULT (female) up to 60 mg (maximum 12 ml).

Caudal block in surgery, using 0.25–0.5% solution, ADULT up to 150 mg (maximum 30 ml).

Caudal block in labour, using 0.25–0.5% solution, ADULT (female) up to 100 mg (maximum 20 ml).

NOTE: MAXIMUM CUMULATIVE SAFE DOSE FOR ADULTS AND CHILDREN OF A 0.25% SOLUTION OF BUPIVACAINE IS 1.5 MG/KG.

USE LOWER DOSES FOR DEBILITATED, ELDERLY, EPILEPTIC, OR ACUTELY ILL PATIENTS.

DO NOT USE SOLUTIONS CONTAINING PRESERVATIVES FOR SPINAL, EPIDURAL, CAUDAL OR INTRAVENOUS REGIONAL ANAESTHESIA.

POM **Bupivacaine** *(WMF 1.2)*

Injection (Solution for injection), Bupivacaine HCl 2.5 mg/ml (0.25%), in 10-ml ampoule; 5 mg/ml (0.5%), in 10-ml ampoule; 5 mg/ml (0.5%) with glucose 75 mg/ml (7.5%), in 4-ml ampoule.

POM **Bupivacaine** *(EDL 1.4)*

Injection, Bupivacaine HCl 0.25%, 0.5% with or without Adrenaline 1 in 200,000; in 10 ml amp.

LIDOCAINE

Lidocaine is a representative local anaesthetic. Various drugs can serve as alternatives.

Synonym: Lignocaine.

Therapeutic category: Local Anaesthetic; Antiarr-hythmic Agent.

Indications: Surface anaesthesia of mucous membranes; infiltration anaesthesia; peripheral and sympathetic nerve block; dental anaesthesia; spinal anaesthesia; intravenous regional anaesthesia; arrhythmias (section 5.4).

Contra-indications: Adjacent skin infection, inflamed skin; concomitant anticoagulant therapy; severe anaemia or heart disease; spinal or epidural anaesthesia in dehydrated or hypovolaemic patient.

Precautions: Respiratory impairment; hepatic impairment (Appendix 5); epilepsy; porphyria; myasthenia gravis; avoid (or use with great care) solutions containing epinephrine (adreanaline) for ring block of digits or appendages (risk of ischaemic necrosis); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: With excessive dosage or following intravascular injection, light-headedness, dizziness, blurred vision, restlessness, tremors and, occasionally, convulsions rapidly followed by drowsiness, unconsciousness and respiratory failure; cardiovascular toxicity includes hypotension, heart block and cardiac arrest; hypersensitivity and allergic reactions also occur; epidural anaesthesia occasionally complicated by urinary retention, faecal incontinence, headache,

backache or loss of perineal sensation; transient paraesthesia and paraplegia very rare.

Advice to patients: Advise patient of possible temporary loss of sensation and motor activity following epidural or spinal anaesthesia. See also under Bupivacaine.

Nursing considerations: See under Bupivacaine.

Dose: Plain Solutions

Local infiltration and peripheral nerve block, using 0.5% solution, ADULT up to 250 mg (up to 50 ml).

Local infiltration and peripheral nerve block, using 1% solution, ADULT up to 250 mg (up to 25 ml).

Surface anaesthesia of pharynx, larynx, trachea, using 4% solution, ADULT 40–200 mg (1–5 ml).

Surface anaesthesia of urethra, using 4% solution, ADULT 400 mg (10 ml).

Spinal anaesthesia, using 5% solution (with glucose 7.5%), ADULT 50–75 mg (1–1.5 ml).

Solutions containing epinephrine

Local infiltration and peripheral nerve block, using 0.5% solution with epinephrine, ADULT up to 400 mg (up to 80 ml).

Local infiltration and peripheral nerve block, using 1% solution with epinephrine, ADULT up to 400 mg (up to 40 ml).

Dental anaesthesia, using 2% solution with epinephrine, ADULT 20–100 mg (1–5 ml).

NOTE: MAXIMUM SAFE DOSES OF LIDOCAINE FOR ADULT AND CHILD ARE: 0.5% OR 1% LIDOCAINE, 4 MG/KG; 0.5% OR 1% LIDOCAINE + EPINEPHRINE 5 MICROGRAMS/ML (1 IN 200 000), 7 MG/KG.

USE LOWER DOSES FOR DEBILITATED, ELDERLY, EPILEPTIC, OR ACUTELY ILL PATIENTS.

DO NOT USE SOLUTIONS CONTAINING PRESERVATIVES FOR SPINAL, EPIDURAL, CAUDAL OR INTRAVENOUS REGIONAL ANAESTHESIA.

POM **Lidocaine** *(WMF 1.2)*

Injection (Solution for injection), Lidocaine HCl 5 mg/ml (0.5%), in 20-ml ampoule; 10 mg/ml (1%), in 20-ml ampoule; 50 mg/ml (5%), in 2-ml ampoule to be mixed with glucose 75 mg/ml (7.5%).

Injection (Solution for injection) with epinephrine, Lidocaine HCl 10 mg/ml (1%) with epinephrine 5 micrograms/ml (1 in 200 000), in 20-ml ampoule.

Injection (Solution for injection) with epinephrine (dental use), Lidocaine HCl 20 mg/ml (2%) with epinephrine 12.5 micrograms/ml (1 in 80 000), in 2.2-ml dental cartridge.

Topical gel or solution, Lidocaine HCl 20–40 mg/ml (2–4%).

POM **Lidocaine** *(EDL 1.4)*

Injection, Lignocaine HCl 1%, 2%, 5%; in vial.

Injection, Lignocaine HCl 1, 2% plus Adrenaline 1 in 200,000; in vials.

Cream or Ointment, Lidocaine HCl 2-5%.

Gel or Solution, Lidocaine HCl 2-4%.

Aerosol, Lidocaine HCl 10%.

Dental Cartridges, Lidocaine HCl 2% plus Adrenaline 1 in 80,000.

POM **Lidocaine** *(Dizpharm)*

Injection, Lidocaine HCl 2%.

2 ml x 50.

Vasoconstrictors

The sympathetic block from spinal or epidural anaesthesia may cause hypotension. Such hypotension is managed by giving intravenous fluids (usually prophylactically) and oxygen, and elevating legs and giving a pressor drug such as ephedrine. In addition to vasoconstriction, ephedrine also accelerates the heart rate and can therefore counter bradycardia (but atropine sulfate is used to reverse persistent bradycardia).

EPHEDRINE

Ephedrine HCl is a complementary drug.

Indications: Prevention of hypotension during delivery under spinal or epidural anaesthesia.

Precautions: Hyperthyroidism; diabetes mellitus; ischaemic heart disease, hypertension; angle-closure glaucoma; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Anorexia, hypersalivation, nausea, vomiting; tachycardia (also in fetus), arrhythmias, anginal pain, vasoconstriction with hypertension, vasodilation with hypotension; dyspnoea; headache, dizziness, anxiety, restlessness, confusion, tremor; difficulty in micturition; sweating, flushing; changes in blood-glucose concentration.

Dose: *To prevent hypotension during delivery under spinal anaesthesia*, by slow intravenous injection of solution containing 3 mg/ml, ADULT (female) 3–6 mg (maximum single dose 9 mg),

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repeated if necessary every 3–4 minutes; maximum cumulative dose 30 mg.

POM **Ephedrine** *(WMF 1.2)*
Injection (Solution for injection), Ephedrine HCl 30 mg/ml, in 1-ml ampoule.

EPINEPHRINE

Synonym.: Adrenaline.
Indications: Vasoconstrictor to retard systemic absorption of infiltrated local anaesthetics.
Contra-indications: Ring block of digits, penis or other situations where there is risk of local ischaemia.
Precautions: Hypertension, atherosclerotic heart disease, cerebral vascular insufficiency, heart block; thyrotoxicosis or diabetes mellitus; **interactions**: Appendix 1.
Dose: Final concentration 5 micrograms/ml (1 in 200 000); *in dental surgery*, in which small volumes are injected, concentrations of up to 12.5 micrograms/ml (1 in 80 000) commonly used; total dose should not exceed 500 micrograms.

3.5 Analgesics and opioid antagonists

Opioid analgesics, such as **morphine**, may be used to supplement general anaesthesia, usually in combination with nitrous oxide–oxygen and a muscle relaxant. Repeated doses of intra-operative analgesics should be given with care, since respiratory depression may persist into the postoperative period.

The specific opioid antagonist **naloxone** will immediately reverse this respiratory depression but the dose may need to be repeated. Other resuscitative measures must also be available. It is important to remember that naloxone will also antagonize the analgesic effect of opioids.

Paracetamol and **nonsteroidal anti-inflammatory drugs** may be useful alternatives (or adjuncts) for the relief of postoperative pain; they do not affect respiration and gastrointestinal motility.

For further information on opioid analgesics, see section 1.8.2; for paracetamol (see section 1.8.1) and nonsteroidal anti-inflammatory drugs (see section 2.1.1).

Opioid analgesics

MORPHINE

Drug subject to international control under the Single Convention on Narcotic Drugs (1961).
Indications: Adjunct during major surgery; postoperative analgesia; pain, myocardial infarction, acute pulmonary oedema (section 1.8.2).
Contra-indications: Acute respiratory depression; increased intracranial pressure, head injury or brain tumour; severe hepatic impairment (Appendix 5); adrenocortical insufficiency; hypothyroidism; convulsive disorders; acute alcoholism, delirium tremens; diverticulitis and other spastic conditions of colon; recent surgery on biliary tract; diarrhoea due to toxins.
Precautions: Asthma, emphysema, or heart failure secondary to chronic lung disease; ability to maintain airway; if used in biliary colic, antispasmodic needed; renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); **overdosage**: section 19.2.3; **interactions**: Appendix 1.
Adverse effects: Respiratory depression; anorexia, nausea, vomiting, constipation; euphoria, dizziness, drowsiness, confusion, headache; dry mouth; spasm of urinary and biliary tract; circulatory depression, hypotension, bradycardia, palpitations; miosis; allergic reactions; physical dependence.
Dose: *Premedication*, by subcutaneous or intramuscular injection 1 hour before surgery, ADULT 150–200 micrograms/kg; by intramuscular injection 1 hour before surgery, CHILD 50–100 micrograms/kg. *Intra-operative analgesia*, by intravenous injection, ADULT and CHILD 100 micrograms/kg, repeated every 40–60 minutes as required. *Postoperative analgesia*, by intramuscular injection, ADULT 150–300 micrograms/kg every 4 hours, CHILD 100–200 micrograms/kg; or by intravenous infusion ADULT 8–10 mg over 30 minutes, then 2–2.5 mg/hour.

POM **Morphine** *(WMF 1.5)*
Injection (Solution for injection), Morphine (as HCl or sulfate) 10 mg/ml, in 1-ml ampoule.

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POM **Morphine** *(EDL 1.2)*
Injection, Morphine (as sulphate or HCl) 10 mg per ml; in 1 ml amp.

FENTANYL

Therapeutic category: Narcotic Analgesic.
Indications: Sedation, relief of pain, preoperative medication, adjunct to general or regional anaesthesia.
Contra-indications: Hypersensitivity to fentanyl or any component; increased intracranial pressure; severe respiratory depression; severe liver or renal insufficiency.
Precautions: Bradycardia; rapid I.V. infusion may result in skeletal muscle and chest wall rigidity, impaired ventilation, respiratory distress, apnoea, bronchoconstriction, laryngospasm; inject slowly over 3 - 5 minutes; non-depolarizing skeletal muscle relaxant may be required.
Adverse effects: Hypotension, bradycardia, respiratory depression, CNS depression, drowsiness, nausea, vomiting, constipation, cardiac arrhythmias.
Nursing considerations: •Monitor respirations of newborns exposed to drug during labour.
•Monitor cardiovascular and respiratory status, B.P., pulse rate.
•For better analgesic effect, give before patient has intense pain.
•Monitor bladder function in postoperative patient.
•Respiratory depression, hypotension, profound sedation, and coma may result if used with other narcotic analgesics, general anaesthetics, tranquilizers, alcohol, sedatives, hypnotics, TCAs, or MAOIs. The doses of the above drugs should be reduced if they have to be used together.
Dose: *Sedation for minor procedures/ analgesia*, by I.M., I.V., Adult and Child (over 12 years), 0.5 - 1 mcg/kg/dose; may be increased in major procedures. Child (1-12 years), 1-2 mcg/kg/dose; may repeat at 30-60 minute intervals.
Preoperative sedation, adjunct to regional anaesthesia, postoperative pain, by I.M., I.V., Adult, 50-100 mcg/ dose.
Adjunct to general anaesthesia, by I.M., I.V., Adult, 2-50 mcg/kg.

POM **Fentanyl** *(EDL 1.2)*
Injection, Fentanyl (as citrate) 0.05 mg per ml; in 10 ml amp.

Opioid antagonists

NALOXONE

Indications: To counteract respiratory depression induced by opioids during anaesthesia; opioid overdosage (see also section 19.2.3).
Precautions: Dependence on opioids; cardiovascular disease.
Adverse effects: Nausea and vomiting; hypertension and hypotension reported; left ventricular failure; pulmonary oedema; seizures; arrhythmias such as ventricular tachycardia or fibrillation, particularly in pre-existing cardiac disease.
Dose: *Opioid-induced respiratory depression*, by intravenous injection, ADULT 100–200 micrograms, repeated every 2–3 minutes to obtain required response; CHILD initially 10 micrograms/kg, if no response followed by 100 micrograms/kg.
Opioid-induced respiratory depression at birth, by subcutaneous, intramuscular, or intravenous injection, NEONATE 10 micrograms/ kg immediately after delivery.

POM **Naloxone** *(WMF 1.5)*
Injection (Solution for injection), Naxolone HCl 400 micrograms/ml, in 1-ml ampoule.

3.6 Blood substitutes and solutions for correcting fluid imbalance

Fluid requirements must be assessed before, during and after major surgery. Replacement fluids should correspond as nearly as possible in volume and composition to those lost. Blood transfusion is essential to restore oxygen-carrying capacity when more than 15% of the circulating blood volume is lost but should be avoided whenever screening for human immunodeficiency viruses and hepatitis B virus is impracticable. Isotonic sodium chloride solution may be used for short-term volume replacement. Plasma expanders such as dextran 70 or polygeline may be useful. Provided renal function is maintained, fluid is most simply replaced by intravenous administration of **sodium chloride solution** (sodium chloride 9 mg/ml, 0.9%) or the more physiologically appropriate **compound solution of sodium lactate**. In emergency cases, there is usually an existing fluid deficit, which must be assessed and corrected before surgery. Isotonic **glucose/ sodium chloride** mixtures (most commonly glucose 4%/ sodium chloride

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0.18%) are preferred in children to avoid the danger of sodium overload and hypoglycaemia. When fluids are administered intravenously for more than 24 hours, potassium chloride is required to prevent potassium depletion. In order to avoid serious arrhythmias, especially in patients with impaired renal function, the required dose of potassium should be determined, whenever possible, by monitoring plasma concentrations of potassium.

See also sections 6.5 (plasma substitutes) and 6.10 (solutions for correcting water, electrolyte, and acid-base disturbances).

4. Drugs used in gastrointestinal diseases

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4.1 Antacids and other antiulcer drugs
4.1.1 Antacids
4.1.2 Ulcer Healing Drugs
4.2 Antispasmodic drugs
4.3 Other smooth muscle relaxants
4.4 Drugs used in diarrhea
4.4.1 Oral rehydration
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4.6 Antiemetic drugs
4.7 Antihaemorrhoidal drugs
4.8 Anti-inflammatory drugs

4.1 Antacids and other antiulcer drugs

4.1.1 Antacids
4.1.2 Ulcer healing drugs

Gastric and duodenal ulcer, or peptic ulcer disease (PUD), Zollinger–Ellison Syndrome (ZE), and gastro–oesophageal reflux disease (GRD) or heartburn are upper gastrointestinal disorders sharing a common abnormality: too much acid and pepsin activity for the degree of local tissue resistance. Hydrolytic and proteolytic digestion of the exposed mucosa occur followed by inflammation, necrosis, and ulceration.

Antacids (usually containing aluminium or magnesium compounds) can often relieve symptoms in ulcer dyspepsia and in non-erosive gastro-oesophageal reflux; they are also sometimes used in non-ulcer dyspepsia but the evidence of benefit is uncertain. Antacids are best given when symptoms occur or are expected, usually between meals and at bedtime, 4 or more times daily; additional doses may be required up to once an hour. Conventional doses for example 10 ml 3 or 4 times daily of liquid magnesium–aluminium antacids promote ulcer healing, but less well than antisecretory drugs (such as an H_2-receptor antagonist); proof of a relationship between healing and neutralizing capacity is lacking. Liquid preparations are more effective than solids.

Aluminium- and **magnesium-containing** antacids (for example aluminium hydroxide, and magnesium hydroxide), being relatively insoluble in water, are long-acting if retained in the stomach. They are suitable antacids for most purposes. Magnesium-containing antacids have a laxative effect whereas aluminium-containing antacids may be constipating.

H_2-receptor antagonists heal gastric and duodenal ulcers by reducing the secretion of gastric acid as a result of histamine H_2-receptor blockade; they can also relieve gastro-oesophageal reflux disease. High

doses of H_2-receptor antagonists have been used in the Zollinger–Ellison syndrome, but a proton-pump inhibitor is now preferred.

Maintenance treatment with low doses has largely been replaced in *Helicobacter pylori* positive patients by eradication regimens (see below). Maintenance treatment may occasionally be used for those with frequent severe recurrences and for the elderly who suffer ulcer complications.

Treatment of undiagnosed dyspepsia with H_2-receptor antagonists may be acceptable in younger patients but care is required in older people because their symptoms may be caused by gastric cancer.

H_2-receptor antagonist therapy can promote healing of NSAID-associated ulcers (particularly duodenal). Treatment also reduces the risk of acid aspiration in obstetric patients at delivery (Mendelson syndrome).

PEPTIC ULCER

Ulcer disease is caused by peptic ulceration that involves the stomach, duodenum, and lower oesophagus. General and inexpensive measures like introducing healthy life-style, stopping smoking and taking antacids should be promoted. The possibilitiy of malignant disease should be considered in all patients over the age of 40 years who are suspected of having an ulcer.

Gastric and duodenal ulcers are healed by 4–8 weeks treatment with H_2-receptor antagonists but there is a high rate of relapse (greater than 70% over 2 years) requiring maintenance therapy. Relapses can be prevented very sucessfully by eradicating *Helicobacter pylori* which is causally associated with most peptic ulcers (except those related to NSAID use). Eradication of *H. pylori* reduces the relapse rate to about 4–8%. This is undoubtedly cost-effective compared to the alternatives of long-term maintenance therapy with low-dose H_2-receptor antagonists or repeated treatment of recurrent ulcers. It is recommended that the presence of *H. pylori* is confirmed before starting eradication treatment, particularly for gastric ulcers. The urea breath test is used widely to test for H. pylori , but it may produce false negative results if used soon after proton pump inhibitors or antibacterials. Eradication regimens are based on a combination of an acid-reducing ('antisecretory') drug and antibiotics.

The following model eradication regimen is suggested on the basis of its efficacy and simplicity (only doses suitable for adults are shown):

omeprazole 40 mg daily for 1 week
plus
metronidazole 400 mg three times daily for 1 week
plus
amoxicillin 500 mg three times daily for 1 week

The decision on choosing an eradication regimen for a particular country should take into account local resistance to antibacterials, cost and availability of the necessary drugs.

NSAID-ASSOCIATED ULCERS

Gastrointestinal bleeding and ulceration may occur with NSAID use. To avoid this, emphasis should be on stopping NSAID use but this is not always possible. A proton pump inhibitor may be considered for protection against NSAID-associated gastric and duodenal ulcers. An H_2-receptor antagonist may be effective for protection against NSAID-associated duodenal ulcers only.

Patients who must continue NSAID therapy after ulcer development may take high-dose H_2-receptor antagonists concomitantly, but ulcers tend to heal more slowly with H_2-receptor antagonists if NSAIDs are continued. A proton-pump inhibitor such as omeprazole is more effective but it is also more expensive.

In patients who can discontinue NSAID therapy after ulcer development, treatment with an H_2-receptor antagonist is effective, but a treatment period of up to 8 weeks may be necessary. A proton pump inhibitor usually produces the most rapid healing. After healing, continued prophylaxis is required.

DYSPEPSIA

Dyspepsia covers pain, fullness, early satiety, bloating, or nausea. It can occur with gastric and duodenal ulceration and gastric cancer but most commonly it is of uncertain origin.

Patients with non-ulcer dyspepsia should be advised to avoid smoking, alcohol and aggravating foods, and to eat small regular meals to aid digestion. Non-ulcer dyspepsia tends to be self-limiting but antacids and H_2-receptor antagonists are often used to suppress gastric acid.

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Effective treatment is important in the presence of severe oesophageal ulceration to prevent longer term complications such as oesophageal stricture and carcinoma.

GASTRO-OESOPHAGEAL REFLUX DISEASE

Gastro-oesophageal reflux disease (including non-erosive gastro-oesophageal reflux and erosive oesophagitis) is characterized by symptoms which include heartburn, acid regurgitation, and sometimes difficulty in swallowing (dysphagia); oesophageal inflammation (oesophagitis), ulceration, and stricture formation may occur and there is an association with asthma.

The management of gastro-oesophageal reflux disease includes drug treatment, lifestyle changes and, in some cases, surgery. Initial treatment is guided by the severity of symptoms and treatment is then adjusted according to response.

For mild symptoms of gastro-oesophageal reflux disease, initial management may include the use of antacids. H_2-receptor antagonists suppress acid secretion and they may relieve symptoms and permit reduction in antacid consumption. Severe symptoms initially require a short-course of a proton-pump inhibitor.

ZOLLINGER–ELLISON SYNDROME

Management of Zollinger–Ellison syndrome requires high dose H_2-receptor antagonist treatment. The proton pump inhibitors are more effective particularly for cases resistant to other treatment but they are more expensive.

4.1.1 Antacids

ALUMINIUM HYDROXIDE

Indications: Ulcer and non-ulcer dyspepsia; gastro-oesophageal reflux; hyperphosphataemia.

Contra-indications: Hypophosphataemia; undiagnosed gastrointestinal or rectal bleeding; appendicitis; porphyria.

Precautions: Impaired renal function and renal dialysis (Appendix 4); hepatic impairment (Appendix 5); constipation; dehydration; fluid restriction; gastrointestinal disorders associated with decreased bowel motility or obstruction; **interactions**: Appendix 1.

Adverse effects: Constipation; intestinal obstruction (large doses); hypophosphataemia with increased bone resorption, hypercalciuria and risk of osteomalacia (patients on low phosphate diet or prolonged therapy); hyperaluminaemia—resulting in osteomalacia, encephalopathy, dementia, microcytic anaemia (in chronic renal failure treated with aluminium hydroxide as phosphate-binding agent).

Advice to patients: Do not take other medicines within 2–4 hours of aluminium hydroxide preparations. May be taken with water to reduce constipating adverse effects.

See also Label 24 in Appendix 6.

Nursing considerations: •Administer after shaking liquid. Dose should be followed by water. Tablets should be thoroughly chewed before swallowing with water.

•May increase fluid, bulk in diet to prevent constipation.

•Advise patient not to take oral drugs within 1-2 hours of taking an antacid; may impair absorption of other drugs.

•Patient should notify the physician if relief is not obtained or if there are any signs to suggest bleeding from the GIT.

•Laxative or stool softener may be given if constipation becomes troublesome; may alternate with magnesuim-containing antacids (if patient does not have renal disease).

•May rupture enteric-coated tablet causing premature release of drugs into the stomach; separate doses by 1 hour.

Dose: *Dyspepsia, gastro-oesophageal reflux*, by mouth, ADULT 1–2 tablets chewed 4 times daily and at bedtime or 5–10 ml suspension 4 times daily between meals and at bedtime; CHILD 6–12 years 5 ml up to three times daily.

Hyperphosphataemia, by mouth , ADULT 2–10 g daily in divided doses with meals.

OTC **Aluminium Hydroxide** *(WMF 17.1)*
Tablets, Aluminium hydroxide 500 mg.
Oral suspension, Aluminium hydroxide 320 mg/5 ml.

OTC **Aluminium Hydroxide** *(EDL 18.1)*
Tablet, (chewable), Aluminium hydroxide 500 mg
Mixture, Aluminium hydroxide mixture B.P. Pack - 200 ml; 500 ml.

OTC **ALUDROX®** *(Wyeth/Delpitano)*
Suspension, Aluminium hydroxide mixture B.P. Pack - 200 ml; 500 ml.

OTC **NEUTRACID®** *(Afrab-Chem)*
Tablet, Aluminium hydroxide 500 mg; white scored tab. marked afrab.

ALUMINIUM HYDROXIDE plus MAGNESIUM HYDROXIDE (with or without SIMETICONE)

Synonym: Magaldrate plus Activated Dimeticone.
Therapeutic category: Antacid, antigas agent.
Pharmacology: Magaldrate is a combination of Aluminium and Magnesium hydroxides and sulphates. Simethicone, an antigas, is activated dimethylpolysiloxane. Magaldrate is an antacid bringing about its action by the neutralization of hydrochloric acid in the gastic secretions. Magaldrate may be absorbed systematically with magnesium posing a risk to patients with renal failure. It is excreted in faeces, some Alminium and Magnesium may also be excreted in breast milk. Simethicone is an antifoam/antigas agent. It acts by lowering surface tension and when administered by mouth, causes bubbles of gas in the GIT to coalesce thus aiding their dispersion. It is excreted in the faeces.
Indications: Symptomatic relief of: GI disorders associated with hyperacidity such as peptic ulcer, dyspepsia, gastro-esophageal reflux disease, gastritis; Pyrosis and heartburn in pregnancy; Flatulence and abdominal discomfort due to excess GI gas.
Contra-indications: Known hypersensitivity to any of its constituents; Colostomy or ileostomy; Renal failure or impairment; Appendicitis or undiagnosed rectal and gastrointestinal bleeding; Ulcerative colitis, chronic diarrhea; Gastric outlet obstruction
Precautions: Patients with decreased gastrointestinal motility; kidney disease.
Interactions: May inhibit the absorption of phenothiazine (especially chlorpromazine); May decrease the absorption of quinolones, tetracycline, chenodiol, antimuscarinics, coumarin, diazepam, chlordiazepoxide, vitamin A, isoniazid, digoxin and phosphates thereby lessening their effectiveness; May increase levodopa absorption, increasing the risk of toxicity; May cause premature release of enteric-coated drugs.
Adverse effects: Mild diarrhea, constipation, fatigue and very rarely weight loss.
Nursing considerations: See under Aluminum Hydroxide.
Dose: *Peptic ulcer*, 2 to 4 tabs to be repeated if necessary. *Gastric hyperacidity*, 1 to 2 tabs between meals or as required. *Heartburn of Pregnancy*, 1 to 2 tabs before breakfast and between meals or as required.
To be chewed and swallowed with water or milk.
See also under the proprietary preparations below.

OTC **Aluminium and Magnesium Hydroxides** *(EDL 18.1)*
Tablet, Aluminium hydroxide 250-600 mg, magnesium hydroxide 200-400 mg with or without simeticone 25-250 mg.
Mixture, Aluminium hydroxide mixture 4.75 ml, magnesium hydroxide 100 mg with or without simeticone 125 mg per 5 ml.

OTC **ACTAL®** *(GSK)*
Tablet, Aluminium hydroxide 200 mg, magnesium hydroxide 150 mg; white tab. marked 'ACTAL'.
Pack - 20; 400.

OTC **ALMAC®** *(Hovid)*
Tablet, (Chewable), Magnesium trisilicate 250 mg, dried aluminium hydroxide 125 mg, simeticone 30 mg; white scored tab. with peppermint flavour.
Pack -10 x 10 (blister).
Suspension, Magnesium hydroxide 200 mg, aluminium hydroxide 200 mg, simeticone 30 mg per 5 ml; white opaque suspension with peppermint flavour.
Pack -100 ml.
Dose: Adult, 1-2 tabs to be chewed after or between meals and at bedtime OR 10-20 ml suspension 4 times daily to be taken 20 mins to 1 hour after meals and at bedtime.

OTC **GASCOL®** *(Fidson)*
Suspension, Magaldrate 540 mg, Simethicone 100 mg per 5 ml.
Pack – 150 ml (in a blue coated plastic bottle).
Advice to patients: Take with a small amount of water or fruit juice; take 1-2 hours apart from other oral medications.
Dose: 5-10 ml between meals and at bedtime; not exceeding 90 ml in a 24-hour period.

OTC **LOCID®** *(Interpharma)*
Suspension, Dried aluminium hydroxide USP 325 mg eqiuvalent to Alumimium HCl 248.62 mg, magnesium hydroxide USP 100 mg, activated polymethylsiloxane USP 125 mg.
Pack - 200 ml.

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OTC **MAALOX PLUS**® *(May & Baker)*
Tablet, Dried Aluminium hydroxide gel 200 mg, magnesium hydroxide 200 mg, simeticone 25 mg; mint flavoured tab.
Dose: Chew 1–4 tabs 20 minutes to 1 hour after meals and at bedtime; not exceeding 4 times a day.

OTC **MAALOX TC**® *(May & Baker)*
Tablet, Aluminium hydroxide gel 600mg, magnesium hydroxide 300mgl; mint flavoured tab.
Dose: *Prevention of duodenal ulcer recurrence*, chew 3 tabs in the morning after food and 3 tabs at bedtime.
Management of Symptoms of Severe hyperacidity, chew 1—2 tabs 20 minutes to 1 hour after meals and at bedtime; not exceeding 4 times a day.

OTC **POLYCROL FORTE**® *(Swipha)*
Tablet, Aluminium hydroxide gel (dried) 400 mg, Magnesium hydroxide 200 mg, Activated methylpolysiloxane 25 mg.
Pack - 10.
Dose: Adult, One tablet; Child (6-12 years), ½ a tablet. To be chewed after meals and at bedtime.
Gel, Aluminium hydroxide gel 4.75 ml, Magnesium hydroxide 100 mg, Activated methylpolysiloxane 125 mg per 5 ml.
Pack - 100 ml.
Dose: 5-10 ml between meals or at bedtime

OTC **RULOX**® *(SKG)*
Suspension, Dried aluminium hydroxide gel 468.1 mg, magnesium hydroxide 100 mg, activated methylpolysiloxane 125 mg per 5 ml.
Pack - 100 ml; 200 ml.
Dose: 5-10 ml to be taken between meals and at bedtime.

MAGNESIUM HYDROXIDE

Therapeutic category: Antacid; Laxative.
Indications: Ulcer and non-ulcer dyspepsia; gastro-oesophageal reflux.
Contra-indications: Severe renal impairment.
Precautions: Renal impairment (Appendix 4); hepatic impairment (Appendix 5); **interactions**: Appendix 1
Adverse effects: Diarrhoea; in renal impairment—hypermagnesaemia resulting in loss of deep tendon reflexes and respiratory depression, with other symptoms including nausea, vomiting, flushing of skin, thirst, hypotension, drowsiness, confusion, muscle weakness, bradycardia, coma and cardiac arrest.
Dose: *Dyspepsia, gastro-oesophageal reflux*, by mouth, ADULT 5–10 ml repeated according to patient's needs.

OTC **Magnesium Hydroxide** *(WMF 17.1)*
Oral suspension, Magnesium hydroxide equivalent to magnesium oxide 550 mg/ 10 ml.

OTC **Magnesium Hydroxide** (*EDL 18.1)*
Tablet, Magnesium hydroxide 500 mg.
Mixture, Magnesium hydroxide 250 mg per 5 ml.

MAGNESIUM TRISILICATE plus ALUMINIUM HYDROXIDE

Indications: Gastric hyperacidity, indigestion, heartburn.
Advice to patients: See Label 24 in Appendix 6.
Nursing considerations: See under Aluminium Hydroxide.
Dose: Adult, 1-2 tabs to be chewed or sucked after meals or as required.
Child (6-12 years), half the adult dose.

OTC **Magnesium Trisilicate plus Aluminium Hydroxide** *(EDL 18.1)*
Tablet (chewable), Magnesium trisilicate 300 mg, aluminium hydroxide 250 mg.

OTC **Magnesium Trisilicate** *(EDL 18.1)*
Tablet (chewable), Magnesium trisilicate 500 mg
Mixture, Magnesium trisilicate 250 mg per ml.

OTC **ANTASIL**® *(Pharma–Deko)*
Tablet, Dried aluminium hydroxide gel 250 mg, magnesium trisilicate 500 mg.
Suspension, Dried aluminium hydroxide gel 310 mg, magnesium trisilicate 620 mg.

OTC **BELL'S ANTACID MIXTURE**® *(De-Sears)*
Mixture, Magnesium trisilicate 2.5%, magnesium carbonate light 2.5%, sodium bicarbonate 2.5%.
Pack - 200 ml.
Dose: By mouth, Adult, 30 ml 3-4 times a day or as required.

OTC **DANACID**® *(Dana)*
Tablet (Chewable), Magnesium trisilicate BP 250 mg, dried aluminium hydroxide BP 120 mg.
Pack - 8 x 12's; 1000's.

OTC **DIGICID**® *(Strides Vital)*
Tablet, Magnesium trisilicate, Aluminium hydroxide.
Pack – 96's.

OTC **EMTRISIL**® *(Emzor)*
Suspension, Magnesium trisilicate 250 mg, light magnesium carbonate 250 mg, sodium bicarbonate 250 mg per 5 ml
Pack - 180 ml; 2 L.

OTC **GELACID**® *(Adler)*
Tablet, Magnesium trisilicate 300 mg, aluminium hydroxide 250 mg.
Pack - 24.

OTC **GELUSIL**® *(Pharma-Deko)*
Tablet, Magnesium trisilicate 500 mg, dried aluminium hydroxide 250 mg.

OTC **GESTID**® *(Ranbaxy)*
Tablet, Dried aluminium hydroxide BP 300 mg, magnesium trisilicate BP 50 mg, magnesium hydroxide USP 25 mg, activated polymethylsiloxane 10 mg.
Pack - 5 x 4's.
Dose: 1-2 tabs 4 times daily; to be chewed and swallowed after meals or as required.
Suspension, Dried aluminium hydroxide gel USP 4.75 ml, magnesium hydroxide USP 100 mg, activated polymethylsiloxane 125 mg, carboxymethylcellulose sodium 50 mg per 5 ml.
Pack - 100 ml; 200 ml.
Dose: Adult, 5-10 ml 3-4 times daily after meals.
Child (5-12 years), 5 ml after every meal.

OTC **JAWASIL**® *(Jawa)*
Suspension, Magnesium trisilicate 300 mg, dried aluminium hydroxide gel 600 mg, magnesium hydroxide 200 mg, dimethylpolysiloxane 50 mg per 10 ml.
Pack - 100 ml; 200 ml.
Dose: Adult, 10-20 ml 3-4 times daily
Child, 5-15 ml 3-4 times daily.

OTC **JULISIL**® *(Juhel)*
Suspension, Magnesium trisilicate BP 250 mg, Light magnesium carbonate BP 250 mg, Sodium bicarbonate BP 250 mg per 5 ml.
Pack – 200 ml.

OTC **Magnesium Trisilicate Comp.** *(Emzor)*
Tablet (Chewable), Magnesium trisilicate 300 mg, aluminium hydroxide 250 mg.
Pack - 500; 1000.
Mixture, Magnesium trisilicate 250 mg per ml.
Pack - 180 ml.

OTC **Magnesium Trisilicate** *(Leady)*
Suspension, Magnesium trisilicate 250mg, light magnesium carbonate 250 mg, Sodium bicarbonate 250 mg per 5 ml.
Pack - 200 ml.

OTC **Magnesium Trisilicate** *(Novel)*
Tablet, Magnesium trisilicate 500 mg; white tab. marked 'G' on one side and 'NOVEL' on the reverse.
500 mg - 1000.

OTC **Magnesium Trisilicate** *(Pharchem)*
Suspension, Magnesium trisilicate 500 mg, light magnesium carbonate 500 mg, sodium bicarbonate 500 mg, conc. peppermint emulsion 0.25 ml, d/s chloroform water 5 ml per 10 ml.

OTC **MAG-O-SIL**® *(Sam)*
Tablet, (chewable), Magnesium trisillicate 250 mg, dried aluminium hydroxide gel 120 mg
Pack - 1000.

OTC **MAGSIL**® *(Leady)*
Tablet (chewable), Dried aluminium hydroxide 250 mg, magnesium trisilicate 100 mg.
Suspension, Magnesium trisilicate 250 mg, light magnesium carbonate 250 mg, sodium bicarbonate 250 mg per 5 ml.
Pack - 200 ml.

OTC **MOKO MIST. MAG. TRISILICATE**® *(New Healthway)*
Suspension, Magnesium trisilicate 250 mg, light magnesium carbonate 250 mg, sodium bicarbonate 250 mg per 5 ml.
Pack - 200 ml.
Dose: Adult, 10-20 ml 3-4 times daily.

OTC **SUPERMAG**® *(Mopson)*
Suspension, Mist. Magnesium Trisilicate BPC.
Pack - 180 ml, 2 L.

OXETHAZAINE plus ALUMINA GEL plus MAGNESIUM HYDROXIDE

Therapeutic category: Antacid/demulcent/mucosal anaesthetic.
Pharmacology: Alumina gel and magnesium hydroxide react chemically to neutralize or buffer existing quantities of stomach acid but have no direct effect on its production. This action increases gastric pH, providing symptomatic relief of hyperacidity. Alumina gel, especially when swallowed undiluted,

forms a diffuse coating over the inflammed gastric mucosa for a variable period of time. Because of this adherent vehicle, oxethazaine exerts a prolonged topical anaesthetic action. Oxethazaine is a topical anaesthetic which when applied to the mucous membranes produces a more potent anaesthesia of longer duration than either cocaine hydrochloride or lidocaine hydrochloride.

Indications: As an adjunct in the treatment of oesophagitis and peptic ulcer.

Contra-indications: Appendicitis due to the danger of perforation or rupture that may result from the constipating or laxative effects of aluminium and magnesium antacids; hypophosphataemia due to the phosphate binding properties of aluminium salts (except aluminium phosphate); severe renal dysfunction due to increased danger of occurrence of hypermagnesaemia.

Precautions: Renal disease, pregnancy, breast-feeding; not recommended for use in children.

Adverse effects: Hypersensitivity reactions including skin eruptions, pruritus; dizziness, faintness, or drowsiness especially when daily doses exceed 60ml; diarrhoea (due to the magnesium); constipation (due to the aluminium).

Dose: For adult only, 5-10 ml 4 times a day; to be taken 15 minutes before meals and at bedtime. Do not exceed the recommended dosage.

POM **MUCAINE®** *(Wyeth/Delpitano)*
Suspension, Oxethazaine in alumina gel 10 mg, milk of magnesia 1.25 ml.
Pack - 200 ml.

SODIUM BICARBONATE

Therapeutic category: Antacid and carminative.

Indications: Symptomatic relief of wind, griping pain, colic, dyspepsia.

Nursing considerations: •Patient should chew tablet before swallowing and drink a full glass of water.
•Taking antacid with milk may cause milk-alkali syndrome; teach patient the symptoms namely confusion, headache, nausea, vomiting, anorexia, urinary stones, hypercalcemia and to avoid such combination.
Advise patient to report to the doctor if symptoms persist after 2 weeks of starting therapy; if indigestion is accompanied by chest pain, dyspnea, diarrhea, dark, tarry stools.
Patients on sodium-restricted diet should avoid sodium bicarbonate containing antacids unless prescribed.

Dose: New born infant, 2.5 ml; 1-6 months, 5 ml; 6 months - 2 years, 10 ml; 2 years and above, 10-15 ml.
The above doses may be repeated as required up to 6 times daily.

OTC **DILLEX GRIPE MIXTURE®** *(BCN)*
Mixture, Dill oil 0.001%, anise oil 0.006%, sodium bicarbonate 1%, sodium citrate 0.05%, caraway oil 0.012%, spearmint oil 0.003%, rectified spirit 2.40%.
Pack - 110ml.

OTC **DR. MEYER'S GRIPE WATER®** *(Farmex-Meyer)*
Mixture, Dill oil 0.005 ml, fennel oil 0.0007 ml, sodium bicarbonate 50 mg per 5 ml.
Pack - 200 ml.

OTC **Moko Bicarbonate of Soda** *(New Healthway)*
Powder, Sodium bicarbonate 100 g per packet.

OTC **SODAMINT®** *(Juhel)*
Tablet, Sodium bicarbonate 300 mg.
300 mg - 1000.

OTC **WOODWARD'S GRIPE WATER®** *(SKG)*
Mixture, Paediatric Sodium Bicarbonate Mixture B.P.C. 1973.
Pack - 100 ml; 150 ml.

4.1.2 Ulcer healing drugs

CIMETIDINE

Therapeutic category: Histamine H_2-receptor antagonist.

Indications: Duodenal ulcer, benign gastric ulcer, recurrent and stomal ulceration, Oesophageal reflux disease and other conditions where reduction of gastric acid is beneficial such as persistent dyspeptic symptoms particularly meal-related.

Contra-indication: Hypersensivity to cimetidine.

Precautions: Reduce dose in renal and hepatic impairment; avoid I.V. injection in high dosage and in cardiovascular impairment; pregnancy, breast feeding.

Adverse effects: Diarrhoea, dizziness, rash, tiredness. Gynaecomastia, occasional reversible liver damage, confusion. Very rarely interstitial nephritis, acute pancreatitis, thrombocytopaenia, headache, myalgia, arthralgia.

Advice to patients: Take with or immediately after meals; take 1 hour before or 2 hours after antacids; may cause drowsiness, impaired judgement, or coordination; avoid smoking

cigarette, excessive alcohol, pepper, caffeine, harsh spices/high temperatures of foods.

Nursing considerations: •Give with meals so that the drug's peak effect occurs at the proper time (peak inhibition of gastric acid secretion occurs at 1 and 3 hours after dosing in fasting subjects and approximately 2 hours in non-fasting subjects; this correlates well with the time food is no longer in the stomach offering a buffering effect). If needed, give antacids 1 hr before or 1 hr after cimetidine.

•If I.V. cimetidine is to be infused, it should not be given too rapidly to prevent bradycardia, circulatory overload (infusion over a period of 30 minutes is recommended).

•Cigarette smoking may increase gastric acid secretion and worsen disease; making the drug less effective.

•Advise patient to avoid pepper, caffeine, alcohol, spices, very hot or cold foods that seem to worsen the condition.

•Inform patient that drug may cause drowsiness, dizziness and if affected, to avoid activities that require alertness.

Dose: By mouth, 400 mg twice daily at breakfast and bed time or 200 mg 3 times daily with meals and 400mg at bedtime (1 g/day).

Acute treatment, 800 mg at bedtime. Duration of therapy is 4 weeks (6 weeks in benign gastric ulceration).

Maintenance therapy, 400 mg at bedtime.

Persistent acid-related dyspeptic symptoms, 400 mg twice daily for 4 weeks.

Oesophageal reflux disease, 400 mg 4 times daily with meals and at bedtime.

Zollinger-Ellison syndrome and other hypersecretory conditions, 1.6 g or more daily in divided doses.

See lit. for details.

Note: H_2-receptor blockers are now taken in the night (nocte) for more effective ulcer healing. Antacids are taken during daytime to neutralise acidity.

POM **Cimetidine** *(EDL 18.7)*
Tablets, Cimetidine 200 mg, 400 mg.
Injection, Cimetidine 100 mg per ml; in 2 ml amp.

POM **ALTRAMET®** *(Taylek)*
Tablets, Cimetidine 200mg, 400 mg.
200 mg - 20; 35; 50; 100; 150; 1000
400 mg - 10; 20; 50; 100; 1000.
Injection, Cimetidine HCl 200 mg per 2 ml.
Pack - 10; 50.

POM **APO-CIMETIDINE®** *(Lahams)*
Tablets, Cimetidine 200 mg, pale green, f-c tab. marked 'APO 200'; 400 mg, pale green, oval, f-c tab. marked 'APO 400'.
200 mg - 100; 1000
400 mg - 100; 500.

POM **CEMTAB®** *(Fill Pharma)*
Tablets, Cimetidine USP 200 mg, 400 mg; film-coated tabs.
200 mg - 500
400 mg - 500

POM **CEPTOR®** *(Dana)*
Tablet, Cimetidine (as HCl) 200 mg; f-c tab.
200 mg - 10 x 10's.

POM **CIMEDINE®** *(Supreme)*
Tablets, Cimetidine 200 mg, 400 mg.
200 mg - 50
400 mg - 24.

POM **CIMESAM®** *(Sam)*
Tablet, Cimetidine 200 mg
200 mg - 500

POM **CIMETAG®** *(Hovid)*
Tablets, Cimetidine 200 mg, 400 mg.
200 mg - 10 x 10 (blister)
400 mg - 10 x 10 (blister).

POM **CIMETIDINUM®** *(St. Michael)*
Tablet, Cimetidine 200 mg.
200 mg - 100 (blister).

POM **DUODIN®** *(L.B.S.)*
Tablets, Cimetidine 200 mg, f-c tab. marked with maker's name and logo; 400 mg, capsule-shaped tab. marked with maker's name.
Pack - 10 x 6; 10 x 10; 500; 1000.

POM **GASTROL®** *(Sam)*
Tablet, Cimetidine 200 mg.
200 mg - 10 x 10; 500.

POM **TAGAMET®** *(GSK)*
Tablets, Cimetidine 200 mg, pale green f-c tab.; 400 mg, pale green oblong f-c tab. Both marked TAGAMET, SK & F and tab. strength.
200 mg - 56
400 mg - 20.
Injection, Cimetidine 200 mg per 2 ml.
2 ml x 10.

ESOMEPRAZOLE

Therapeutic category: Gastric acid secretion inhibitor.

Pharmacology: Esomeprazole, the S-isomer of omeprazole, reduces gastric acid secretion

through a specific targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. Esomeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the secretory canaliculi of the parietal cell, where it inhibits the enzyme H^+K^+-ATPase - the acid pump and inhibits both basal and stimulated acid secretion. Food intake had no significant influence on the effect of esomeprazole on intragastric acidity. During treatment with antisecretory drugs serum gastrin increases in response to the decreased acid secretion.

Pharmacokinetics - *Absorption and distribution*: Esomeprazole is acid labile and is administered orally as enteric-coated granules. *In vivo* conversion to the R-isomer is negligible. Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. The absolute bioavailability is 89% after repeated once daily administration. The apparent volume of distribution at steady state in healthy subjects is approximately 0.22 L/kg body weight. Esomeprazole is 97% protein bound.

Metabolism and excretion: Esomeprazole is completely metabolised by the cytochrome P450 system (CYP).

Indications: *Gastroesophageal Reflux Disease (GERD)*:

- treatment of erosive reflux esophagitis;
- long-term management of patients with healed esophagitis to prevent relapse;
- symptomatic treatment of gastroesophageal reflux disease (GERD).

In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori and

- healing of *Helicobacter pylori* associated duodenal ulcer;
- prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcer disease.

Contra-indications: Known hypersensitivity to esomeprazole, substituted benzimidazoles or any other constituents of the formulation.

Precautions: In the presence of any alarm symptom (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melaena) anad when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with esomeprazole may alleviate symptoms and delay diagnosis. Patients on long term treatment (particularly those treated for more than 1 year) should be kept under regular surveillance. Pregnancy and lactation.

Adverse effects: The following adverse drug reactions have been identified or suspected in the clinical trials programme for esomeprazole. None was found to be dose-related.

Common (>1/100, <1/10): Headache, abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation.

Uncommon (>1/1000, <1/100): Dermatitis, pruritus, urticaria, dizziness, dry mouth'

Nursing considerations: •Administer whole, at least 1 hr before eating.

•Inform patient that drug may cause drowsiness, dizziness and if affected, to avoid activities that require alertness.

•Advise patient to avoid alcohol, salicylates, ibuprofen; may cause GI irritation.

•Discontinue medication and notify doctor if patient reports severe diarrhoea.

Dose: The tablets should be swallowed whole with liquid. The tablets should not be chewed or crushed.

Gastro-esophageal Reflux Disease (GERD)

- *Treatment of erosive reflux esophagitis*: 40 mg once daily for 4 weeks. An additional 4 weeks treatment is recommended for patients in whom esophagitis has not healed or who have persistent symptoms.
- *Long-term management of patients with healed esophagitis to prevent relapse*: 20 mg once daily.
- *Symptomatic treatment of gastro-esophageal reflux disease (GERD)*: 20 mg once daily in patients without esophagitis. If symptoms control has not been achieved after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using an on demand regimen taking 20 mg once daily, when needed.

In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori and

- *Healing of Helicobacter pylori associated with duodenal ulcer*: 20 mg with 1 g Amoxicillin and 500 mg Clarithromycin, all twice daily for 7 days.
- *Prevention of relapse of peptic ulcers in patients with Helicobacter pylori as associated ulcer disease*: 20 mg with 1 g Amoxicillin and 500 mg Clarithromycin, all twice daily for 7 days.

Children No experience with esomeprazole in children.

Impaired renal function Dose adjustment is not required in patients with impaired renal function. Due to limited experience

in patients with severe renal insufficiency, such patients should be treated with caution.
Impaired hepatic function Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, a dose of 20 mg esomeprazole should be used. (see "pharmacokinetics).
Elderly Dose adjustment is not required in the elderly.

POM **NEXIUM®** *(Reals)*
Tablets, Esomeprazole (as Magnesium trihydrate) 20 mg, light pink f-c tab. marked '20 mg' on one side and 'AEH' on the reverse; 40 mg, pink f-c tab. marked '40 mg' on one side and 'AEI' on the reverse. Both contain esomeprazole as enteric-coated pellets (MUPS).

FAMOTIDINE

Therapeutic category: Antihistamine, H_2 Blocker; Histamine-2 Antagonist.
Indications: Duodenal ulcer and gastric ulcer.
Contra-indications: Hypersensitivity to famotidine, nursing mothers.
Precautions: Children; renal impairment (reduce the dosage usually by half when creatinine clearance ml/min.); pregnancy (avoid during the first trimester).
Adverse effects: Rarely headache, dizziness, constipation and diarrhoea; dry mouth, nausea and/or vomiting, rash, abdominal discomfort or distension, anorexia, and fatigue.
Nursing considerations: •Give with meals or liquids. If needed, give antacids 1 hr before or 2 hr after famotidine.
•Advise patient to avoid pepper, caffeine, alcohol, spices, aspirin, very hot or cold foods that seem to worsen the condition.
•Inform patient that drug may cause drowsiness, dizziness and if affected, to avoid activities that require alertness.
•Cigarette smoking may increase gastric acid secretion and worsen disease; making the drug less effective.
•Advise patient not to take drug for longer than 8 weeks except if ordered by the physician.
Dose: By mouth, *duodenal or gastric ulcer*, 40 mg at night; *Maintenance (duodenal ulcer)*, 20 mg at night; the doses may be increased if necessary.

POM **FAMODAR®** *(Supreme)*
Tablets, Famotidine 20 mg, 40 mg.
20 mg – 30.
40 mg – 10.

POM **FAMOTAB®** *(Hovid)*
Tablet, Famotidine 40 mg; square, light orange, f-c tab.
40 mg -10 x 10 (blister).

POM **PEPDINE®** *(Bolax/APP)*
Tablets, Famotidine 20 mg, 40 mg.
20 mg – 30.
40 mg – 15.

POM **PEPTI®** *(Silva Hill)*
Tablets, Famotidine 20 mg, 40 mg.
20 mg - 10 x10.
40 mg - 10 x 10.

LANSOPRAZOLE

Therapeutic category: Gastric acid secretion inhibitor.
Pharmacology: Lansoprazole is a substituted benzimidazole proton pump inhibiotor. It suppresses gastric acid secretion by the specific inhibition of the (H+, K+) ATPase enzyme system (acid pump) at the surface of gastric parietal cells, resulting in the blocking of the final step of acid production and so the inhibition of both basal and stimulated acid secretion regardless of the stimulus. The enteric coated pellet formulation ensures that the drug is absorbed only after it leaves the stomach, with an absolute bioavailability over 80%, a plasma half-life of 1.5 hrs, and a duration of action $\geq$ 24 hrs. It is extensively metabolised in the liver into two inactive metabolites that undergo significant biliary excretion.
Indications: Short-term treatment of active duodenal ulcer; Maintenance of healed duodenal ulcer; Eradication of *H. pylori* infection to prevent DU recurrence; Short-term treatment of active benign gastric ulcer; Short-term treatment of erosive esophagitis; Maintenance of healing of erosive esophagitis; Long-term treatment of pathological hypersecretory conditions including Zollinger-Ellison syndrome.
Contra-indications: Hypersensitivity to Lansoprazole or any component of the product.
Precautions: As with other antiulcerants symptomatic response to treatment with Lansoprazole does not preclude gastric malignancy.
Pregnancy and Lactation: Use during pregnancy if clearly needed. It is not known if Lansoprazole is excreted in human breast milk, the physician should decide to discontinue nursing or to discontinue the drug according to the importance of the drug to the mother.
Children: Safety and efficacy are not estab-

lished in children < 18 yrs.
Liver impairment: Consider dosage reduction in severe cases of hepatic impairment.
Elderly: Doses > 30 mg daily should be administered only if additional acid suppression is needed.
Dysphagia: For patients with difficulty in swallowing, capsule can be opened and pellets can be swallowed immediately, without crushing or chewing the pellets.
Adverse effects: Diarrhea, nausea, abdominal pain, headache and skin rashes may occur.
Nursing considerations: •Administer capsule whole 30 min before eating for best results.
•Inform patient that drug may cause drowsiness, dizziness and if affected, to avoid activities that require alertness.
•Advise patient to avoid alcohol, salicylates, ibuprofen; may cause GI irritation.
•Discontinue medication and notify doctor if patient reports severe diarrhoea.
Dose: *Duodenal ulcer,* Short term treatment, 15-30 mg once daily for 4 weeks; Maintenance of healed duodenal ulcer, 15 mg once daily.
Eradication of H. pylori to prevent DU recurrence, Suggested regimens:
Triple therapy: 30 mg Lansoprazole, 1 g Amoxicillin and 500 mg clarithromycin, all given b.i.d. (every 12 hours) for two weeks. Alternatively, Lansoprazole 30 mg b.i.d. on days 1-4, Azithromycin 500 mg once daily on days 2-4, and Tinidazole 2000 mg once on day 4.
Dual therapy: 30 mg Lansoprazole and 1 g Amoxicillin t.i.d. for 2 weeks.
Active benign gastric ulcer, Short term treatment, 30 mg once daily for up to 8 weeks.
Erosive esophagitis, Short term treatment, 30 mg once daily for 8 weeks; additional 8 weeks may be needed for patients who do not heal. In case of recurrence consider another 8 weeks. Healing maintenance: 15 mg once daily.
Pathological hypersecretory conditions including ZE syndrome: The dosage should be individualized according to the desired patient response for as long as needed. The usual starting dose is 60 mg once daily. Daily doses > 120 mg should be administered in divided doses.
Note: For best result take the capsules 30 minutes before meals. Use the drug within one month from opening date. If you have difficulty in swallowing the capsule, open it and swallow the content immediately without chewing or crushing the pellets. No dosage adjustment is necessary in elderly or renal impairment patients. Adjust dosage in case of severe liver impairment.

POM **LANZOTEC®** *(Afrab-Chem)*
Capsules, Lansoprazole 15 mg, 30 mg; e-c pellets in capsules.
15 mg - 14
30 mg - 14.

OMEPRAZOLE

Therapeutic category: Gastric acid secretion inhibitor.
Pharmacology: Omeprazole, a proton-pump-inhibitor (PPI), is an acid-activated pro-drug. It inhibits H+K+ATPase of the gastric pump. With a pKa of about 4.0, it selectively accumulates in acid spaces of pH < 4.0. This level of acidity is achieved only in the secretory canaliculus of the parietal cell when the cell is secreting acid. After accumulation in this acid space, acid activation converts omeprazole to cationic sulphonamide, which then binds covalently to cysteine on the luminal face of the gastric H+K+ATPase thereby inhibiting the gastric pump. As this action inhibits the final stage of gastric acid formation, there is effective inhibition of both basal and stimulated acid secretion irrespective of the stimulus to acid formation.
The onset of action is rapid, and reversible control of gastric acid secretion is achieved with once a day dosing.
Indications: Treatment of heartburns (pyrosis); gastroesophageal reflux disease (GORD); stress ulceration; gastric and duodenal ulcers; Zollinger-Ellison syndrome; acid related disorders; prophylaxis in long-term NSAID therapy and acid aspiration.
Contra-indications: Pregnancy and lactation.
Precautions: When gastric ulcer is suspected, the possibility of malignancy should be excluded as treatment may exacerbate symptoms and delay diagnosis.
Pregnancy and lactation: Use of omeprazole in pregnancy and lactation should be avoided except where considered essential. There is no evidence of foetal toxicity or teratogenicity with the use of omeprazole.
Experience in Children: New documentation has been completed demonstrating that omeprazole satisfies an outstanding medical need in children with erosive esophagitis refractory to conventional treatment. In a pivotal international multi-centre study involving children aged 1-16 yrs with erosive esoghagitis of grade 2 or worse, esophagitis was healed in 94% of patients after a single two week course

of omeprazole and the remaining 6% after a second course. Reflux-related symptoms improved dramatically in almost all patients, and 90% of children gained weight during treatment an important positive outcome. Omeprazole provides major benefits in these severely ill children.

Elderly: Bioavailability may be increased in geriatric patients.

Impaired renal and hepatic function: Dosage adjustment in patients with impaired renal or liver function is not required.

Adverse effects: Nausea, headache, diarrhoea, contipation and flatulence which are mild and transient.

Nursing considerations: •Give before meals.

•Capsules should be swallowed whole; not chewed, crushed or opened.

•Inform patient that drug may cause drowsiness, dizziness and if affected, to avoid activities that require alertness.

•Advise patient to avoid alcohol, salicylates, ibuprofen; may cause GI irritation.

•Discontinue medication and notify doctor if patient reports severe diarrhoea.

Dose: By mouth, Adult, *Active duodenal ulcer*, 20 mg/day usually for 2 weeks and up to 4 - 8 weeks in severe cases. *Gastric ulcer*, 20 mg/day for up to 4 - 8 weeks.

Erosive oesophagitis, heartburn, symptoms associated with GORD, 20mg/day for up to 4-8 weeks depending on the type of oesophagitis. Maintenance of healing erosive oesophagitis: 20mg daily.

Duration of treatment: In patients with duodenal ulcer, gastric ulcer or reflux oesophagitis, symptoms relief is rapid and healing occurs within 2 weeks in most cases. For those patients who may not have fully healed after the initial course, healing usually occurs during a further 2 week treatment period with duodenal ulcer, and a further 4 week treatment for patients with gastric ulcer or reflux oesophagitis.

In patients refractory to other treatment regimens, 40 mg omeprazole once daily has been used and healing achieved usually within 4 weeks in patients with duodenal ulcer and within 8 weeks in patients with gastric ulcer or reflux oesophagitis.

Zollinger-Ellison syndrome, initially 60 mg once daily; adjusted according to individual response. In refractory cases, 20-12 0mg daily; doses above 80 mg should be divided during administration.

Maintenance Therapy: The safety of omeprazole in long term treatment of indicated ailments has been established. Patients have been treated for upward of 3 years with omeprazole with out any harzadous clinical results.

Eradication of H. pylori, 20 mg daily with Amoxicillin 500 mg t.d.s and Metronidazole 400 mg b.d for 7 days. Alternatively, 20 mg daily with Amoxicillin 500 mg t.d.s and Clarithromycin 500 mg b.d for 7 days. See also under the proprietary preparations.

Overdosage and treatment: *Symptoms* of overdosage include: confusion, drowsiness, blurred vision, tachycardia, nausea, diaphoresis, flushing, headache, dry mouth.

Treatment: Symptomatic and supportive. Omeprazole is not readily dialyzable.

POM **EUCID®** *(Didachons)*

Capsule, Omeprazole 20 mg; enteric-coated granules.

POM **LOSEC®** *(Reals)*

Capsules, Omeprazole 10 mg, 20 mg, 40 mg.

Dose: *Duodenal ulcer*, 20-40 mg once daily for 2-4 weeks. To prevent relapse, the recommended dose is 10 mg once daily which may be increased to 20-40 mg once daily if needed.

Gastric ulcer, 20-40 mg once daily for 4-8 weeks. For prevention of relapse in poorly responsive patients, 20-40 mg once daily.

NSAID associated ulcers, 20 mg once daily for 4-8 weeks. For prevention of NSAID associated ulcers, 20 mg once daily.

Helicobacter pylori eradication regimens in peptic ulcer, Triple therapy regimens: Losec 20 mg, amoxicillin 1 g and clarithromycin 500 mg, all twice daily for one week or Losec 20 mg, clarithromycin 250 mg and metronidazole 400 mg (or tinidazole 500 mg), all twice dailly for one week.

Dual therapy regimens: Losec 40-80 mg daily with amoxicillin 1.5 g daily in divided doses for two weeks. In clinical studies, daily doses of 1.5-3 g of amoxicillin have been used or Losec 40 mg once daily and clarithromycin 500 mg three times a day for two weeks.

Reflux oesophagitis, 20 mg once daily for 4-8 weeks. *For severe reflux oesophagitis*, Losec 40 mg once daily for 8 weeks is recommended. For long term management of patients with healed

reflux oesophagitis the recommended dose is 10 mg once daily which may be increased to 20-40 mg once daily if needed.
Symptomatic GERD, 10-20 mg once daily for 4 weeks. If symptom control is not achieved after 4 week-treatment with Losec 20 mg once daily, further investigation is recommended.
Zollinger-Ellison syndrome, Adjust dose individually and continue treatment as long as clinically indicated. Initial treatment, 60 mg daily. Maintenance dose, Losec 60-20 mg daily. Divide daily dose if it exceeds 80 mg.

POM **MEPRASIL®** *(Fidson)*
Capsule, Omeprazole USP 20 mg; e-c granules in hard gelatin capsule with an opaque green body and cap marked 'Meprasil 20 mg.'
Pack - 14.
Injection, Omeprazole (as Sodium salt) BP 40 mg per vial; in 10 ml amber coloured tubular vial.
Dose: 40 mg once daily.

POM **OLIT®** *(Interpharma)*
Capsule, Omeprazole 20 mg.

POM **OMEZOLE®** *(Hovid)*
Capsule, Omeprazole 20 mg; e-c pellets in hard gelatin cap. marked 'Omezole/Hovid'.
20 mg - 4 x 7 (in alu-alu blisters).

POM **RAMEZOLE®** *(Pharmabox)*
Capsule, Omeprazole USP 20 mg; reddish brown cap and pink body filled with white to light brown enteric coated granules.

RABEPRAZOLE

Therapeutic category: Gastric acid secretion inhibitor.
Pharmacology: **Mechanism of Action** - Rabeprazole belongs to the class of anti-secretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H_2 histamine antagonist properties, but suppress gastro acid secretion by the specific inhibition of the H^+/K^+-ATPase enzyme (the acid or proton pump). The effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus. Animal studies indicate that after administration, rabeprazole sodium rapidly disappears from both the plasma and gastric mucosa. As a weak base, rabeprazole is rapidly absorbed following all doses and is concentrated in the acid environment of the parietal cells. Rabeprazole is converted to the active sulfonamide form through protonation and it subsequently reacts with the available cysteines on the proton pump.
Indications: Treatment of active duodenal ulcer; active benign gastric ulcer; symptomatic erosive or ulcerative gastro-oesophageal reflux disease (GORD); Gastro-Oesophageal Reflux Disease long- term management (GORD Maintenance).
Contra-indications: Known hypersensitivity to rabeprazole sodium, substituted benzimidazoles or to any excipients used in the formulation; Pregnancy and during breast feeding.
Precautions: Symptomatic response to therapy with rabeprazole sodium does not preclude the presence of gastric or oesophageal malignancy, therefore the possibility of malignancy should be excluded prior to commencing treatment.
Hepatic dysfunction. Ability to drive and operate complex machinery may be impaired.
Adverse effects: The observed undesirable effects have generally been mild/moderate and transient in nature. The most common adverse events (incidence $\geq$ 5%) were headache, diarrhoea and nausea.
Other adverse events (incidence <5% and $\geq$ 2%) were rhinitis, abdominal pain, asthenia, flatulence, pharyngitis, vomiting, nonspecific pain/back pain, dizziness, flu like symptoms, infection, cough, constipation and insomnia. Further less frequent adverse events (incidence $\geq$ 1%) were rash, myalgia, chest pain, dry mouth, dyspepsia, nervousness, somnolence, bronchitis, sinusitis, chills, eructation, leg cramps, urinary tract infection, arthralgia and fever.
In isolated cases, anorexia, gastritis, weight gain, depression, pruritus, vision or taste disturbances, stomatitis, sweating, leucocytosis have been observed.
Nursing considerations: •Administer whole, in the morning after breakfast.
•Inform patient that drug may cause dizziness and if affected, to avoid activities that require alertness.
•Advise patient to avoid alcohol, salicylates, NSAIDs; may cause GI irritation.
•Discontinue medication and notify doctor if patient reports severe diarrhoea.
Dose: *Adults/Elderly, Active Duodenal Ulcer and Active Benign Gastric Ulcer*, 20 mg to be taken once daily in the morning. Some patients with active duodenal ulcer may respond to one 10 mg tablet to be taken once daily in the morning. Most patients with active duodenal ulcer heal within 4 weeks. A few refractory

patients may require an additional 4 weeks of therapy to achieve healing. Most patients with active benign gastric ulcer heal within 6 weeks. A few refractory patients may require an additional 6 weeksof therapy to achieve healing.

Erosive or Ulcerative Gastro-Oesophageal Reflux Disease (GORD), 20 mg to be taken once daily for 4-8 weeks.

Gastro-oesophageal reflux Disease Long-term Management (GORD Maintenance), For long-term management, a maintenance dose 10-20 mg once daily can be used depending upon patient's response.

Note: Tablets should be taken in the morning, before eating; and although neither the time of day nor food intake was shown to any effect on rabeprazole sodium activity, this regimen will facilitate treatment compliance.

Advise patient not to chew nor crush the tablets; tablets should be swallowed whole.

Renal and hepatic impairment: No dosage adjustment is necessary for patients with renal or hepatic impairment.

Children: Not recommended for use in children.

Overdosage and treatment: *Symptoms* - There is no experience to date with deliberate overdose. Dosages of up to 80 mg/day have been well tolerated.

Treatment - No specific antidote is known. Rabeprazole sodium is extensively protein bound and is therefore not readily dialysable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

POM **PARIET®** *(Janssen-Cilag)*

Tablets, Rabeprazole (as Sodium) 10 mg, 20 mg; gastro-resistant tabs.

10 mg - 14's

20 mg - 14's.

RANITIDINE

Ranitidine is a representative H_2-receptor antagonist. Various drugs can serve as alternatives.

Therapeutic category: Histamine H_2-receptor antagonist.

Indications: Benign gastric and duodenal ulceration, gastro-oesophageal reflux, Zollinger–Ellison syndrome, other conditions where gastric acid reduction is beneficial.

Contra-indications: Porphyria

Precautions: Hepatic impairment (Appendix 5); renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); middle-aged or older patients and those whose symptoms change - may mask gastric cancer; **interactions**: Appendix 1.

Adverse effects: Diarrhoea and other gastrointestinal disturbances, headache, dizziness, rash, tiredness, acute pancreatitis, bradycardia, AV block, confusion, depression; rarely hallucinations (particularly in the elderly or the very ill), hypersensitivity reactions (including fever, arthralgia, myalgia, anaphylaxis), blood disorders (including agranulocytosis, leukopenia, pancytopenia, thrombocytopenia), hepatitis, tachycardia, agitation, visual disturbances, erythema multiforme, alopecia, gynaecomastia and impotence.

Advice to patients: See Label 13 in Appendix 6 (for the effervescent preparations). It may take several days before this medicine begins to relieve stomach pain; antacids may be taken with ranitidine unless otherwise instructed by the physician; wait 30-60 minutes between taking the antacid and ranitidine; may cause drowsiness, impair judgement, or co-ordination. Avoid smoking as this may increase gastric acid secretion and worsen disease.

Nursing considerations: •Administer with meals for prolonged effect. may give antacids 1 hr before or 1 hr after ranitidine.

•I.M. solution does not need to be diluted before use.

•I.V. must be diluted and may be administered by continuous infusion over 24 hours.

•Monitor creatinine clearance for renal impairment.

•Observe caution in patients with renal and hepatic impairment.

•See also under Cimetidine.

Dose: *Benign gastric and duodenal ulceration*, by mouth , adult 150 mg twice daily or 300 mg at night for 4–8 weeks, up to 6 weeks in *chronic episodic dyspepsia*, and up to 8 weeks in *NSAID-associated ulceration* (in *duodenal ulcer* 300 mg can be given twice daily for 4 weeks to achieve a higher healing rate); maintenance, 150 mg at night; CHILD (*peptic ulcer*) 2–4 mg/kg twice daily, maximum 300 mg daily.

Benign gastric and duodenal ulceration, reflux oesophagitis, Zollinger–Ellison syndrome, by intramuscular injection, adult 50 mg every 6–8 hours or by slow intravenous injection , 50 mg diluted to 20 ml and given over at least 2 minutes, may be repeated every 6–8

hours or by intravenous infusion, 25 mg/hour for 2 hours, may be repeated every 6–8 hours.
Duodenal ulceration associated withH. pylori, see notes above.
Prophylaxis of NSAID-induced duodenal ulcer, by mouth , adult 150 mg twice daily
Reflux oesophagitis, by mouth , adult 150 mg twice daily or 300 mg at night for up to 8 weeks, or if necessary 12 weeks (moderate to severe, 150 mg 4 times daily for up to 12 weeks); *long-term treatment of healed oesophagitis*, 150 mg twice daily.
Zollinger–Ellison syndrome, by mouth, adult 150 mg 3 times daily; up to 6 g daily in divided doses has been used.
Gastric acid reduction (prophylaxis of acid aspiration) in obstetrics, by mouth, adult 150 mg at onset of labour, then every 6 hours; *surgical procedures*, by intramuscular or slow intravenous injection, adult 50 mg 45–60 minutes before induction of anaesthesia (intravenous injection diluted to 20 ml and given over at least 2 minutes), or by mouth, 150 mg 2 hours before induction of anaesthesia, and also, when possible on the preceding evening.
Prophylaxis of stress ulceration, adult initial slow intravenous injection of 50 mg diluted to 20 ml and given over at least 2 minutes then by continuous intravenous infusion, 125–250 micrograms/kg per hour (may be followed by 150 mg twice daily by mouth when oral feeding commences).

Note: H_2 - receptor blockers are taken in the night (nocte) for more effective ulcer healing. Antacids are taken during daytime to neutralise acidity.

POM **Ranitidine** *(WMF 17.1)*
Tablets, Ranitidine (as HCl) 150 mg
Oral solution, Ranitidine (as HCl) 75 mg/5 ml.
Injection (Solution for injection), Ranitidine (as HCl) 25 mg/ml, 2-ml ampoule.

POM **Ranitidine** *(EDL 18.7)*
Tablets, Ranitidine (as HCl) 150 mg, 300 mg.
Injection, Ranitidine (as HCl) 25 mg per ml; in 2 ml amp.

POM **ACILOC**® *(Interpharma)*
Tablets, Ranitidine 150 mg, 300 mg; both are f-c tabs.
150 mg - 10 x 10's.
300 mg - 2 x 10's.

POM **APO-RANITIDINE**® *(Lahams)*
Tablets, Ranitidine 150 mg, white f-c tab. marked 'APO 150'; 300 mg, white, scored, oblong f-c tab. marked 'APO 300'.
150 mg - 100.
300 mg - 100.

POM **HISTAC**® (*Ranbaxy)*
Tablets, Ranitidine (as HCl) BP 150 mg, 300 mg; both are f-c tabs.
150 mg - 10's
300 mg - 10's.

POM **RANITAL**® *(Taylek)*
Tablets, Ranitidine (as HCl) 150 mg, 300 mg.

POM **ZANTAC**® *(GSK)*
Tablets, Ranitidine (as HCl) 150 mg, white, round f–c tab. marked 'GLAXO' and 'ZANTAC 150'; 300 mg, white, capsule–shaped, f–c tab., marked 'GLAXO' on one face and 'ZANTAC 300' on the other.
150 mg - 20; 60.
300 mg - 10; 30.
Effervescent Tablets, Ranitidine (as HCl) 150 mg, 300 mg; white to pale yellow, round, flat, bevel–edged tabs which effervesce on dissolution in water to give a clear, grapefruit/orange flavoured solution.
Effervescent Granules, Ranitidine (as HCl) 150 mg, 300 mg; white to pale yellow, free flowing granules which effervesce on dissolution in water to give a clear, grapefruit/orange flavoured solution.
Injection, Ranitidine (as HCl) 25 mg per ml; 2 ml aqueous solution in amp.

RANITIDINE BISMUTH CITRATE

Synonym: Ranitidine Bismutrex.
Therapeutic category: Histamine H_2-Receptor Antagonist.
Indications: Treatment of duodenal ulcer and benign gastric ulcer; also used in eradication regimen for *Helicobacter pylori* with other drugs.
Contra-indications: Moderate to severe renal impairment; long-term (maintenance) therapy; porphyria; pregnancy, breast-feeding.
Precautions: May mask symptoms of gastric carcinoma (exclude malignancy before therapy); renal impairment, elderly (excreted

via the kidneys).

Adverse effects: May cause blackening of the stools and tongue (due to bismuth); rarely hypersensitivity reactions including pruritus, skin rash, anaphylaxis; GI disturbances; headache; transient changes in the liver enzymes; mild anaemia.

Advice to patients: May cause blackening of the stools and tongue.

Nursing considerations: •See under Ranitidine.

Dose: By mouth, *Duodenal ulcer*, 400 mg twice daily for 4 weeks; may be extended for another 4 weeks if required.
Benign gastric ulcer, 400 mg twice daily for 8 weeks.
Eradication of Helicobacter pylori (combination therapy), 400 mg twice daily plus **Amoxycillin** 1 g twice daily plus **Metronidazole** 400 mg twice daily for a total of 4-8 weeks.

Note: Not recommended for children. Ranitidine bismuth citrate is not indicated for long term (maintenance) therapy; more than two 8-week courses in any one year should be avoided because of the possibility of accumulation of bismuth. If 4-week courses of therapy are given, up to a maximum of 16 weeks treatment may be given in any one year.

POM **PYLORID**® *(GSK)*
Tablet, Ranitidine bismuth citrate 400 mg; light blue octagonal capsule shaped f-c tab.

PIRENZEPINE

Therapeutic category: Antimuscarinic.

Indications: Hyperacidity and peptic ulcer.

Adverse effects: Occasionally dry mouth, visual disturbances.

Advice to patients: See Label 22 in Appendix 6.

Dose: By mouth, 50 mg twice daily; up to a max. 150 mg daily in 3 divided doses. See lit. for details.

POM **Pirenzepine** *(EDL 18.7)*
Tablet, Pirenzepine HCl 50 mg.

MUCOSAL PROTECTIVE AGENTS

Sucralfate

Sucralfate, or aluminum sucrose sulphate, is a sulphated disaccharide developed for use in peptic ulcer disease.

It binds selectively to necrotic ulcer tissue, where it may act as a bile to acid, pepsin, and barrier. In addition, sucralfate may directly absorb bile salts. It is effective in the healing of duodenal ulcers. It is not absorbed systemically, and few adverse effects have been reported. The dosage is 1g 4 times daily on an empty stomach (at least 1 hour before meals). It also requires an acid pH to be activated and so should not be administered simultaneously with antacids or an H_2–receptor antagonist.

Colloidal Bismuth Compounds

Like sucralfate, these compounds seem to work by selective binding to an ulcer and by coating it to protect the ulcer from acid and pepsin. **Tripotassium dicitrato bismuthate** has been shown to be superior to placebo in the healing of both duodenal and gastric ulcers.

Carbenoxolone

Carbenoxolone, a synthetic derivative of glycyrrhizinic acid (an extract from liquorice), is effective in healing both gastric and duodenal ulcers. Its mechanism of action may involve an increase in the production, secretion, and viscosity of intestinal mucus. Its clinical usefulness has been limited by aldosterone–like side effects such as hypertension, fluid retention, and hypokalaemia. The concurrent administration of spironolactone controls the fluid retention but also abolishes the ulcer–healing effect; thiazides prevent sodium retention without abolishing the beneficial effect in peptic disease.

OTHER ULCER HEALING DRUGS

Misoprostol is a prostaglandin analogue particularly useful in the prevention of NSAID-induced gastric ulcers. It is a synthetic prostaglandin E_1 analogue that replaces the protective prostaglandins consumed with prostaglandin-inhibiting therapies, e.g. nonsteroidal anti-inflammatory drugs. It is taken orally and usually adult dosage is 200 mcg 4 times daily with food. If not tolerated, the dose may be decreased to 100 mcg 4 times daily with food or 200 mcg twice daily with food.

Pantoprazole is another gastric acid secretion inhibitor.

4.2 Antispasmodic drugs

The smooth muscle relaxant properties of anticholinergic (more correctly termed antimuscarinic) and other antispasmodic drugs may be useful in dyspepsia, irritable bowel syndrome, and in diverticular disease. The gastric antisecretory effects of conventional anticholinergic drugs are of little practical significance since dosage is limited by atropine-like adverse effects. Moreover they have been superseded by

more powerful and specific antisecretory drugs, including the histamine H_2-receptor antagonists.

Anticholinergics that are used for gastrointestinal smooth muscle spasm include **atropine** and **hyoscine butylbromide**.

Nursing Considerations:- Anticholinergics
•Give with or after meals to prevent GI upset; may give with fluids other than water. Hard candy, frequent drinks, sugarless gum may be needed to relieve dry mouth.
•Monitor patient for urinary retention (may palpate bladder); constipation (increase fluids, bulk, exercise); mood changes.
•Advise patient to avoid driving or other hazardous activities as drowsiness may occur. OTC medications for cough & cold with alcohol, antihistamines should be avoided unless prescribed by doctor.

ATROPINE

Atropine sulfate is a representative antispasmodic drug. Various drugs can serve as alternatives.

Indications: Dyspepsia, irritable bowel syndrome, diverticular disease; premedication (section 3.2); mydriasis and cycloplegia (section 13.3.1); poisoning (section 19.2.3).

Contra-indications: Angle-closure glaucoma; myasthenia gravis; paralytic ileus; pyloric stenosis; prostatic enlargement.

Precautions: Children, elderly and Down syndrome (increased risk of adverse effects); gastro-oesophageal reflux; diarrhoea; ulcerative colitis; acute myocardial infarction; hypertension; hyperthyroidism; cardiac insufficiency, cardiac surgery—conditions characterized by tachycardia; pyrexia; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Constipation; transient bradycardia (followed by tachycardia, palpitations and arrhythmias); reduced bronchial secretions, urinary urgency and retention; dilatation of pupils with loss of accommodation, photophobia, dry mouth, flushing and dryness of skin; occasionally confusion (particularly in the elderly), nausea, vomiting and giddiness.

Dose: *Dyspepsia, irritable bowel syndrome, diverticular disease*, by mouth, ADULT 0.6–1.2 mg at night.

POM **Atropine** *(WMF 17.5)*
Tablets, Atropine sulfate 600 micrograms.

BELLADONNA ALKALOIDS

Pharmacology: It competitively blocks acetylcholine, which decreases GI motility and inhibits gastric acid secretion.

Indications: GI disorders associated with smooth muscle spasm.

Contra-indications: Glaucoma.

Precautions: Cardiac disease, paralytic ileus, urinary retention, elderly, breast-feeding.

Adverse effects: Tachycardia, difficulty with micturition and constipation, dry mouth, dry skin.

Nursing considerations: •Give drug 30-60 minutes before meals.
•Elderly patients should be given lower doses because of slowing down of metabolism.
•Encourage patient to drink fluids to prevent constipation.
•Teach patient to rinse mouth frequently or chew gum to relieve dryness of mouth.
•Instruct patient to avoid driving and hazardous activities if he/she is drowsy or has blurred vision.
•Teach patient to report skin rash or local eruption of rashes, dryness of mouth.

Dose: See lit.

POM **Belladonna Mixture** *(EDL 18.4)*

CARBACHOL

Synonym: Carbacholine.

Therapeutic category: Parasympathomimetic.

Indications: Urinary retention; postoperative intestinal atony.

Contra-indications: Asthma, Addison's disease, intestinal or urinary obstruction, coronary occlusion, hyperthyroidism, peptic ulcer.

Precautions: Elderly, Cardiovascular disease, epilepsy, parkinsonism.

Adverse effects: Parasympathomimetic effects such as nausea, vomiting, sweating, blurred vision, bradycardia, intestinal colic.

Advice to patients: See label 22 in Appendix 6.

Dose: By mouth, 2 mg 3 times daily.
By s.c. injection (acute cases), 250 mcg repeated at 30-minute intervals if necessary.

POM **Carbachol** *(EDL 18.4)*
Tablet, Carbachol 2 mg.
Injection, Carbachol 0.25 mg per ml; 1 ml amp.

HYOSCINE N-BUTYLBROMIDE

Synonym: Scopolamine

Therapeutic category: Anticholinergic Agent; Antispasmodic/Antimuscarinic.

Pharmacology: Hyoscine N-butylbromide inhibits muscarinic actions of acetylcholine on autonomic effectors innervated by postganglionic cholinergic neurons. It has a special site of action at the parasympathetic ganglia in the walls of the viscera. Because of this, it exerts a specific antispasmodic action on the smooth muscle of the GI, biliary and urinary tracts, this action being produced long before side effects characteristic of atropine-like substances occur, hence, no side effects on the CNS or salivary glands are observed when the drug is administered in therapeutic doses.

Indications: Gastric and duodenal ulcers, gastro-intestinal spasm and hypermotility, pylorospasm in infants, post-operative vomiting, spastic constipation, biliary dyskinesia and spasm of urinary tract, delayed relaxation of the lower uterine segment, dysmenorrhoea.

Contra-indications: Glaucoma, urinary retention, mechanical stenoses in the GIT, tachycardia, megacolon.

Precautions: Patients over 40 years (may cause glaucoma); prolonged administration (tolerance may develop); asthma; hypertension; myasthenia gravis; ulcerative colitis; urinary retention; reflux oesophagitis may be aggravated; paralytic ileus or pyloric stenosis (may lead to obstruction); pregnancy, breast - feeding, children, elderly.

Interactions:

•Tricyclic antidepressants, amantadine, some antihistamines, phenothiazines, butyrophenones (these drugs have anticholinergic properties and co-administration may enhance the effect of hyoscine).

•Alcohol or other CNS depressants; MAOIs; Sympathomimetics.

Adverse effects: Dry mouth and skin; increased pulse rate; transient disturbance of accommodation which can affect vision; constipation; photophobia; urinary urgency and retention. Occasionally nausea, vomiting and giddiness, particularly in the elderly.

Nursing considerations: •Parental dose should be given slowly and keep patient in bed for at least an hour to prevent hypotension.

•Give oral dose with or after meals, and with fluids to reduce GI upset; chewing gum and sips of water will relieve dry mouth.

•Increase fluid intake if constipation occurs. Instruct patient to notify physician if urinary hesitancy or retention occurs.

•Instruct patient to avoid OTC medications for cough and cold, which contain alcohol, antihistamine unless prescribed by the physician.

•Advise patient not to discontinue drug abruptly and to avoid hazardous activities that require mental alertness and physical coordination until the CNS effects of the drug are established.

Dose: By mouth, Adult and child (over 6 years), 10-20 mg 3-5 times daily.
Child (under 6 years): not recommended
By S.C., I.M. or slow I.V., *acute spasm*, 20 mg, repeated after 30 minutes if required.

POM **Hyoscine N-Butylbromide** *(EDL 18.4)*
Tablet, Hyoscine N-butylbromide 10 mg.
Liquid, Hyoscine N-butylbromide 5 mg per 5 ml.
Injection, Hyoscine N-butylbromide 20 mg per ml; in 1 ml amp.

POM **COLIPAN®** *(NGC)*
Tablet, Hyoscine-N-butylbromide 10 mg; round whte biconvex s-c tab.
10 mg - 20; 100.
Syrup, Hyoscine-N- butylbromide 5 mg per 5 ml; clear yellow viscous liquid.
Pack - 100 ml.
Injection, Hyoscine-N-butylbromide 20 mg per ml; in 1 ml amp.

POM **COLOSPAN®** *(Hovid)*
Tablet, Hyoscine butylbromide 10 mg; s.c. tab.
10 mg - 40; 1000.

POM **Hyoscine Butyl Bromide** *(Doyin)*
Injection, Hyoscine-N-butylbromide 20 mg per ml; in 1 ml amp.
20 mg - 100.

POM **LOCIN®** *(Beta Drugs)*
Injections, Hyoscine N-butylbromide BP 10 mg, 20 mg per 1-ml ampoule.
Pack – 1-ml x 10's.

POM **SCOPBUTAN®** *(Dizpharm)*
Tablet, Hyoscine-N- butylbromide 10 mg.
10 mg - 1000.

HOMATROPINE METHYLBROMIDE

Therapeutic category: Antimuscarinic Agent; Antispasmodic.

Indications: Treatment of gastro-intestinal spasms and as adjunct in the treatment of peptic ulcer.

Contra-indications: Myasthenia gravis; closed or nervous angle glaucoma.

Precautions: Acute myocardial infarction, thyrotoxicosis, cardiac insufficiency.

Interactions:

•Co-administration with other antimuscarinic drugs such as atropine, hyosine, antihistamines, butyrophenones, phenothiazine, and TCAs may

potentiate the effects of homatropine.
Adverse effects: Mydriasis, cycloplegia; prolonged use may lead to cardiovascular side effects such as bradycardia followed by relaxed tachycardia with palpitation; in high doses urinary urgency, difficulty and retention, constipation due to reduction in gut motility (paralytic ileus) may occur; dryness of mouth; difficulty in swallowing.
Dose: By mouth, Adult, 10-20 mg 3-4 times daily; Child (up to 3 months), 2-4 drops 3-4 times 3-6 months, 4-6 drops 3-4 times daily; 6-12 months, 6-9 drops 3-4 times daily; 1-3 years, 2.5 ml 2-3 times daily; 3-6 years, 5 ml 2-3 times daily; 6-12 years, 10 mg 2-3 times daily.
Note: Infant doses are to be taken 10-15 minutes before feeding.

POM **NOSPAMIN**® *(Afrab-Chem)*
Tablet, Homatropine methylbromide 10 mg.
10 mg - 20; 100; 500.
Syrup, Homatropine methylbromide
5 mg per 5 ml.
Pack - 6 ml.
Paediatric drops, Homatropine methylbromide
2 mg per ml.
Pack - 15 ml (with dropper).

PROPANTHELINE

Therapeutic category: Anticholinergic Agent; Antispasmodic Agent.
Pharmacology: It competitively blocks acetylcholine, which decreases GI motility and inhibits gastric acid secretion.
Indications: Spasm of the GIT; as an adjunct in gastric and duodenal ulcer.
Contra-indications, Precautions, etc.: See under Hyoscine butylbromide.
Advice to patients: See Label 22 in Appendix 6. Take 30-60 minutes before meals and at bedtime. Maintain good oral hygiene habits, because lack of saliva may increase chance of cavities. Observe caution while driving or performing other tasks requiring alertness, as may cause drowsiness, dizziness, or blurred vision. Notify physician if skin rash, flushing, or eye pain occurs; or if difficulty in urinating, constipation, or sensitivity to light becomes severe or persists.
Nursing considerations: •Give before meals so that the drug's peak effect occurs at the proper time (peak inhibition of gastric acid secretion occurs at 1 and 3 hours after dosing in fasting subjects and approximately 2 hours in non-fasting subjects; this correlates well with the time food is no longer in the stomach offering a buffering effect).
•Bedtime dose can be larger and should be given at least 2 hours after the last meal.
•Provide increased fluids, bulk, exercise, to decrease constipation.
•Tell patient to avoid alcohol or other CNS depressants; they enhance sedating properties of the drug.
•Give chewing gum or sips of water to relieve dry mouth.
Dose: By mouth, 15 mg 3 times daily and 30 mg at night; up to a max. 120 mg daily.

POM **Propantheline***(EDL 18.4)*
Tablet, Propantheline bromide 15 mg.

POM **PROBANTHINE**® *(Morison)*
Tablet, Propantheline bromide 15 mg; pink scored tab.
15 mg - 40.

4.3 Other smooth muscle relaxants

DROTAVERINE

Indications: Spasms of smooth muscles in cholelithiasis, nephrolithiasis, cholecystitis, pyelitis, cystitis, vescal tenesmus. As adjuvant in ventricular and duodenal ulcer, cardia and pylorus spasm, irritable colon syndrome, hypertension, angina pectoris, and intermittent claudication. Also effective in dysmenorrhoea, strong labour pains, tetanus uteri, imminent abortion.
Contra-indications: Severe liver, renal and cardiac insufficiency.
Adverse effects: Headache, dizziness, nausea, palpitation, and hypotension may occur.
Dose: Adult, by mouth, usually 120-240 mg daily in 3 divided doses; by s.c. or i.m. injection, 40-240 mg daily in 1-3 divided doses. *Acute stone colic*, by i.v. injection, 40-80 mg.
Child (1-6 years), by mouth, 40-120 mg daily in 2-3 divided doses; over 6 years, 80-200 mg daily in 2-5 divided doses.

POM **NO-SPA**® *(Sanofi)*
Tablet, Drotaverine HCl 40 mg.
40 mg - 20; 100; 1000.
Injection, Drotaverine HCl 20 mg per ml; in 2 ml amp.
Pack - 5; 25; 50.

MEBEVERINE

Therapeutic category: Antispasmodic.
Pharmacology: Mebeverine is a musculotropic antispasmodic with a direct action on the smooth muscle of the GIT, relieving spasm without affecting normal gut motility. Since this action is not mediated by the autonomic

nervous system, the usual anticholinergic side effects are absent. But like all antispasmodics, mebeverine should be avoided in paralytic ileus.

Indications: Symptomatic treatment of abdominal pain and cramps, bowel disturbances and intestinal discomfort related to irritable bowel syndrome (IBS); GI spasm secondary to organic disease; functional disorders of the GIT associated with abdominal pain in children over 3 years of age.

Precautions: Paralytic ileus; pregnancy and breast-feeding; avoid in porphyria.

Dose: By mouth, Adult and child over 10 years, 135 mg 3 times daily until therapeutic response is achieved; then gradually reduce dose after a few weeks. To be taken preferably 20 minutes before meals.

POM **DUSPATALIN**® *(NGC)*
Tablet, Mebeverine HCl 135 mg; white s-c tab. 135 mg - 50.

4.4 Drugs used in diarrhoea

4.4.1 Oral rehydration
4.4.2 Antimotility drugs
4.4.3 Adsorbents and bulk-forming drugs

Acute diarrhoeal diseases are a leading cause of childhood morbidity and mortality; frail and elderly patients are also at risk. In adults acute diarrhoea is the most frequent health problem of travellers to developing countries and is increasingly common among HIV-infected persons. Assessment and correction of dehydration and electrolyte disturbance is the priority in all cases of acute diarrhoea. Symptomatic relief (section 4.3.2) in adults may be warranted in some cases but antidiarrhoeals should never be used in children since they do not reduce fluid and electrolyte loss and may cause adverse effects.

Diarrhoea persisting for longer than a month is known as chronic diarrhoea. A mild malabsorption syndrome, tropical enteropathy, is apparent in most healthy indigenous populations of tropical countries. However the majority of cases of chronic diarrhoea have non-infectious causes including gluten-sensitivity, inherited metabolic disorders or inflammatory bowel disease.

Bloody diarrhoea is usually a sign of invasive enteric infection and should be treated with an appropriate anti-infective agent.

4.4.1 Oral rehydration

Acute diarrhoea in children should always be treated with oral rehydration solution according to plan A, B or C as shown. Severely dehydrated patients must be treated initially with intravenous fluids until they are able take fluids by mouth. For oral rehydration it is important to administer the solution in small amounts at regular intervals as indicated below.

Treatment of dehydration: WHO recommendations

According to the degree of dehydration, health professionals are advised to follow one of 3 management plans.

Plan A: no dehydration. Nutritional advice and increased fluid intake are sufficient (soup, rice, water and yoghurt, or even water). For infants aged under 6 months who have not yet started taking solids, oral rehydration solution must be presented before offering milk. Mother's milk or dried cow's milk must be given without any particular restrictions. In the case of mixed breast-milk/formula feeding, the contribution of breastfeeding must be increased.

Plan B: moderate dehydration. Whatever the child's age, a 4-hour treatment plan is applied to avoid short-term problems. Feeding should not therefore be envisaged initially. It is recommended that parents are shown how to give approximately 75 ml/kg of oral rehydration solution with a spoon over a 4-hour period, and it is suggested that parents should be watched to see how they cope at the beginning of the treatment. A larger amount of solution can be given if the child continues to have frequent stools. In case of vomiting, rehydration must be discontinued for 10 minutes and then resumed at a slower rate (about one teaspoonful every 2 minutes). The child's status must be re-assessed after 4 hours to decide on the most appropriate subsequent treatment. Oral rehydration solution should continue to be offered once dehydration has been controlled, for as long as the child continues to have diarrhoea.

Plan C: severe dehydration.

Hospitalization is necessary, but the most urgent priority is to start rehydration. In hospital (or elsewhere), if the child can drink, oral rehydration solution must be given pending, and even during, intravenous infusion (20 ml/kg every hour by mouth before infusion, then 5 ml/kg every hour by mouth during intravenous rehydration). For intravenous supplementation, it is recommended that compound solution of sodium lactate (see section 26.2) is administered at a rate adapted to the child's age (infant under 12 months: 30 ml/kg over 1 hour then 70 ml/kg over 5 hours; child over 12 months: the same amounts over 30 minutes and 2.5 hours respectively). If the intravenous route is unavailable, a nasogastric tube is also suitable for administering oral rehydration solution, at a rate of 20 ml/kg every hour. If the child vomits, the rate of administration of the oral solution should be reduced.

ORAL REHYDRATION SALTS

Glucose salt solution

sodium chloride	2.6 g/litre of clean water
sodium citrate	2.9 g/litre of clean water
potassium chloride	1.5 g/litre of clean water
glucose (anhydrous)	13.5 g/litre of clean water

When glucose and sodium citrate are not available, they may be replaced by

sucrose (common sugar)	27 g/litre of clean water
sodium bicarbonate	2.5 g/litre of clean water

NOTE: THE SOLUTION MAY BE PREPARED EITHER FROM PREPACKAGED SUGAR/SALT MIXTURES OR FROM BULK SUBSTANCES AND WATER. SOLUTIONS MUST BE FRESHLY PREPARED, PREFERABLY WITH RECENTLY BOILED AND COOLED WATER. ACCURATE WEIGHING AND THOROUGH MIXING AND DISSOLUTION OF INGREDIENTS IN THE CORRECT VOLUME OF CLEAN WATER IS IMPORTANT. ADMINISTRATION OF MORE CONCENTRATED SOLUTIONS CAN RESULT IN HYPERNATRAEMIA.

CHOLERA: IN CASES OF CHOLERA, ORAL REHYDRATION SALTS CONTAINING A HIGHER CONCENTRATION OF SODIUM MAY BE REQUIRED TO PREVENT HYPONATRAEMIA.

Indications: Dehydration from acute diarrhoea.

PRECAUTIONS: Renal impairment.

ADVERSE EFFECTS: Vomiting—may indicate too rapid administration; hypernatraemia and hyperkalaemia may result from overdose in renal impairment or administration of too concentrated a solution.

DOSE: *Fluid and electrolyte loss in acute diarrhoea*, by mouth , ADULT 200–400 ml solution after every loose motion; INFANT and CHILD according to Plan A, B or C (see notes above).

*OTC***Oral Rehydration Salt** *(EDL 18.6.2)*
Powder, Glucose 20g, Potassium chloride 1.5g, Sodium citrate dihydrate 2.9g (or Sodium bicarbonate 2.5g), Sodium chloride 3.5g.

OTC **AQUALYTE®** *(Farmex–Meyer)*
Solution, Sodium chloride 1.404g, potassium chloride 0.97g, sodium citrate 1.25g, sodium phosphate 0.71g, calcium lactate 0.6168g, magnesium dicitrate 0.9674g, citric acid 0.4693g, anhydrous dextrose 20.0g, distilled water to 1000ml; ready to use oral rehydration solution.
Pack - 250 ml.

Dose: By mouth, Adult and children above 5 years: 25 ml 2-3 hourly; not more than 10 doses in 24 hours.
Child (up to 5 years): 250 ml 2-3 times during the first 4-6 hours; then 250 ml 2-3 times during the next 18-24 hours and 250 ml 2 times within the following 24 hours.

4.4.2 Antimotility drugs

Opioids such as **codeine** are used in the symptomatic relief of uncomplicated, acute diarrhoea in adults but not in young children. They act on opioid receptors in the gut wall and decrease bowel motility. In dehydration, fluid and electrolyte replacement (section 4.3.1) are of primary importance.

Diphenoxylate and Loperamide
Both are phenylpiperidine derivatives that are used to reduce the motility of the gut. In acute diarrhoeas, they are used as adjuncts to fluid and electrolyte replacement but are not recommended for young children.
As an antidiarrheal drug, diphenoxylate is usually used in combination with atropine (**Lomotil®**). The adult dosage is 2 tablets every 6 hours until the diarrhoea is controlled. Loperamide (**Imodium®**) does not have the sedative or respiratory depressant effects of diphenoxylate. The usual dose is 4mg to start and then 2mg after each diarrhoeal stool for up to 5 days.

Propantheline
Anticholinergic (antimuscarinic) drugs diminish intestinal motility. They sometimes have a beneficial effect on diarrhoea, but are frequently of great value in relieving colicky abdominal pain if this is an accompaniment to

the diarrhoea (see section 4.2). They should not be used for primary treatment.

CODEINE

DRUG SUBJECT TO INTERNATIONAL CONTROL UNDER THE SINGLE CONVENTION ON NARCOTIC DRUGS (1961).

Indications: Short-term symptomatic relief of acute diarrhoea in adults; pain (section 1.8.2).

Contra-indications: Children; conditions where inhibition of peristalsis should be avoided; abdominal distension; acute diarrhoeal conditions such as ulcerative colitis or antibiotic-associated colitis; acute respiratory depression.

Precautions: Tolerance or dependence may occur with prolonged use; elderly and debilitated patients; hepatic impairment (Appendix 5); renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); **overdosage**: see section 19.2.2; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, constipation, drowsiness; respiratory depression and hypotension (large doses); dependence; difficulty with micturition; ureteric or biliary spasm; dry mouth, sweating, headache, facial flushing, vertigo, bradycardia, tachycardia, palpitations, hypothermia, hallucinations, dysphoria, mood changes, miosis, decreased libido or potency, rash, urticaria, pruritus; convulsions (large doses).

Dose: *Symptomatic relief of acute diarrhoea*, by mouth, ADULT 30 mg 3–4 times daily

CD **Codeine** *(WMF 17.7.2)*
Tablets, Codeine phosphate 30 mg.

LOPERAMIDE

Therapeutic category: Antidiarrhoeal.

Indications: Symptomatic control of acute and chronic diarrhoea when inhibition of peristalsis is indicated; to decrease the volume ileostomy discharge.

Contra-indications: Child under 2 years; acute dysentery; acute ulcerative colitis or pseudomembranous colitis associated with broad-spectrum antibiotics; conditions in which inhibition of peristalsis should be avoided such as acute diarrhoea due to ingestion of poison.

Precautions: Infants (approprate fluid and electrolyte replacement therapy should be given); acute diarrhoea (discontinue therapy if no improvement within 48 hours); hepatic dysfunction (monitor closely for CNS toxicity); pregnancy, breast-feeding.

Interactions:
•CNS depressants, phenothiazines, TCAs may ptentiate the adverse effects.

Adverse effects: Hypersensitivity reactions (including skin rash); abdominal pain, distension or discomfort; nausea and vomiting; constipation, tiredness, drowsiness, dry mouth.

Advice to patients: Do not take more than 8 capsules in 24 hours; may cause drowsiness.

Nursing considerations: •Relieve dry mouth with sips of water, hard candy.
•Therapy for chronic diarrhoea should not exceed 10 days; if acute diarrhoea lasts longer than 48 hours, discontinue therapy and consult physician.
•Advise patient to avoid driving or operating machinery if he feels dizzy or drowsy.
•Monitor children for signs of dehydration, CNS problems.

Dose: *Acute diarrhoea,* Adult, by mouth, initially 4 mg, followed by 2 mg after each loose stool; Child (over 5 years), by mouth, 2 mg, followed by 2 mg after each loose stool.
Chronic diarrhoea, Adult and child (over 5 years), by mouth, initially 4 mg daily (2 mg for child); adjusted between 2-12 mg daily until 1-2 solid stools a day are obtained.
Maximum dose for acute and chronic diarrhoea is 16 mg (8 capsules) daily for adults and for a child, 6 mg (3 capsules) per 20 kg b. wt.

POM **IMODIUM®** *(Janssen-Cilag)*
Capsule, Loperamide HCl 2 mg.
2 mg - 6; 240.

4.4.3 Adsorbents and bulk-forming drugs

Kaolin and Pectin

These are adsorbents and their action is through their ability to adsorb compounds from solution, presumably binding potential intestinal toxins. Kaolin and Morphine Mixture B.P.C. are still used for control of mild chronic diarrhoea.

KAOLIN

Indications: Mild chronic diarrhoea.

Contra-indications: Obstructive bowl lesions.

Adverse effects: Constipation.

Nursing considerations: •Administer after shaking suspension.
•Don't use for more than 2 days; not a replacement for specific therapy for the underlying cause.
•May reduce absorption of other PO drugs; separate administration times at least 2 hr apart.

Dose: Adult, 30 ml every 4-6 hours.
Child, 5-30 ml every 4-6 hours.

OTC **Kaolin with or without Morphine** *(EDL 18.6.1)*
Mixture, See B.P. 1988.

OTC **DIAPEC®** *(Pfizer/Neimeth)*
Suspension, Kaolin light 1 g per 5 ml.
Pack - 60 ml.
Dose: Adult, by mouth, 15-20 ml 3 times daily.
Child (2-5 years), 2.5 ml 4 hourly; 6-10 years, 7.5-15 ml 4 hourly; 11-15 years, 10-15 ml 3 times daily.

OTC **FURAPEC®** *(Food & Pharma)*
Suspension, Light kaolin 1000 mg per 5 ml; in a flavoured base.
Pack - 60 ml.
Dose: Child (under 1 year), 5 ml 1-3 times daily; 1-4 years, 10 ml 1-3 times daily.

OTC **GALWAYS ADM®** *(SKG)*
Suspension, Light kaolin 6 g, diarex 250 mg per 30 ml; fruit flavoured susp.
Pack - 60 ml.
Dose: By mouth, Adult, 30 ml; Child (under 3 years), 2.5 ml; 3-6 years, 10 ml; 6-12 years, 15ml.
To be taken at half-hourly intervals until symptoms abate; usually 3-4 doses should be sufficient. Shake before use.

OTC **Moko Mist Kaolin** *(New Healthway)*
Suspension, Light kaolin BP 1000 mg, sodium bicarbonate BP 250 mg, light magnesium carbonate BP 250 mg per 5 ml.

OTC **NEIPEC®** *(Neimeth)*
Suspension, Kaolin light 1 g per 5 ml.
Pack - 60 ml.

SULPHAGUANIDINE plus KAOLIN plus NEOMYCIN SULPHATE

Therapeutic category: Antidiarrhoeal
Indications: Diarrhoea of bacteria origin, gastroenteritis and food poisoning.
Contra-indications: Ulcerative colitis, intestinal obstruction.
Precaution: Prolonged use may cause overgrowth of non-susceptible micro-organisms.
Dose: Adult and child (over 12 years), by mouth 30 ml initially, followed by 15 ml 4 times daily. Child (6-12 years), 15 ml initially, followed by 10 ml 4 times daily; 1-6 years, 5-10 ml initially, followed by 2.5-5 ml 4 times daily.

POM **IVAX®** *(BCN)*
Suspension, Sulphaguanidine 0.7 g, light kaolin 1.05 g, neomycine sulphate 53.33 mg per 5 ml.
Pack - 60 ml.

4.5 Laxatives

A balanced diet, including adequate fluid intake and fibre is of value in preventing constipation.

Before prescribing laxatives, it is important to be sure that the patient is constipated and that the constipation is not secondary to an underlying undiagnosed complaint. It is also important that the patient understands that bowel habit can vary considerably in frequency without doing harm. For example some people consider themselves constipated if they do not have a bowel movement each day. A useful definition of constipation is the passage of hard stools less frequently than the patient's own normal pattern and this should be explained to the patient since misconceptions about bowel habits have led to excessive laxative use which in turn has led to hypokalaemia and an atonic non-functioning colon.

Laxatives should generally be avoided except where straining will exacerbate a condition such as angina or increase the risk of rectal bleeding as in haemorrhoids. Laxatives are of value in drug-induced constipation, for the expulsion of parasites after anthelminthic treatment and to clear the alimentary tract before surgery and radiological procedures. Prolonged treatment of constipation is rarely necessary except occasionally in the elderly.

There are many different laxatives. These include **bulk-forming laxatives** which relieve constipation by increasing faecal mass and stimulating peristalsis, **stimulant laxatives** which increase intestinal motility and often cause abdominal cramp, **faecal softeners** which lubricate and soften impacted faeces and **osmotic laxatives** which act by retaining fluid in the bowel by osmosis. **Bowel cleansing solutions** are used before colonic surgery, colonoscopy or radiological examination to ensure that the bowel is free of solid contents; they are **not** a treatment for constipation.

BISACODYL

Therapeutic category: Stimulant laxative.
Pharmacology: Stimulates persistalsis by directly irritating the smooth muscle of the intestine, possibly the colonic intramural plexus; alters water and electrolyte secretion producing net intestinal fluid accumulation and laxation. Less than 5% is absorbed systemically. Onset of action is 6-10 hours (oral) and 0.25-1 hour (rectal). It is metabolised in the liver and the conjugated metabolites are excreted in milk, bile and urine.
Indications: Treatment of constipation (preferred for constipation caused by narcotic analgesics); bowel clearance before surgery, labour or radiological examination.
Contra-indications: Abdominal pain, nausea, vomiting, or other symptoms of appendicitis or acute surgical abdomen; rectal fissures or ulcerated haemorrhoids; intestinal obstruction.
Precautions: Children, abdominal pain, pregnancy.
Interactions:
•Milk, antacids (decreased effect).
•Decreased effect of warfarin.
Adverse effects: Mild abdominal cramps, nausea, vomiting, rectal burning, vertigo, electrolyte and fluid imbalance.
Advice to patients: See Labels 5 and 25 in Appendix 6.
Nursing considerations: •Increased pH may dissolve the enteric coating leading to GI distress; do not crush or chew enteric coated drug product.
•Administer tablets 2 hours prior to, or 4 hours after antacids.
•Insert suppository as high as possible into the rectum; position against the rectal wall, not embedded in faecal matter because it may cause delay in onset of action.
•Teach patient to use for short term treatment and prevent abuse; prolonged use may cause loss of bowel tone.
•Tell patient that dietary intake of bulk found in cereals, fresh fruits and vegetables improve bowel movement.
•Onset of action is 6-10 hours (oral) and 25 to 60 minutes (rectal); time administration of drug so as not to intefere with scheduled activities or sleep.
•Inform patient not to use medication if symptoms of appendicitis occur namely abdominal pain, nausea, vomiting.
Dose: By mouth, Adult, 10 mg at night;
increased to 15-20 mg if necessary.
Child: 5 mg.
By rectum, Adult, 10 mg in the morning.
Child: 5 mg.

POM **Bisacodyl** *(EDL 18.5)*
Tablet, Bisacodyl 5 mg.
Suppositories, Bisacodyl 5 mg, 10 mg.

POM **APO-BISACODYL®** *(Lahams)*
Tablet, Bisacodyl 5 mg; yellow e-c tab. marked "5".
5 mg - 1000.

POM **BISCOLAX®** *(Adler)*
Tablet, Bisacodyl 5 mg; e–c tab.
5 mg - 100.

POM **DULCOLAX®** *(NGC)*
Tablet, Bisacodyl 5 mg; e-c tab.
Suppositories, Bisacodyl 10 mg.
Paediatric suppositories, Bisacodyl 5 mg.

POM **LAXADIN®** *(Dizpharm)*
Tablet, Bisacodyl 5 mg; e-c tab.

OLIVE OIL

Indications: Olive oil is nutritious, demulcent and mildly laxative.
Dose: By mouth, Adult, *as a purgative*, 15-60 ml.

OTC **BELL'S OLIVE OIL®** *(De-Sears)*
Liquid, Olive Oil BP 1973; a pale yellow or greenish-yellow oil.
Pack - 70 ml, 150 ml.

PSYLLIUM

Therapeutic category: Bulk-producing Laxative.
Pharmacology: Adsorbs water in the intestine to form a viscous liquid which promotes peristalsis and reduces transit time. Onset of action is 12-24 hours, but full effect may take 2-3 days.
Indications: Treatment of chronic atonic or spastic constipation and in constipation associated with rectal disorder; management of irritable bowel syndrome.
Contra-indications: Faecal impaction, GI obstruction or ulceration, appendicitis; hypersensitivity to psyllium or any component.
Precautions: Oesophageal strictures, ulcers, strenosis, or intestinal adhesions; elderly may have insufficient fluid intake which may predispose them to faecal impaction and bowel obstruction.
Interactions:
•Decreased effect of warfarin, digitalis, potassium-sparing diuretics, salicylates, tetracyclines, nitrofurantoin.
Adverse effects: Intestinal obstruction, diarrhoea, constipation, abdominal cramps; bronchospasm upon inhalation in susceptible

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individuals.

Advice to patients: See Label 13 in Appendic A. Must be mixed in a glass of water or juice; drink a full glass of liquid with each dose; do not use for longer than 1 week without the advice of a physician.

Nursing considerations: •Mix with cold pleasant-tasting liquid such as orange juice to mask the grittiness, stir; instruct patient to drink it immediately, otherwise the mixture will congeal. Follow with additional glass of liquid.

•Teach patient that adequate fluid intake, exercise and dietary intake of bulk which include fresh vegetables, cereals and fruits will improve bowel movement; laxative effect of drug is observed in 12-24 hours and may be delayed for 3 days.

•Inhalation of psyllium dust may cause sensitivity to psyllium (runny nose, watery eyes, wheezing).

•Do not use in the presence of symptoms of appendicitis namely abdominal pain, nausea, vomiting; notify doctor if constipation is not relieved or if symptoms of electrolyte imbalance occur viz muscle cramps, pains, weakness, dizziness and excessive thirst.

Dose: By mouth, Adult, 1-2 satchets in a glass of liquid 1-3 times daily; follow with additional glass of water.
Child (over 6 years), 1 level teaspoonful in half a glass of liquid at bedtime.

Note: Administer at least 3 hours before or after drugs.

POM **Psyllium** *(EDL 18.5)*
Granules, Psyllium 3.5 g per sachet.

SENNA

Senna is a representative stimulant laxative. Various drugs can serve as alternatives.

Therapeutic category: Stimulant laxative.

Indications: Constipation; acts in 8–12 hours.

Contra-indications: Intestinal obstruction; undiagnosed abdominal symptoms.

Precautions: Avoid prolonged use unless indication for prevention of faecal impaction; breastfeeding (Appendix 3).

Adverse effects: Abdominal discomfort; atonic non-functioning colon and hypokalaemia (with prolonged use or overdosage).

Advice to patients: See Labels 5 and 25 in Appendix 6.

Nursing considerations: •Before giving for constipation, determine if patient has adequate fluid intake, exercise and diet; tell patient about dietary sources of bulk including fresh fruits and vegetables.

•Use for short-term treatment because drug is very potent and gives thorough, strong bowel action 6-10 hours after administration.

•Give oral dose in the morning or evening; cramping, rectal bleeding, nausea, vomiting may be due to overdosage (discontinue drug).

•Teach patient that faeces and urine may turn yellowish brown in colour.

•Patient should not use in the presence of of symptoms of appendicitis namely abdominal pain, nausea and vomiting.

•Notify the physician if constipation is not relieved or if symptoms of electrolyte imbalance occur viz muscle cramps, pain, weakness, dizziness and excess thirst.

Dose: *Constipation*, by mouth, ADULT 2–4 tablets, usually at night; initial dose should be low, then gradually increased; CHILD over 6 years, half the adult dose in the morning (on doctor's advice).

POM **Senna** *(WMF 17.6)*
Tablets, total Sennosides (calculated as Sennoside B) 7.5 mg.

POM **Senna** *(EDL 18.5)*
Tablets and Granules

LIQUID PARAFFIN

Pharmacology: Liquid paraffin is a mineral oil which is minimally absorbed by the GIT. It is a lubricant laxative. It mixes with and coats the intestinal contents, preventing colonic reabsorption of faecal water and increasing water retention in the stool. This leads to the formation of soft oily faeces. Onset of action is 6-8 hours.

Indications: Constipation.

Contra-indications: Appendicitis, faecal impaction, intestinal obstruction or perforation. Avoid enema in children under 2 years.

Precautions: Elderly or debilitated patients (due to susceptibility to lipid pneumonitis through aspiration, absorption, and transport from intestinal mucosa); children, rectal bleeding.

Adverse effects: Nausea, vomiting, diarrhoea in excessive use; abdominal cramps; decreased absorption of nutrients and fat-soluble vitamins.

Nursing considerations: •Give with fruit juices or carbonated drinks to disguise taste preferably at bedtime.

•May delay passage of food from stomach (do not give with meals or immediately after); more effective on an empty stomach.

•Encourage patient to take adequate fluids, exercise and increased bulk in diet (viz fresh fruits, vegetables, cereals).

Dose: By mouth, *Constipation*, Adult, 15-30 ml as enema.
Child, 5-15 ml at bedtime or 30-60 ml as enema.

Note: Avoid enema in children under 2 years.

OTC **Liquid Paraffin** *(EDL 18.5)*
Oral emulsion, Liquid paraffin 5 ml per 10 ml.

OTC **Moko Liquid Paraffin** *(New Healthway)*
Liquid, Liquid paraffin BP; clear colourless viscous liquid.
Pack - 200 ml.

MAGNESIUM HYDROXIDE

Synonym: Milk of Magnesia; MOM; Magnesia Magma.
Therapeutic category: Saline Laxative; Antacid.
Pharmacology: Promotes bowel evacuation by causing osmotic retention of fluid which distends the colon with increased peristaltic activity; reacts with hydrochloric acid in the stomach to form magnesium chloride. Onset of laxative action is 4-8 hours. The absorbed magnesium ions (up to 30%) are usually excreted by kidneys, unabsorbed drug is excreted in faeces.
Indications: Short-term treatment of occasional constipation and symptoms of hyperacidity.
Contra-indications: Colostomy or ileostomy, intestinal obstruction, faecal impaction, renal failure, appendicitis, hypersensitivity to any component.
Precautions: Renal impairment, elderly.
Advice to patients: Dilute dose in water or juice, shake well.
Nursing considerations: •Shake suspension thoroughly; give with at least a glass of water.
•Encourage patient to take adequate fluids, exercise and increased bulk in diet (viz fresh fruits and vegetables).
•Warn patient that frequent or prolonged use may cause dependence, or loss of bowel tone.
•Don't give oral drugs 1 to 2 hours before or after administration of magnesuim hydroxide.
•Onset of action is 4-8 hours; time administration of drug so as not to interfere with scheduled activities or sleep.
Dose: By mouth, *constipation*, Adult, 15-60 ml. Child (2-6 years), 5-15 ml.

OTC **Magnesium Hydroxide** *(EDL 18.5)*
Mixture, Magnesium hydroxide (as hydrated magnesium oxide) 550 mg per 10 ml.

OTC **DR. MEYER'S MILK OF MAGNESIA®** *(Farmex-Meyer)*
Suspension, Magnesium hydroxide 415 mg per 5 ml.
Pack - 100 ml.

OTC **PHILIP'S MILK OF MAGNESIA®** *(GSK)*
Suspension, Magnesium hydroxide 415 mg; smooth white opaque non-gritty viscous susp.
Pack - 100 ml.

MAGNESIUM SULFATE

Synonym: Epsom Salts
Therapeutic category: Saline Laxative; Antacid.
Pharmacology: Magnesium sulfate is a saline laxative. When taken by mouth in dilute solution it reduces the normal absorption of water from the intestine with the result that the bulky fluid contents distend the bowel, active reflex peristalsis is excited, and evacuation of the contents of the intestine follows.
Indication: Rapid bowel evacuation.
Contra-indications: See under Magnesium hydroxide.
Precautions: Renal and hepatic impairment, elderly, use only occasionally.
Advice to patients: See Labels 13 and 23 in Appendix 6.
Nursing considerations: See under Magnesium Hydroxide.
Dose: 5 -10 g in a tumblerful of water or 10-20 ml, followed by a tumblerful of water, preferably before breakfast.

OTC **Magnesium Sulphate** *(EDL 18.5)*
Mixture, Magnesium sulfate 4 g per 10 ml
Powder, Magnesium sulfate 5 g per sachet.

OTC **ANDREW'S LIVER SALT®** *(GSK)*
Granules (effervescent), Magnesium sulfate 5 g per sachet.
Pack - 10; 50.

OTC **Moko Epsom Salt** *(New Healthway)*
Powder, Magnesium sulfate 25 g per satchet.

OTC **Moko Mist Alba** *(New Healthway)*
Suspension, Magnesium sulfate 80 g.

4.6 Antiemetic drugs

Anti–emetics should be prescribed only when the cause of vomiting is known, particularly in children, otherwise the symptomatic relief that they produce may delay diagnosis. Anti–emetics are unnecessary and sometimes harmful when the cause can be treated, e.g. as in diabetic ketoacidosis, or in excessive digoxin or antiepileptic dosage.
If antinauseant drug treatment is indicated the choice of drug depends on the aetiology of vomiting.

Metoclopramide has antiemetic properties and also stimulates upper gastrointestinal motility. Metoclopramide is effective against nausea and vomiting associated with gastrointestinal disorders or migraine, following surgery and chemotherapy and is also effective against radiation-induced nausea and vomiting. Combining metoclopramide with corticosteroids (such as dexamethasone) can improve its antiemetic effect in chemotherapy-induced nausea and vomiting.

Metoclopramide may be useful in the management of gastro-oesophageal reflux and gastroparesis, as well as preoperatively in the prevention of aspiration syndromes. It is also used to facilitate intubation of the small bowel during radiographic examinations. Metoclopramide is not effective in the prevention or treatment of motion sickness.

Metoclopramide may cause acute dystonic reactions with facial and skeletal muscle spasms and oculogyric crises. These reactions are most common in the young (especially girls and young women) and the elderly; they occur shortly after the start of treatment and subside within 24 hours of drug withdrawal.

Promethazine is a phenothiazine that in addition to D2 dopaminergic blockade has pronounced histamine H1 and muscarinic receptor blocking properties. It is effective in the prevention and treatment of vertigo and motion sickness. Promethazine may be useful in the prevention and treatment of postoperative and drug-induced nausea and vomiting. It has limited effect on chemotherapy-induced mild to moderate emesis.

Chlorpromazine has a powerful sedative and antiemetic action, the latter probably mediated by the chemoreceptor trigger zone. It is of particular value in the treatment of vomiting associated with uraemia, radiation sickness and disseminated malignant disease, where its sedative property may also be appropriate. It is ineffective in motion sickness.

Cyclizine is a histamine H_1-receptor antagonist which causes less sedation than promethazine and has anti–motion sickness activity. It is effective in nausea and vomiting of other causes such as vertigo and nausea associated with Meniere's disease.

Like cyclizine, **meclozine** is an antihistamine with anti–motion sickness activity. It is less sedative than promethazine and is usually available in combination with pyridoxine.

Prochlorperazine is a phenothiazine indicated in the prophylaxis and treatment of vertigo and nausea associated with Meniere's disease. It is used in both acute and chronic forms of vertigo.

Ondansetron is a potent, highly selective 5–HT_3 (Serotonin) receptor–antagonist. Activation of these 5–HT_3 receptors in both the peripheral and CNS by chemotherapeutic agents and radiotherapy initiates a vomiting reflex. Ondansetron blocks the initiation of this reflex.

Tropisetron, like ondansetron, is a highly potent and selective competitive antagonist of the 5–HT_3 receptor. Activation of these 5–HT_3 receptors in both the peripheral neurons and within the CNS by some chemotherapeutic agents and radiotherapy initiates the emesis reflex and its accompanying feeling of nausea. Tropisetron selectively blocks the excitation of the presynaptic 5–HT_3 receptors of the peripheral neurons in this reflex, and may exert additional direct actions within the CNS on 5–HT_3 receptors mediating the actions of vagal input to the area postrema. It has a 24–hour duration of action which allows once–a–day administration. It prevents nausea and vomiting induced by cancer chemotherapy without causing extrapyramidal side effects. Tropisetron is nearly completely absorbed (more than 5%) from the GIT, with a mean half–life of about 20 minutes. The peak plasma concentration is attained within 3 hours.

CHLORPROMAZINE

Therapeutic category: Antipsychotic/anti-emetic.

Indications: Nausea and vomiting of terminal illness.

Contra-indications, Precautions, etc: See Chlorpromazine in Section 1.2.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: See Chlorpromazine in Section 1.2.

Dose: By mouth, 10-25 mg 4-6 hourly.
By deep I.M. injection, 25 mg initially then 25-50 mg 3-4 hourly until vomiting stops.

POM **Chlorpromazine** *(EDL 18.2)*
Tablets, Chlorpromazine HCl 25 mg, 50 mg.
Syrup, Chlorpromazine HCl 25 mg per 5 ml.
Injection, Chlorpromazine HCl 25 mg per ml; in 2 ml amp.

See Chlorpromazine in Section 1.2 for the proprietary preparations.

CINNARIZINE

Indications: Vestibular disorders such as vertigo, tinnitus, giddiness, nausea, and vomiting in Meniere's syndrome; prophylaxis of motion sickness; vascular spasms and arteriosclerosis as in Raynaud's disease, vascular headache, migraine.

Contra-indications: Hypersensitivity to the drug or any component; porphyria.

Precautions: Pregnancy, breast-feeding; elderly (may suffer extrapyramidal symptoms on prolonged therapy); hypotension (high doses); somnolence may occur at the start of therapy.

Interactions:

•May potentiate the sedative effects of CNS depressants and alcohol.

Adverse effects: Somnolence and GI disturbances; allergic skin reactions; fatigue; extrapyramidal symptoms in the elderly (reduce dose or discontinue).

Advice to patients: See label 2 in Appendix 6. To be taken preferably after meals.

Dose: *Vestibular disorders*, 25 mg 3 times daily or 75 mg once daily.
To be taken half an hour before travelling and to be repeated every 6 hours if necessary in prophylaxis of motion sickness.
See lit. for other indications and doses.

POM **STUGERON®** *(Janssen-Cilag)*
Tablet, Cinnarizine 25 mg.
25 mg - 50.
Capsule (forte), Cinnarizine 75 mg; red/yellow cap.
75 mg - 20.

CYCLIZINE

Therapeutic category: Antiemetic; Antihistamine, H_1 Blocker.

Indications: Nausea, vomiting, motion sickness, labyrinthine disorders.

Contra-indications, Precautions, etc: See under Promethazine.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: •Raise bed rails, institute safety measures, assist with ambulation.
•Advise patient to drink plenty of fluids for dry mouth and to prevent constipation.
•Warn patient that drug may cause drowsiness, may impair judgement and coordination, and to avoid alcohol and activities requiring alertness.

Dose: By mouth, 50 mg 3 times daily.
Child (1-10 years), 25 mg 3 times daily.
By I.M. injection, 50 mg 3 times daily.

Note: I.M. injection is not recommended in children.

POM **Cyclizine** *(EDL 18.2)*
Tablet, Cyclizine HCl 50 mg.
Injection, Cyclizine (as lactate) 50 mg per ml; in 1 ml amp.

DOMPERIDONE

Therapeutic category: Antinauseant.

Pharmacology: Domperidone is a dopamine antagonist with anti-emetic properties similar to those of metoclopramide and phenothiazines. Unlike these other drugs, however, domperidone does not readily cross the blood-brain-barrier and hence, is less likely to cause central effects such as sedation and dystonic reactions. It acts at the chemoreceptor trigger zone and so is unlikely to be effective in motion sickness and other vestibular disorders.

Indications: Dyspepsia associated with delayed gastric emptying, gastro-oesophageal reflux and oesophagitis (sense of fullness, abdominal distension, upper abdominal pain, bloating, eructation, flatulence, heartburn, nausea and vomiting). Nausea and vomiting induced by radiotherapy or cytotoxic therapy, levodopa and bromocriptine.

Contra-indications: GI haemorrhage, mechanical obstruction or perforation; prolactinoma (prolactin-releasing pituitary tumour).

Precautions: Infants under 1 year, hepatic impairment, severe renal insufficiency; pregnancy, breast-feeding.

Interactions:

•Anticholinergic drugs (may antagonise the anti-dyspeptic effect of domperidone).
•Antacids may lower oral bioavailability of domperidone.

Adverse effects: Transient intestinal cramps;increase in the plasma prolactin level which may cause galactorrhoea and gynaecomastia; rarely allergic reactions such as rash and urticaria.

Dose: *Chronic dyspepsia*, by mouth, Adult, 10 mg 3 times daily; to be taken 15-30 minutes before meals and, if necessary,once more before retiring;
Child (over 1 year), 2.5 ml per 10 kg b. wt. 3 times daily before meals and, if necessary, once more in the evening.

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These doses can be doubled if necessary in both Adult and Child (over 1 year).

Acute and subacute conditions (particularly nausea and vomiting), Adult, by mouth, 20 mg 3-4 times daily before meals and before bedtime (the dose may be doubled if necessary); by rectum in suppositories, 120-240 mg daily.

Child, by mouth, 5 ml per 10 kg b. wt. 3-4 times daily before meals and before bedtime; by rectum in suppositories, up to 2 years, 10 mg 2-4 times daily; 2-4 years, 30 mg 2 times daily; 4-6 years, 30 mg 3 times daily; above 6 years, 30 mg 4 times daily.

Note: Oral doageforms should be taken before meals. If taken after meals absorption of the drug can be delayed. The tablets are not intended for children below 5 years. Reduce dose in renal insufficiency. The suppositories should preferably be inserted into an empty rectum with the blunt end first.

POM **MOTILIUM®** *(Janssen-Cilag)*
Tablet, Domperidone 10 mg; f-c tab. 10 mg - 30.

MECLOZINE plus PYRIDOXINE

Synonym: Meclizine plus Vitamin B_6.

Therapeutic category: Antiemetic; Antihistamine, H_1 Blocker.

Indications: Nausea and vomiting

Contra-indications, Precautions, etc: See under Promethazine.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: •Give after meals to reduce GI upset.
•Do not discontinue drug abruptly.
•Lowest possible dose in the elderly due to the anticholinergic effects.
•Notify physician if adverse GI effects, fever, or heat intolerance occurs.
•See also under Cyclizine.

Dose: Usually, 1-2 tabs 2-3 times daily.

Severe nausea and vomiting of pregnancy, 2 tabs at bedtime and if necessary 1 tab. in the morning.

POM **Meclozine plus Pyridoxine** *(EDL 18.2)*
Tablet, Meclozine HCl 25 mg, pyridoxine HCl 50 mg.

METOCLOPRAMIDE

Therapeutic category: Antiemetic.

Indications: Nausea and vomiting in gastrointestinal disorders and treatment with cytotoxics (section 12.1) or radiotherapy; gastro-oesophageal reflux; gastroparesis; premedication and postoperatively; aid to gastrointestinal intubation; nausea and vomiting in migraine (section 1.9).

NOTE: IN CHILDREN (AND IN SOME COUNTRIES, PATIENTS UNDER 20 YEARS) USE RESTRICTED TO SEVERE INTRACTABLE VOMITING OF KNOWN CAUSE, VOMITING OF RADIOTHERAPY AND CHEMOTHERAPY, AID TO GASTROINTESTINAL INTUBATION, PREMEDICATION.

Contra-indications: Gastrointestinal obstruction, haemorrhage or perforation; 3–4 days after gastrointestinal surgery; convulsive disorders; phaeochromocytoma.

Precautions: Elderly, children and young adults; hepatic impairment (Appendix 5); renal impairment (Appendix 4); may mask underlying disorders such as cerebral irritation; avoid for 3–4 days after gastrointestinal surgery; pregnancy (Appendix 2); breastfeeding (Appendix 3); Parkinson disease; epilepsy; depression; porphyria; **interactions**: Appendix 1.

Adverse effects: Extrapyramidal symptoms (especially in children and young adults; see notes above); tardive dyskinesias on prolonged use; hyperprolactinaemia; drowsiness, restlessness, dizziness, headache, diarrhoea, depression, hypotension and hypertension reported; rarely, neuroleptic malignant syndrome; rashes, pruritus, oedema; cardiac conduction abnormalities following intravenous administration; rarely methaemoglobinaemia (more severe in G6PD deficiency).

Advice to patients: See Labels 2 and 22 in Appendix 6.

Nursing considerations: •Administer about 30-60 min before meals for better absorption.
•Relieve dry mouth with frequent sips of water, gum, hard candy.
Advise patient to avoid harzadous activities until stabilised on medication; alcohol, other CNS depressants that may increase sedative effects of the drug.
•Notify physician if involuntary movements occur.

Dose: *Nausea and vomiting, gastro-oesophageal reflux, gastroparesis*, by mouth or by intramuscular injection or by slow intravenous injection (over 1–2 minutes), ADULT 10 mg 3 times daily; young ADULT 15–19 years (under 60 kg) 5 mg 3 times daily; CHILD up to 1 year (up to 10 kg) 1 mg twice daily, 1–3 years (10–14 kg) 1 mg 2–3 times daily, 3–5 years (15–19 kg) 2 mg 2–3 times daily, 5–9 years (20–29 kg) 2.5 mg 3 times daily,

9–14 years (30 kg and over) 5 mg 3 times daily (usual maximum 500 micrograms/kg daily, particularly for children and young adults).
Premedication, by slow intravenous injection , ADULT 10 mg as a single dose.
Aid to gastrointestinal intubation, by mouth or by intramuscular injection or by slow intravenous injection, ADULT 10–20 mg as a single dose 5–10 minutes before examination; young ADULT (15–19 years), 10 mg; CHILD under 3 years 1 mg, 3–5 years 2 mg, 5–9 years 2.5 mg, 9–14 years 5 mg.

NOTE: HIGH DOSE METOCLOPRAMIDE WITH CYTOTOXIC CHEMOTHERAPY, SEE SECTION 8.2.

POM **Metoclopramide** *(WMF 17.2)*
Tablets, Metoclopramide HCl 10 mg.
Injection (Solution for injection), Metoclopramide HCl 5 mg/ml, 2-ml ampoule.

POM **Metoclopramide** *(EDL 18.2)*
Tablet, Metoclopramide (as HCl) 10 mg.
Syrup, Metoclopramide (as HCl) 5 mg per 5 ml.
Injection, Metoclopramide (as HCl) 5 mg per ml; in 2 ml amp.

POM **HEPDIN®** *(Justeen)*
Injection, Metoclopramide 10 mg per 2 ml.
Pack – 2 ml x 10's.

POM **METOPRONE®** *(Beta Drugs)*
Injection, Metoclopramide HCl BP 10 mg per ampoule; sterile solution of metoclopramide HCl in water for injections.
Pack - 1-ml x 100 amps; 2-ml x 10 amps; 2-ml x 100 amps

ONDANSETRON

Therapeutic category: Antiemetic.
Indications: Nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy; post–operative nausea and vomiting (PONV).
Precautions: Pregnancy and breast–feeding.
Adverse effects: Constipation, headache, a sensation of flushing or warmth in the head and epigastrium; occasional alteration in liver enzymes; rarely hypersensitivity reactions.
Dose: Adult, *Highly Emetogenic chemotherapy, e.g., regimens containing cisplatin*: Initially by slow intravenous injection or 15 minute infusion of 8 mg immediately before chemotherapy, followed by a continuous intravenous infusion of 1 mg/hour for up to 24 hours or by a further two doses of 8 mg given by slow intravenous injection or 15 minute infusion four hours apart; then 8 mg by mouth every 8 hours for up to 5 days.
Less Emetogenic chemotherapy, e.g., regimens containing cyclophosphamide, doxorubicin, carboplatin: By slow intravenous injection or 15 minute infusion of 8 mg, immediately before chemotherapy, or 8mg by mouth 1-2 hours before chemotherapy; then 8 mg by mouth every 8 hours for up to 5 days.
Radiotherapy induced Nausea and Vomiting: By mouth, 8 mg every 8 hours, the first dose to be taken 1-2 hours before starting radiotherapy; the duration of treatment depends on the length of the course of radiotherapy.
Post-operative nausea and vomiting (PONV), Prevention, 4 mg as a single dose by slow i.v. injection at induction; alternatively, 8 mg by mouth 1 hour prior to anaesthesia followed by 2 further 8 mg doses at 8 hourly intervals.
Treatment, 4 mg as a single dose by slow i.v. injection.
There is no experience of PONV in children and limited experience in the elderly.
Elderly, as for younger adults.
Child (above 4 years), by slow intravenous injection or by intravenous infusion over 15 minutes, 5 mg/m^2; then, 4 mg by mouth every 8 hours for up to 5 days.

POM **ZOFRAN®** *(GSK)*
Tablets, Ondansetron HCl 4 mg, 8 mg; both are yellow, oval, f–c tabs marked 'GLAXO' on one face, and '4' and '8' respectively on the other.
Injection, Ondansetron HCl 2 mg per ml; aqueous solution in 2 ml and 4 ml amps.

PROCHLORPERAZINE

Therapeutic category: Antiemetic; Antipsychotic Agent.
Pharmacology: Prochlorperazine acts on the chemoreceptor zone to inhibit nausea and vomiting. See notes above.
Indications: Vertigo due to Menier's disease and other labyrinthe disorders, severe nausea and vomiting; migraine.
Contra-indications: Comatose states, bone marrow depression, liver damage.

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Precautions: Undiagnosed and prolonged vomiting; warn patients of impaired judgement and dexterity.

Interactions: CNS depressants, alcohol, analgesics,antihypertensives, antidepre- ssants, anticonvulsants, antidiabetics.

Adverse effects: CNS disturbances, anticholinergic effects, allergic effects and extrapyramidal symptoms - occur rarely at low dosage.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: •Dilute oral solution with fruit juice, milk, carbonated drink, or water.

•Give I.M. deep; avoid S.C. route. Do not mix with other drugs in the same syringe.

•Observe closely for orthostatic hypotension especially when given I.V.

•Avoid skin contact with oral solution or injection, contact dematitis has occured.

•Warn patient that drug may cause drowsiness, impair judgement and co-ordination.

•Inform patient that drug may cause photosensitivity, to avoid excessive sunlight.

•Observe for extrapyramidal symptoms; advise patient to notify physician of involuntary movements or feelings of restlessness.

Dose: By mouth, *nausea and vomiting, acute attack,* 20 mg initially then 10 mg after 2 hours; prevention, 5-10 mg 2-3 times daily.
Child (Over 10 kg), 0.25 mg/kg 2-3 times daily. Not recommended for children under 10 kg.
See lit. for details.

POM **Prochlorperazine** *(EDL 18.2)*
Tablets, Prochlorperazine (as maleate) 5 mg, 25 mg.
Syrup, Prochlorperazine (as mesylate) 5 mg per 5 ml
Injection, Prochlorperazine (as mesylate) 12.5 mg per ml; in 1 ml, 2 ml amps.

POM **STEMETIL**® *(May & Baker)*
Tablet, Prochlorperazine maleate 5 mg; cream tab. marked with tab. name and strength.
5 mg - 25; 250.

PROMETHAZINE

Therapeutic category: Antiemetic; Antihistamine, H_1 Blocker; Sedative.

Indications: Nausea, vomiting, labyrinthine disorders, motion sickness; premedication (section 3.2).

Contra-indications: Porphyria.

Precautions: Prostatic hypertrophy; urinary retention; glaucoma; hepatic disease (Appendix 5); epilepsy; elderly and children (more susceptible to adverse effects); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Drowsiness, dizziness, sedation (but paradoxical stimulation may occur, especially with high doses or in children and elderly); headache, psychomotor impairment; urinary retention, dry mouth, blurred vision, gastrointestinal disturbances; hypersensitivity reactions; rashes, photosensitivity reactions; jaundice; blood disorders; cardiovascular adverse effects—after injection; venous thrombosis at site of intravenous injection; pain on intramuscular injection.

Advice to patients: See Label 2 in Appendix 6. May cause drowsiness, impair judgement and coordination; may cause photosensitivity, sunscreening agent and protective clothing may be used; avoid excessive sunlight; notify physician of involuntary movements or feelings of restlessness.

Nursing considerations: •Give with food or milk to reduce GI distress; food may slightly reduce absorption.

•Give I.M. deep into a large muscle mass and rotate injection sites. Avoice S.C route.

•I.V. dose must be diluted to a max. concentration of 25-50 mg/9 ml and infused at max. rate of 25 mg/2 minute. Rapid I.V. administration may cause a transient fall in B.P.

•Coffee or tea may reduce drowsiness; give chewing gum or ice chips to relieve dry mouth.

Dose: *Nausea and vomiting (including postoperative)*, by mouth or by intramuscular injection or by slow intravenous injection (diluted to 2.5 mg/ml in water for injection), ADULT 12.5–25 mg, repeated at intervals of not less than 4 hours (usual maximum, 100 mg in 24 hours).
Motion sickness, prevention, by mouth, ADULT 20–25 mg at bedtime on night before travel, repeated on day of travel if necessary; CHILD 2–5 years, 5 mg at night and on day of travel, if necessary; 5–10 years, 10 mg at night and on day of travel, if necessary.

DILUTION AND ADMINISTRATION: INTRAVENOUS INJECTION, ACCORDING TO MANFACTURER'S DIRECTIONS.

POM **Promethazine** *(WMF 17.2)*
Tablets, Promethazine HCl 10 mg, 25 mg
Elixir (Oral solution), Promethazine HCl 5 mg/5 ml.
Injection (Solution for injection),

Promethazine HCl 25 mg/ml, 2-ml ampoule.

POM **Promethazine** *(EDL 18.2)*
Tablets, Promethazine HCl 10 mg, 25 mg; or promethazine theoclate 25 mg.
Syrup, Promethazine HCl 5 mg per 5 ml.
Injection, Promethazine HCl 25 mg per ml; in 1 ml, 2 ml amps.

POM **AVOMINE®** *(May & Baker)*
Tablet, Promethazine theoclate 25 mg; white scored tab. marked 'AVOMINE'.
25 mg - 10; 250 .

See Section 8.1 for other Preparations.

TROPISETRON

Indications: Prevention of cancer-chemotherapy-induced nausea and vomiting.
Contra-indications: Hypersensitivity to tropisetron or any other components of the formulations; pregnancy.
Precautions: Patients who drive or operate machinery (may cause fatigue and dizziness); uncontrolled hypertension (daily doses higher than 10mg should be avoided since they may cause a further increase in blood pressure); breast-feeding (to be avoided since it is not known whether tropisetron is excreted into human milk.
Interactions:
•Rifampicin or other liver enzyme-inducing drugs e.g. phenobarbital (concomitant administration lowers plasma concentration of tropisetron which will necessitate increase in dosage for extensive metabolisers but not for poor metabolisers).
•Ingestion of the capsule with food causes slight increase in bioavailability which is not clinically relevant.
Adverse effects: Headache, constipation, dizziness, fatigue, and G.I. disorders such as abdominal pain and diarrhoea. Some of these may be caused by the concomitant chemo-therapy or the underlying disease.
Advice to patients: See Label 2 in Appendix 6.
Dose: *Adult*, as a 6-day course of 5 mg daily, given I.V. on day 1 shortly before cancer chemotherapy either as an infusion (1 ampoule diluted in 100 ml of a common infusion fluid such as normal saline, Ringer's solution, glucose 5%, or levulose 5%) or as a slow injection, followed by oral administration on days 2 to 6. Capsules should be taken with water in the morning immediately upon rising, one hour before food intake.
Child (over 2 years of age), 0.2 mg/kg, up to a maximum daily dose of 5 mg per day.
To be administered as 6-day course as for adult (see under *adult* above).
Tropisetron can be given as a drink solution immediately after diluting the appropriate amount of tropisetron from the ampoule in orange juice or cola, and should be taken in the morning, one hour before food intake.

POM **NAVOBAN®** *(Novartis)*
Capsule, Tropisetron (as HCl) 5 mg.
Injection, Tropisetron (as HCl) 5 mg per 5 ml; in 5 ml amp.

4.7 Antihaemorrhoidal drugs

Haemorrhoids are enlarged or varicose veins of the tissues at the anus or rectal outlet. They are the most frequent cause of rectal bleeding. Anal and perianal pruritus, soreness and excoriation occur commonly in patients suffering from haemorrhoids, fistulas and proctitis. Careful local toilet with attention to any minor faecal soiling, adjustment of the diet to avoid hard stools, the use of bulk-forming materials such as bran and a high residue diet are helpful.
Soothing preparations containing mild astringents such as bismuth subgallate, zinc oxide and hamamelis with lubricants, vasoconstrictors or mild antiseptics, in the form of topical ointments, creams and suppositories, are used to provide symptomatic relief. Local anaesthetics are included in some preparations to relieve pain. Corticosteroids may be combined in such preparations (but should only be used after exclusion of infection); they are suitable for occasional short-term use, but prolonged use can cause atrophy of the anal skin.

Anal and perianal pruritus, soreness and excoriation occur commonly in patients suffering from haemorrhoids, fistulas, and proctitis. These conditions are best treated by application of bland ointments, suppositories, and dusting–powders. Adjustment of diet to avoid hard stools is also helpful.
Bland Soothing Preparations contain mild astringents such as bismuth subgallate or oxide, zinc oxide, balsam peru may give symptomatic relief in haemorrhoids.

Vasoconstrictors such as phenylephrine may also be included in the preparations for haemorrhoids.

Local Anaesthetics are used to relieve pain associated with haemorrhoids, and pruritus ani. They include lignocaine and pramoxine. They should not be used for longer than 2 weeks since they may cause sensitisation of the anal skin.

Corticosteroids such as **Betamethasone** and **Hydrocortisone** are often combined with antibiotics, local anaesthetics, and soothing agents for short–term use in haemorrhoids but not in the presence of herpes infection.

Administration: Suppository should be inserted into the rectum night and morning and after a bowel movement.

Rectal Ointments and creams are applied night and morning and after a bowel movement, externally or by rectum using a rectal nozzle.

BETAMETHASONE plus LIGNOCAINE plus PHENYLEPHRINE

Indications: Haemorrhoids and associated ano-rectal disorders.

Dose: One suppository morning and night.
Ointment, apply 2-3 times daily.

POM **Bethamethasone plus Lignocaine plus Phenylephrine** *(EDL 18.3)*

Rectal ointment, Betamethasone valerate 0.05%, lignocaine HCl 2.5%, phenylephrine HCl 0.1%.

Suppository, 0.5 mg + 40 mg + 2 mg respectively.

BENZYLBENZOATE plus BISMUTH OXIDE plus BALSAM PERU B.P.C. plus RESORCINOL plus ZINC OXIDE plus BISMUTH SUBGALLATE *(EDL 18.3)*

Suppository, 33 mg + 24 mg + 49 mg + 24 mg + 296 mg + 59 mg respectively.

Indications: Haemorrhoids and other ano-rectal conditions.

Dose: 1 suppository night and morning, and after defecation.
Not recommended for children.

POM **ANUPROCT**® *((Pharma-Deko)*

Suppository, As above.

PHENYLEPHRINE plus HYDROCORTISONE

Indications: Haemorrhoids and the associated pain, itching and burning.

Dose: 1 suppository 3-5 times daily, especially at night, in the morning and after each bowel movement.
Ointment, apply to the affected rectal area 3-5 times daily as for the suppository. Lubricate applicator before each application and thoroughly cleanse after each use.
Not recommended for children under 12 years.

POM **PREPARATION H**® *(Matbeny)*

Suppository/Ointment, Phenylephrine HCl 0.25%, hydrocortisone 1%, shark liver oil 3%, cocoa butter 85.5%.

Pack (suppository) - 12; ointment, 26 g.

PRAMOXINE HCL plus HYDROCORTISONE plus BENZYL BENZOATE plus BISMUTH OXIDE plus BALSAM PERU B.P.C. plus ZINC OXIDE plus BISMUTH SUBGALLATE *(EDL 18.3)*

Suppository, 27 mg + 5 mg + 33 mg +24 mg + 49 mg + 296 mg + 59 mg respectively.

Indications: Haemorrhoids and other ano–rectal conditions.

PREDNISOLONE plus CINCHOCAINE

Indications: Local treatment of haemorrhoids, proctitis, anal fissures.

Dose: Insert 1 suppository daily after a bowel movement, for 5-7 days (in severe cases initially 2-3 times daily).
Ointment, apply twice daily for 5-7 days (3-4 times daily on 1st day if necessary), then once daily for a few days after symptoms have cleared.

POM **SCHERIPROCT** ® *(CHI/Schering)*

Suppository/Rectal Ointment, Prednisolone caproate, cinchocaine HCl.

Pack - 12 Suppositories/Pack; 10 g Ointment/tube.

TRIBENOSIDE plus LIDOCAINE

Indications: External and internal haemorrhoids.

Contra-indications: Hypersenitisivity to the active substances.

Precautions: Pregnancy, breast-feeding.

Adverse effects: Slight burning sensation, pain, increased intestinal motility.

Dose: One suppository mornings and evenings later reduced to one supp. daily.

POM **Tribenoside plus Lidocaine** *(EDL 18.3)*

Rectal cream, Tribenoside 5%, lidocaine HCl

2%.
Suppository, Tribenoside 400 mg, lidocaine HCl 40 mg.

POM **PROCTO-GLYVENOL**® *(Oculus)*
Suppositories, Tribenoside 400 mg, lignocaine HCl 40 mg.
Rectal cream, Tribenoside 5%, lignocaine HCl 2%.
Pack - 30 g.

4.8 Anti-inflammatory drugs

Ulcerative colitis and Crohn disease are inflammatory diseases of the intestinal tract.

ULCERATIVE COLITIS
Acute attacks of ulcerative colitis require treatment with local corticosteroids such as **hydrocortisone** in the form of suppositories or retention enemas. Because of the risk of intestinal perforation, rectal administration of hydrocortisone must be used with extreme caution in patients with severe ulcerative disease and should not be given to such patients without conducting a thorough proctological examination. More extensive disease requires oral corticosteroid treatment and severe extensive or fulminant disease needs hospital admission and intravenous corticosteroid administration; other therapy may include intravenous fluid and electrolyte replacement, blood transfusion, and possibly parenteral nutrition and antibiotics.

The aminosalicylate **sulfasalazine** is useful in the treatment of symptomatic disease. It also has value in the maintenance of remission in ulcerative colitis for which corticosteroid treatment is unsuitable because of adverse effects. In resistant or frequently relapsing cases azathioprine 2–2.5 mg/kg daily (section 12.2) given under close supervision may be helpful. Laxatives are required to facilitate bowel movement when proctitis is present. Antimotility drugs such as codeine and antispasmodic drugs should not be used in active ulcerative colitis because they can precipitate paralytic ileus and megacolon. Diarrhoea resulting from reduced bile salt absorption may improve with colestyramine. General nutritional care and appropriate supplements are essential. High-fibre or low-residue diets should be used as appropriate. Irritable bowel syndrome during remission of ulcerative colitis requires avoidance of a high-fibre diet and possibly treatment with an antispasmodic (see section 4.2).

CROHN DISEASE
Treatment of Crohn disease of the colon is similar to that of ulcerative colitis. In small bowel disease **sulfasalazine** may have marginal benefit. Symptoms and inflammation associated with disease exacerbation are suppressed by oral corticosteroids such as prednisolone. **Metronidazole** may be beneficial in the treatment of active Crohn disease particularly with perianal involvement, possibly through its antibacterial activity. Other antibacterials should be given if specifically indicated (for example, sepsis associated with fistulas and perianal disease) and for managing bacterial overgrowth in the small bowel. General nutritional care and appropriate supplements are essential.

HYDROCORTISONE

Hydrocortisone retention enema is a representative rectal corticosteroid preparation (other than suppository). Various formulations can serve as alternatives.
Hydrocortisone rectal preparations are complementary drugs.

Indications: Ulcerative colitis, proctitis, proctosigmoiditis; anaphylaxis (section 8); skin (section 15.3); adrenocortical insufficiency (section 10.3).
Contra-indications: Use of enemas in bowel obstruction, bowel perforation, or extensive fistulas; untreated infections.
Precautions: Proctological examination required before treatment; systemic absorption may occur (see section 10.3); prolonged use should be avoided; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Local pain or burning sensation; rectal bleeding (reported with use of enema); exacerbation of untreated infections; suppositories may stain fabrics; systemic adverse effects (section 10.3).
Dose: *Ulcerative colitis, proctitis*, by rectum (suppositories), ADULT 25 mg twice daily for 2 weeks; may be increased to 25 mg 3 times daily or 50 mg twice daily in severe cases; in factitial proctitis treatment may be required for 6–8 weeks
Ulcerative colitis, ulcerative proctitis,

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ulcerative proctosigmoiditis, by rectum (retention enema), ADULT 100 mg at night for 21 days or until clinical and proctological remission; if no clinical and proctological improvement after 21 days, discontinue; treatment for 2–3 months may be required for proctological remission; when used for more than 21 days, discontinue gradually using 100 mg every other night for 2–3 weeks.

POM **Hydrocortisone** *(WMF 17.4)*
Suppositories, Hydrocortisone acetate 25 mg.
Retention enema (Rectal solution), Hydrocortisone 100 mg; in 60-ml bottle.

SULFASALAZINE

Sulfasalazine is a representative aminosalicylate. Various drugs can serve as alternatives.

Indications: Ulcerative colitis; Crohn disease; severe rheumatoid arthritis (section 2.1.2).

Contra-indications: Hypersensitivity to salicylates or sulfonamides; child under 2 years; porphyria; intestinal or urinary obstruction; severe renal impairment

Precautions: Renal impairment (Appendix 4); hepatic impairment; G6PD deficiency; slow acetylator status; monitor blood counts and liver function initially and at monthly intervals for first 3 months; monitor kidney function initially and at intervals during treatment; history of allergy; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

BLOOD DISORDERS: PATIENTS SHOULD BE ADVISED TO REPORT ANY UNEXPLAINED BLEEDING, BRUISING, PURPURA, SORE THROAT, FEVER OR MALAISE OCCURRING DURING TREATMENT; BLOOD COUNT SHOULD BE PERFORMED AND SULFASALAZINE STOPPED IMMEDIATELY IF THERE IS SUSPICION OR EVIDENCE OF BLOOD DISORDER.

Adverse effects: Nausea, exacerbation of colitis; diarrhoea, loss of appetite, fever, blood disorders (including Heinz body anaemia, megaloblastic anaemia, leukopenia, neutropenia, thrombocytopenia); hypersensitivity reactions (including rash, urticaria, Stevens-Johnson syndrome (erythema multiforme), exfoliative dermatitis, epidermal necrolysis, pruritus, photosensitization, anaphylaxis, serum sickness, interstitial nephritis, lupus erythematosus-like syndrome); lung complications (including eosinophilia, fibrosing alveolitis); ocular complications (including periorbital oedema); stomatitis, parotitis; ataxia, aseptic meningitis, vertigo, tinnitus, alopecia, peripheral neuropathy, insomnia, depression, headache, hallucinations; kidney reactions (including proteinuria, crystalluria, haematuria); oligospermia; rarely acute pancreatitis, hepatitis; urine may be coloured orange; some soft contact lenses may be stained.

Dose: *Ulcerative colitis*, by mouth, ADULT 1–2 g 4 times daily in acute attack until remission, reducing to maintenance dose of 500 mg 4 times daily; CHILD over 2 years, 40–60 mg/kg daily in acute attack, reducing to maintenance dose of 20–30 mg/kg daily.

Active Crohn disease, by mouth , ADULT 1–2 g 4 times daily in acute attack until remission occurs; CHILD over 2 years, 40–60 mg/kg daily in acute attack.

Ulcerative colitis, Crohn colitis, by rectum (suppositories, used alone or in conjunction with oral therapy), ADULT 0.5–1 g morning and evening after a bowel movement; by rectum (retention enema), ADULT 3 g at night retained for at least an hour; CHILD not a suitable formulation.

POM **Sulfasalazine** *(WMF 17.4)*
Tablets, Sulfasalazine 500 mg.
Suppositories, Sulfasalazine 500 mg.
Retention enema (Rectal solution), Sulfasalazine 3 g; in 100-ml bottle.

5. Cardiovascular system drugs

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5.1 Drugs used in heart failure

5.2 Diuretics

5.2.1 Thiazide diuretics

5.2.2 Loop diuretics

5.2.3 Potassium-sparing diuretics

5.2.4 Osmotic diuretics

5.3 Antihypertensive drugs

5.3.1 Beta–adrenoceptor blocking drugs

5.3.2 Vasodilators

5.3.3 Alpha-adrenoceptor blocking drugs

5.3.4 Centrally acting antihypertensive drugs

5.3.5 Angiotensin-converting enzyme (ACE) inhibitors

5.3.6 Calcium-channel blockers

5.3.7 Diuretics (see also section 5.2)

5.4 Antiarrhythmic drugs

5.5 Antianginal drugs

5.6 Antithrombotic drugs and myocardial infarction

5.7 Lipid–regulating drugs

5.1 Drugs used in heart failure

Treatment of heart failure aims to relieve symptoms, improve exercise tolerance, reduce incidence of acute exacerbations, and reduce mortality. Drugs used to treat heart failure due to left ventricular systolic dysfunction include ACE inhibitors, diuretics, cardiac glycosides and vasodilators. In addition, measures such as weight reduction, moderate salt restriction, and appropriate exercise should be introduced.

The primary treatment of heart failure is with angiotensin-converting enzyme inhibitors (ACE inhibitors) such as **enalapril** which can be used in all stages of chronic heart failure to prevent further deterioration and progression of heart disease.

A thiazide diuretic such as **hydrochlorothiazide** is used in the management of mild to moderate heart failure when the patient has mild fluid retention and severe pulmonary oedema is not present; however thiazides are ineffective if renal function is poor. In these patients, and in more severe fluid retention, a loop diuretic such as **furosemide** (section 5.2.2) is required. In severe fluid retention, intravenous furosemide produces relief of breathlessness and reduces preload sooner than would be expected from the time of onset of diuresis. Hypokalaemia may develop, but is less likely with the shorter-acting loop diuretics than with the thiazides; care is needed to avoid hypotension.

A combination of a thiazide and a loop diuretic may be required to treat refractory oedema. The combination often produces a synergistic effect on solute and water excretion, which relieves symptoms in the diuretic-resistant heart failure patient. However, the combination may produce excessive intravascular volume depletion and electrolyte disturbances including potentially life-threatening hypokalaemia.

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The aldosterone antagonist **spironolactone** (section 5.2.3) may be considered for patients with severe heart failure who are already receiving an ACE inhibitor and a diuretic; a low dose of spironolactone (usually 25 mg daily) reduces symptoms and mortality rate in these patients. Close monitoring of serum creatinine and potassium is necessary with any change in treatment or in the patient's clinical condition.

Digoxin, a cardiac glycoside, increases the strength of cardiac muscle contractions and increases cardiac output. In mild heart failure, digoxin inhibits the sympathetic nervous system and produces arterial vasodilation. It produces symptomatic improvement, increases exercise tolerance, and reduces hospitalization, but it does not reduce mortality. It is considered for patients with atrial fibrillation and those who remain symptomatic despite treatment with an ACE inhibitor, a diuretic, and a suitable beta-blocker.

Vasodilators are used in heart failure to reduce systemic vascular resistance. **Isosorbide dinitrate** (section 5.5) produces mainly venous dilatation, which reduces left ventricular preload, leading to a reduction in pulmonary congestion and dyspnoea. **Hydralazine** (section 5.3.2) produces mainly arterial vasodilation, which reduces left ventricular afterload, and increases stroke volume and cardiac output. Isosorbide dinitrate and hydralazine can be used in combination when an ACE inhibitor cannot be used.

Dopamine, an inotropic sympathomimetic, may be given for short periods in the treatment of severe heart failure. Dosage is critical; at low doses it stimulates myocardial contractility and increases cardiac output, however, higher doses (more than 5 micrograms/kg per minute) cause vasoconstriction, with a worsening of heart failure.

DIGOXIN

Therapeutic category: Cardiac glycoside; Anti-arrhythmic agent.

Indications: Heart failure; arrhythmias (section 5.4)

Contra-indications: Hypertrophic obstructive cardiomyopathy (unless also severe heart failure); Wolff-Parkinson-White syndrome or other accessory pathway, particularly if accompanied by atrial fibrillation; intermittent complete heart block; second-degree atrioventricular block.

Precautions: Recent myocardial infarction; sick sinus syndrome; severe pulmonary disease; thyroid disease; elderly (reduce dose); renal impairment (Appendix 4); avoid hypokalaemia; avoid rapid intravenous administration (nausea and risk of arrhythmias); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Usually associated with excessive dosage and include anorexia, nausea, vomiting, diarrhoea, abdominal pain; visual disturbances, headache, fatigue, drowsiness, confusion, delirium, hallucinations, depression; arrhythmias, heart block; rarely rash, intestinal ischaemia; gynaecomastia on long-term use; thrombocytopenia reported.

Advice to patients: Do not discontinue medication without checking with physician; notify physician if loss of appetite or visual changes occur.

Nursing considerations: •Give with or without food; tablet may be crushed and mixed with food or fluids.
•Give I.V infusion slowly over at least 5 minutes with close monitoring.
•Obtain baseline data before giving first dose namely heart rate and rhythm, B.P., and electrolytes.
•Loading dose may need to be reduced if patient has received cardiac glycoside within the previous 2-3 weeks.
•Apical-radial pulse should be taken for a full minute and significant changes reported to the physician.
•Withhold drug and notify physician if pulse rate falls below 60 beats/minute; may be sign of digitalis toxicity. Other noncardiac signs of toxicity include nausea, vomiting, anorexia, visual disturbances, blurred vision, confusion, and depression.
•Monitor serum potassium and encourage patient to eat potassium-rich foods to avoid hypokalaemia viz banana, orange juice.
•Dosage should be reduced by 20% to 25% when changing from oral to parenteral therapy.

Dose: *Heart failure*, by mouth, ADULT 1–1.5 mg in divided doses over 24 hours for rapid digitalization or 250 micrograms 1–2 times daily if digitalization less urgent; maintenance 62.5–500 micrograms daily (higher dose may be divided), according to renal function and heart rate response; usual range 125–250 micrograms daily (lower dose more appropriate in elderly).
Emergency loading dose, by intravenous infusion over at least 2 hours, ADULT 0.75–1 mg.

NOTE: INFUSION DOSE MAY NEED TO BE REDUCED IF DIGOXIN OR OTHER CARDIAC GLYCOSIDE GIVEN IN PREVIOUS 2 WEEKS.

POM **Digoxin** *(WMF 12.4)*
Tablets, Digoxin 62.5 micrograms, 250 micrograms.
Oral solution, Digoxin 50 micrograms/ml.
Injection (Solution for injection), Digoxin 250 micrograms/ml; in 2-ml ampoule.

POM **Digoxin** *(EDL 12.4)*
Tablets, Digoxin 0.0625 mg, 0.25 mg.
Elixir, Digoxin 0.05 mg per 5 ml
Injection, Digoxin 0.1 mg, 0.25 mg per ml; in 1 ml and 2 ml amps resp.

POM **DIGOXIN-SANDOZ®** *(Novartis)*
Tablet, Digoxin 0.25 mg.
Injection, Digoxin 0.25 mg per ml; in 2 ml amp.

POM **LANOXIN®** *(GSK)*
Tablet, Digoxin 0.25 mg; scored tab.
Pack - 20.
Injection, Digoxin 0.25 mg per ml; in 2 ml amp.

POM **LANOXIN–PG®** *(GSK)*
Tablet, Digoxin 0.0625 mg; blue tab.
Pack - 20.
Elixir, Digoxin 0.05 mg per 5 ml; yellow coloured elixir. To be used undiluted.
Pack - 60 ml.

DOPAMINE

Dopamine HCl is a complementary drug for inotropic support.

Therapeutic category: Sympathomimetic.

Indications: Cardiogenic shock in myocardial infarction or cardiac surgery.

Contra-indications: Tachyarrhythmia, ventricular fibrillation; ischaemic heart disease; phaeo-chromocytoma; hyperthyroidism.

Precautions: Correct hypovolaemia before, and maintain blood volume during treatment; correct hypoxia, hypercapnia, and metabolic acidosis before or at same time as starting treatment; low dose in shock due to myocardial infarction; history of peripheral vascular disease (increased risk of ischaemia of extremities); elderly; **interactions**: Appendix 1.

Adverse effects: Nausea and vomiting; peripheral vasoconstriction; hypotension with dizziness, fainting, flushing; tachycardia, ectopic beats, palpitations, anginal pain; headache, dyspnoea; hypertension particularly in overdosage.

Nursing considerations: •Administer into large vein to prevent the possibility of extravasation; monitor continuously for free flow; in case of extravasation, due to the short half-life of dopamine, withdrawal of drug is often the only necessary treatment. Use phentolamine as antidote; mix 5 mg with 9 ml of NS; inject a small amount of this dilution into extravasated area; blanching should reverse immediately. Monitor site; repeat the antidote if blanching should recur.
•Monitor B.P., pulse rate, urine output, temperature frequently during infusion.
•Observe patient for adverse effects and notify doctor immediately if they occur; dosage may need to be adjusted or discontinued.

Dose: *Cardiogenic shock*, by intravenous infusion into large vein, ADULT initially 2–5 micrograms/kg/minute; gradually increased by 5–10 micrograms/kg/minute according to blood pressure, cardiac output and urine output; seriously ill patients up to 20–50 micrograms/kg/minute.

Dilution and administration: According to manufacturer's directions.

POM **Dopamine** *(WMF 12.4)*
Concentrate for infusion (Concentrate for solution for infusion), Dopamine HCl 40 mg/ml; in 5-ml ampoule.

POM **Dopamine** *(EDL 12.4)*
Injection, Dopamine HCl 40 mg per ml; in 5 ml vial.

ENALAPRIL

Enalapril is a representative angiotensin-converting enzyme inhibitor. Various drugs can serve as alternatives.

Indications: Heart failure (with a diuretic); prevention of symptomatic heart failure and prevention of coronary ischaemic events in patients with left ventricular dysfunction; hypertension (section 5.3).

Contra-indications: Hypersensitivity to ACE inhibitors (including angioedema); renovascular disease; pregnancy (Appendix 2).

Precautions: Use with diuretics; hypotension with first doses, especially in patients on diuretics, on a low-sodium diet, on dialysis, if dehydrated, or with heart failure; peripheral vascular disease or generalized atherosclerosis (risk of clinically silent renovascular disease); use with great care in severe or symptomatic aortic stenosis; monitor renal function before and during treatment; renal impairment (reduce dose, see also

Appendix 4); liver impairment (Appendix 5); possibly increased risk of agranulocytosis in collagen vascular disease; history of idiopathic or hereditary angioedema (use with care or avoid); breastfeeding (Appendix 3); **interactions**: Appendix 1.

USE WITH DIURETICS: RISK OF VERY RAPID FALLS IN BLOOD PRESSURE IN VOLUME-DEPLETED PATIENTS; TREATMENT SHOULD THEREFORE BE INITIATED WITH VERY LOW DOSES. HIGH-DOSE DIURETIC THERAPY (FUROSEMIDE DOSE GREATER THAN 80 MG DAILY) SHOULD BE DISCONTINUED, OR DOSE SIGNIFICANTLY REDUCED, AT LEAST 24 HOURS BEFORE STARTING ENALAPRIL (MAY NOT BE POSSIBLE IN HEART FAILURE—RISK OF PULMONARY OEDEMA). IF HIGH-DOSE DIURETIC CANNOT BE STOPPED, MEDICAL SUPERVISION ADVISED FOR AT LEAST 2 HOURS AFTER ADMINISTRATION OR UNTIL BLOOD PRESSURE STABLE.

ANAPHYLACTOID REACTIONS: AVOID ENALAPRIL DURING DIALYSIS WITH HIGH-FLUX POLYACRILONITRILE MEMBRANES AND DURING LOW-DENSITY LIPOPROTEIN APHERESIS WITH DEXTRAN SULFATE; ALSO WITHHOLD BEFORE DESENSITIZATION WITH WASP OR BEE VENOM.

Adverse effects: Dizziness, headache; less commonly, nausea, diarrhoea, hypotension (severe in rare cases), dry cough, fatigue, asthenia, muscle cramps, rash and renal impairment; rarely, vomiting, dyspepsia, abdominal pain, constipation, glossitis, stomatitis, ileus, anorexia, pancreatitis, liver damage, chest pain, palpitations, arrhythmias, angioedema, bronchospasm, rhinorrhoea, sore throat, pulmonary infiltrates, paraesthesia, vertigo, nervousness, depression, confusion, drowsiness or insomnia, pruritus, urticaria, alopecia, sweating, flushing, impotence, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, pemphigus, taste disturbance, tinnitus, blurred vision; electrolyte disturbances and hypersensitivity-like reactions (including fever, myalgia, arthralgia, eosinophilia, and photo-sensitivity) reported.

Dose: *Heart failure, asymptomatic left ventricular dysfunction*, by mouth, adult, initially 2.5 mg daily under close medical supervision; usual maintenance dose 20 mg daily in 1–2 divided doses.

POM **Enalapril** *(WMF 12.4)*
Tablets, Enalapril 2.5 mg.

HYDROCHLOROTHIAZIDE

Hydrochlorothiazide is a representative thiazide diuretic. Various drugs can serve as alternatives.

Indications: Heart failure; hypertension (section 5.3); oedema (section 5.2.1)

Contra-indications: Severe renal or severe hepatic impairment; hyponatraemia, hypercalcaemia, refractory hypokalaemia, symptomatic hyperuricaemia; Addison disease.

Precautions: Renal and hepatic impairment (Appendices 4 and 5); pregnancy and breastfeeding (Appendices 2 and 3); elderly (reduce dose); may cause hypokalaemia; may aggravate diabetes mellitus and gout; may exacerbate systemic lupus erythematosus; porphyria; **interactions**: Appendix 1.

Adverse effects: Fluid and electrolyte imbalance leading to dry mouth, thirst, gastrointestinal disturbances (including nausea, vomiting), weakness, lethargy, drowsiness, seizures, headache, muscle pains or cramps, hypotension (including postural hypotension), oliguria, arrhythmias; hypokalaemia, hypomagnesaemia, hyponatraemia, hypochloraemic alkalosis, hypercalcaemia; hyperglycaemia, hyperuricaemia, gout; rashes, photosensitivity; altered plasma lipid concentration; rarely impotence (reversible); blood disorders (including neutropenia, thrombocytopenia); pancreatitis, intrahepatic cholestasis; acute renal failure; hypersensitivity reactions (pneumonitis, pulmonary oedema, severe skin reactions).

Dose: *Heart failure*, by mouth, ADULT initially 25 mg daily on rising, increasing to 50 mg daily if necessary; ELDERLY initially 12.5 mg daily.

POM **Hydrochlorothiazide** *(WMF 12.4)*
Tablets, Hydrochlorothiazide 25 mg.

ISOPRENALINE

Synonym: Isoproterenol

Therapeutic category: Sympathomimetic

Pharmacology: It acts almost exclusively on beta-adrenergic receptors unlike dopamine which has indirect effects on alpha-adrenergic receptors. It stimulates the CNS and the heart, increasing cardiac output, excitability, and rate; it also causes peripheral vasodilation and bronchodilation.

Indications: Bradycardia associated with heart block; cardiac arrest; Stokes - Adams

syndrome.

Contra-indications: Hyperthyroidism, severe cardiovascular disorders, digitalis intoxication.

Precautions: Diabetes mellitus, hypertension.

Adverse effects: Nervousness, tachycardia, palpitations, precordial pain, hypotension, sweating, tremor, headache.

Dose: Usually as a solution of the HCl containing 1 mg in 500 ml of dextrose injection by slow I.V. infusion.

POM **Isoprenaline** *(EDL 12.4)*

Injection, Isoprenaline HCl 1 mg per ml; in 2 ml amp.

5.2 Diuretics

5.2.1 Thiazide diuretics
5.2.2 Loop diuretics
5.2.3 Potassium-sparing diuretics
5.2.4 Osmotic diuretics

Diuretics increase urinary excretion of water and electrolytes and are used to relieve oedema associated with heart failure, nephrotic syndrome or hepatic cirrhosis. Some diuretics are used at lower doses to reduce raised blood pressure. Osmotic diuretics are mainly used to treat cerebral oedema, and also to lower raised intraocular pressure.

Most diuretics increase urine volume by inhibiting the reabsorption of sodium and chloride ions in the renal tubule; they also modify renal handling of potassium, calcium, magnesium and urate. Osmotic diuretics act differently; they cause an increase in urine volume by an osmotic effect.

Although **loop diuretics** are the most potent their duration of action is relatively short, whilst **thiazide diuretics** are moderately potent but produce diuresis for a longer period. **Potassium-sparing diuretics** are relatively weak. Carbonic anhydrase inhibitors are weak diuretics which are rarely used for their diuretic effect and are principally used to lower intraocular pressure in glaucoma (section 13.4.4).

ELECTROLYTE IMBALANCE

The adverse effects of diuretic therapy are mainly due to the fluid and electrolyte imbalance induced by the drugs. *Hyponatraemia* is an adverse effect of all diuretics. The risk of *hypokalaemia*, which may occur with both thiazide and loop diuretics, depends more on the duration of action than on potency and is thus greater with thiazides than with loop diuretics (when given in equipotent doses). Potassium-sparing diuretics can cause *hyperkalaemia*. Other electrolyte disturbances include *hypercalcaemia* (thiazides), *hypocalcaemia* (loop diuretics) and *hypomagnesaemia* (thiazide and loop diuretics).

Symptoms of fluid and electrolyte imbalance include dry mouth, thirst, gastrointestinal disturbances (including nausea, vomiting), weakness, lethargy, drowsiness, restlessness, seizures, confusion, headache, muscle pains or cramps, hypotension (including postural hypotension), oliguria, arrhythmias.

ELDERLY

The elderly are more susceptible to electrolyte imbalance than younger patients. Treatment should begin with a lower initial dose of the diuretic (commonly about 50% of the adult dose) and then adjusted carefully according to renal function, plasma electrolytes and diuretic response.

5.2.1 Thiazide diuretics

Thiazide diuretics, such as **hydrochlorothiazide**, are moderately potent and act by inhibiting sodium and chloride reabsorption at the beginning of the distal convoluted tubule. They produce diuresis within 1–2 hours of oral administration and most have a duration of action of 12–24 hours.

Thiazide diuretics are used in the management of oedema associated with mild to moderate congestive heart failure, renal dysfunction or hepatic disease; however, thiazides are not effective in patients with poor renal function (creatinine clearance of less than 30 ml per minute). In severe fluid retention a loop diuretic may be necessary.

In hypertension, a thiazide diuretic is used at a low dose to lower blood pressure with very little biochemical disturbance; the maximum therapeutic effect may not be seen for several weeks. Higher doses should not be used because they do not necessarily increase the hypotensive response but may cause marked changes in plasma potassium, magnesium, uric acid, glucose and lipids. If a thiazide alone

does not lower blood pressure adequately, it may be used in combination with another antihypertensive such as a beta-adrenoceptor antagonist (section 5.3).

Urinary excretion of calcium is reduced by thiazide diuretics and this property is occasionally utilized in the treatment of idiopathic hypercalciuria in patients with calcium-containing calculi. Paradoxically, thiazide diuretics are used in the treatment of diabetes insipidus, since in this disease they reduce urine volume.

Thiazide diuretics, especially in high doses, produce a marked increase in potassium excretion which may cause hypokalaemia; this is dangerous in patients with severe coronary artery disease and those being treated with cardiac glycosides. In hepatic failure hypokalaemia can precipitate encephalopathy, particularly in alcoholic cirrhosis. Potassium-sparing diuretics are used as a more effective alternative to potassium supplements for prevention of hypokalaemia induced by thiazide diuretics; however supplementation with potassium in any form is seldom necessary with the smaller doses of diuretics used to treat hypertension.

BENDROFLUAZIDE

Synonym: Bendroflumethiazide.
Therapeutic category: Thiazide diuretic.
Pharmacology: Bendrofluazide is a thiazide duuretic that increases urine excretion of sodium and water by inhibiting sodium reabsorption in the cortical diluting site of the ascending loop of Henle.
Indications: Oedema, hypertension.
Contra-indications: Severe renal dysfunction, hypercalcaemia.
Precautions: Potassium supplement may be required, diabetes, pregnancy, breast feeding, elderly.
Adverse effects: Hypokalaemia, gout, fatigue, blood dyscrasias, rash, hyperglycaemia.
Nursing considerations: •Administer in the morning to avoid interference with sleep or nocturia.
•Teach patient to take drug with food to prevent nausea, and to eat food rich in potassium viz tomatoes, bananas, citrus fruits, and dates.
•Teach patient to avoid sudden posture changes, but to rise slowly to avoid orthostatic hypotension.
•Observe patient for glycosuria (if diabetic); monitor blood sugar.
•Watch for signs of hypokalaemia, for example, muscle weakness and cramps.
•Elderly patients are especially susceptible to excessive diuresis.
Dose: *Oedema*, initially 5-10 mg in the morning daily or on alternate days; maintenance, 2.5-10 mg 1-3 times weekly.
Hypertension, 2.5-5 mg in the morning.

POM **Bendrofluazide** *(EDL 16)*
Tablets, Bendrofluazide 2.5 mg, 5 mg.

CHLORTALIDONE plus RESERPINE

Therapeutic category: Diuretic/ antihypertensive
Indications: Hypertension
Contra-indications: Anuria, severe renal or hepatic failure, refractory hypokalaemia and hyponatraemia, hypercalcaemia, symptomatic hyperuricaemia, overt depression, parkinson's disease, epilepsy, electroconvulsive therapy, phaeo-chromocytoma, co-medication with MAO inhibitors, acute peptic ulcer, ulcerative colitis.
Precautions: Coronary or cerebral arterio-sclerosis, renal dysfunction; periodic serum electrolyte determinations (in the event of potassium depletion give potassium medication under surveillance); hypomag- nesaemia, hyponatraemia, hyperuricaemia, impaired glucose tolerance, hyperlipidaemia, history of peptic ulcer or depression; acute erosive gastritis, gall-stones, heart failure, fresh myo-cardial infarction, sinus bradycardia, disorders of cardiac conduction, operations; pregnancy, lactation; road-users.
Adverse effects: Depression, anxiety states, GI upsets, postural hypotension, disturbances affecting potency; hypokalaemia, hyponatraemia, hypomagnasaemia, hyperuricaemia, hyperglycaemia, rise in blood lipid levels, thrombocytopenia, changes in the blood count; sinus bradycardia, GI ulceration; disturbances affecting ejaculation, galactorrhoea, gynaecomastia; cardiac arrhythmia, parkinsonism.
Advice to patients: See Label 2 in Appendix 6. May be taken with food or milk; take early in the day to avoid nocturia; may cause drowsiness, may impair judgement and coordination; impotence, gynaecomastia may occur but is reversible; photosensitivity may occur.
Nursing considerations: •Take B.P. with patient lying down and standing.
•Administer drug in the morning to avoid sleep disturbance or interference and nocturia.
•Weigh patient daily and inform doctor of any weight gain.
•Teach patient to rise slowly to sitting or standing position to avoid orthostatic hypotension.

•Consult dietitian to provide high-potassium diet such as citrus fruits, tomatoes, bananas and dates.
•Observe for mental depression and alert family members to report any symptoms; observe for signs of hypokalaemia (muscle weakness and cramps) which can be relieved with potassium sparing diuretics; blood sugar may increase in the diabetic and hence, insulin requirement.

Dose: By mouth, Adult, initially ½ tablet daily according to the patient's needs. Maintenance, not more than 1 tablet daily.

POM **REGROTON®** *(Novartis)*
Tablet, Chlortalidone 50 mg, reserpine 0.25 mg. Pack - 20, 100.

INDAPAMIDE

Therapeutic category: Diuretic; Antihypertensive.
Pharmacology: A thiazide-like diuretic that inhibits sodium reabsorption at the beginning of distal convoluted tubule. It also has a direct vasodilating effect that may be a result of calcium channel-blocking action.
Indications: Oedema; alone or as an adjunct in hypertension.
Contra-indications: Severe renal or hepatic insufficiency, recent cerebrovascular accidents.
Precautions: Pregnancy, breast-feeding; monitor potassium and uric acid levels especially in those predisposed to hypokalaemia and in patients with gout.
Adverse effects: Hypokalaemia, fatigue, orthostatic hypotension, allergic manifestation.
Advice to patients: May be taken with food or milk; take early in the day to avoid nocturia; photosensitivity reactions may occur with skin rash, redness, itching or sunburn (minimise exposure to sunlight).
Nursing considerations: •Give with food or milk only if nausea occurs, since absorption may be decreased slightly.
•Take B.P. with patient lying down and standing.
•May increase serum glucose in diabetic patients.
•Teach patient to change positions slowly to minimise orthostatic hypotension.
Dose: *Oedema*, 2.5-5 mg daily.
Hypertension, 2.5 mg daily.
Note: There is little therapeutic benefit to increasing the dose > 5 mg/day; there is, however, an increased risk of electrolyte disturbances.

POM **Indapamide** *(EDL 16)*
Tablet, Indapamide 2.5 mg.

HYDROCHLOROTHIAZIDE

Hydrochlorothiazide is a representative thiazide diuretic. Various drugs can serve as alternatives.
Indications: Oedema; diabetes insipidus; hypertension (see also section 5.3); heart failure (section 5.1).
Contra-indications: Severe renal or severe hepatic impairment; hyponatraemia, hypercalcaemia, refractory hypokalaemia, symptomatic hyperuricaemia; Addison disease.
Precautions: Renal (Appendix 4), hepatic impairment (Appendix 5); pregnancy (Appendix 2), breastfeeding (Appendix 3); elderly (reduce dose); may cause hypokalaemia; may aggravate diabetes mellitus and gout; may exacerbate systemic lupus erythematosus; porphyria; **interactions**: Appendix 1.
Adverse effects: Hypokalaemia, hypomagnesaemia, hyponatraemia, hypochloraemic alkalosis (for symptoms of fluid and electrolyte imbalance see introductory notes); hypercalcaemia; hyperglycaemia; hyperuricaemia, gout; rash, photosensitivity; altered plasma lipid concentration; rarely impotence (reversible), blood disorders (including neutropenia, thrombocytopenia); pancreatitis, intrahepatic cholestasis and hypersensitivity reactions (including pneumonitis, pulmonary oedema, severe skin reactions) also reported; acute renal failure.
Dose: *Hypertension*, by mouth, ADULT 12.5–25 mg daily; ELDERLY initially 12.5 mg daily.
Oedema, by mouth, ADULT initially 25 mg daily on rising, increasing to 50 mg daily if necessary; ELDERLY initially 12.5 mg daily.
Severe oedema in patients unable to tolerate loop diuretics, by mouth, ADULT up to 100 mg either daily or on alternate days (maximum 100 mg daily).
Nephrogenic diabetes insipidus, by mouth, ADULT initially up to 100 mg daily.

POM **Hydrochlorothiazide** *(WMF 16.1)*
Tablets, Hydrochlorothiazide 25 mg, 50 mg

5.2.2 Loop diuretics

Loop diuretics, or high-ceiling diuretics, such as **furosemide**, are the most potent and rapidly produce an intense dose-dependent diuresis of relatively short

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duration. Oral furosemide produces diuresis within 30–60 minutes of administration, with the maximum diuretic effect in 1–2 hours. The diuretic action lasts for 4–6 hours. Intravenous furosemide produces diuresis within 5 minutes, with the maximum diuretic effect in 20–60 minutes and diuresis complete within 2 hours.

Loop diuretics inhibit reabsorption from the ascending loop of Henlé in the renal tubule and are useful, particularly in situations where rapid and effective diuresis is needed such as reduction of acute pulmonary oedema due to left ventricular failure . They are also used to treat oedema associated with renal and hepatic disorders and are used in high doses in the management of oliguria due to chronic renal insufficiency. Loop diuretics may be effective in patients unresponsive to thiazide diuretics.

Because of their shorter duration of action, the risk of hypokalaemia may be less with loop diuretics than with thiazide diuretics; if required, potassium-sparing diuretics may be used for prevention of hypokalaemia. Loop diuretics may cause hypovolaemia and excessive use can produce severe dehydration with the possibility of circulatory collapse. Furosemide may cause hyperuricaemia and precipitate attacks of gout. Rapid high-dose injection or infusion of furosemide may cause tinnitus and even permanent deafness.

FUROSEMIDE

Furosemide is a representative loop diuretic. Various drugs can serve as alternatives.

Synonym: Frusemide.

Therapeutic category: Loop diuretic.

Indications: Oedema; oliguria due to renal failure.

CONTRAINDICATIONS: Renal failure with anuria; precomatose states associated with liver cirrhosis.

Precautions: Monitor electrolytes particularly potassium and sodium; hypotension; elderly (reduce dose); pregnancy (Appendix 2), breastfeeding (Appendix 3); correct hypovolaemia before using in oliguria; renal impairment (Appendix 4), hepatic impairment (Appendix 5); prostatic enlargement; porphyria; **interactions**: Appendix 1.

Adverse effects: Hypokalaemia, hypomagnesaemia, hyponatraemia, hypochloraemic alkalosis (for symptoms of fluid and electrolyte imbalance, see introductory notes), increased calcium excretion, hypovolaemia, hyperglycaemia (but less often than with thiazide diuretics); temporary increase in plasma cholesterol and triglyceride concentration; less commonly hyperuricaemia and gout; rarely rash, photosensitivity, bone marrow depression (withdraw treatment), pancreatitis (with large parenteral doses), tinnitus and deafness (with rapid administration of large parenteral doses and in renal impairment; deafness may be permanent if other ototoxic drugs taken).

Advice to patients: May be taken with food or milk to minimise GI upset; rise slowly from a lying or sitting position to minimise dizziness, lightheadedness, or fainting, also use extra care when exercising, standing for long period of time, and during hot weather; take last dose of day early in the evening to prevent nocturia.

Nursing considerations: •Give oral and I.M. doses in the morning to prevent nocturia; second doses should be given in early afternoon; give I.V. slowly over 1-2 minutes..

•Parenteral therapy should only be used in children when oral route is not possible.

•Monitor serum potassium, watch for signs of hypokalaemia, e.g., muscle weakness and cramps.

•Monitor weight and I & 0 daily; in high doses, monitor hearing; check B.P. lying and standing, to monitor postural hypotension (frusemide is a very potent loop diuretic).

•Test urine to assess urinary glucose if patient is diabetic.

•Consult dietician to provide high potassium diet; advise patient to limit alcohol intake and strenous exercise in hot weather to prevent exacerbating orthostatic hypotension.

•Instruct patient to immediately report ringing in the ears, severe abdominal pain or sore throat and fever (these may indicate frusemide toxicity).

•Check for signs of confusion especially in the elderly.

Dose: *Oedema*, by mouth, ADULT initially 40 mg daily on rising; maintenance, 20–40 mg daily; may be increased to 80 mg daily or more in resistant oedema; CHILD 1–3 mg/kg daily (maximum 40 mg daily).

Acute pulmonary oedema, by slow intravenous injection, ADULT 20–50 mg, if necessary increase by 20-mg steps every 2 hours; if effective single dose is more than 50 mg, consider using slow intravenous infusion at a rate not exceeding 4 mg/minute; CHILD 0.5–1.5 mg/kg daily

(maximum 20 mg daily).
Oliguria (glomerular filtration rate less than 20 ml/minute), by slow intravenous infusion at a rate not exceeding 4 mg/minute, ADULT initially 250 mg over 1 hour; if urine output not satisfactory during hour after first dose, infuse 500 mg over 2 hours then, if no satisfactory response during hour after second dose, infuse 1 g over 4 hours; if no response after third dose, dialysis probably necessary.

NOTE: DOSE TO BE DILUTED IN SUITABLE AMOUNT OF INFUSION FLUID, DEPENDING ON HYDRATION OF PATIENT. I.V. injections should be given slowly over 1-2 minutes; maximum rate of administration for infusion is 4 mg/minute; replace parental therapy with oral therapy as soon as possible.

POM **Furosemide** *(WMF 16.2)*
Tablets, Furosemide 40 mg.
Injection (Solution for injection), Furosemide 10 mg/ml; in 2-ml ampoule.

POM **Furosemide** *(EDL 16)*
Tablet, Furosemide 40 mg.
Injection, Furosemide 10 mg per ml; in 2 ml amp.

POM **APO-FUROSEMIDE®** *(Lahams)*
Tablet, Furosemide 40 mg; yellow, scored tab. marked 'APO 40'.
40 mg - 1000.

POM **DIUREMID®** *(Hovid)*
Tablet, Furosemide 40 mg
40 mg - 40; 1000.

POM **FRUMED®** *(Fill Pharma)*
Tablet, Furosemide 40 mg
40 mg - 500.
Injection, Furosemide BP 20 mg per 2 ml; in 2-ml amber ampoule.

POM **FUSID®** *(Dizpharm)*
Tablet, Furosemide 40 mg.
40 mg - 250.
Injection, Furosemide 20 mg per 2 ml.
Pack - 25.

POM **FUZIL®** *(Beta Drugs)*
Injection, Furosemide BP 20 mg per ampoule; sterile solution of furosemide sodium hydroxide and sodium chloride.

POM **NGC-DIUREX®** *(NGC)*
Tablet, Furosemide 40 mg.
40 mg - 10; 1000.

POM **SUPAVIN®** *(Justeen)*
Injection, Furosemide 10 mg per 2 ml.
Pack – 2 ml x 10's.

5.2.3 Potassium-sparing diuretics

Potassium-sparing diuretics include **amiloride** and **spironolactone**; they are weak diuretics and reduce potassium excretion and increase sodium excretion in the distal tubule. Amiloride acts about 2 hours after oral administration, reaching a peak in 6–10 hours and persisting for about 24 hours. Spironolactone, which acts by antagonising aldosterone, has a relatively slow onset of action requiring 2–3 days to achieve maximum diuretic effect, and a similar period of 2–3 days for diuresis to cease after discontinuation of treatment.

Amiloride may be used alone, but its principal use is in combination with a thiazide or a loop diuretic to conserve potassium during treatment of congestive heart failure or hepatic cirrhosis with ascites.

Spironolactone is used in the treatment of refractory oedema due to heart failure, hepatic cirrhosis (with or without ascites), nephrotic syndrome and ascites associated with malignancy. It is frequently given with a thiazide or a loop diuretic, helping to conserve potassium in those at risk from hypokalaemia. A low dose of spironolactone is beneficial in severe heart failure in patients who are already taking an ACE inhibitor and a diuretic. Spironolactone is used in the diagnosis and treatment of primary hyperaldosteronism; presumptive evidence for diagnosis is provided by correction of hypokalaemia and of hypertension.

The most dangerous adverse effect of potassium-sparing diuretics, such as amiloride or spironolactone, is hyperkalaemia, which can be life-threatening. These diuretics are thus best avoided or used very carefully in patients who have or may develop hyperkalaemia, such as those with renal failure, patients receiving other potassium-sparing diuretics and patients taking ACE inhibitors or potassium supplements.

AMILORIDE

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Indications: Oedema associated with heart failure or hepatic cirrhosis (with ascites), usually with thiazide or loop diuretic.

Contra-indications: Hyperkalaemia; renal failure.

Precautions: Monitor electrolytes, particularly potassium; renal impairment (Appendix 4); diabetes mellitus; elderly (reduce dose); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Hyperkalaemia, hyponatreamia (for symptoms of fluid and electrolyte imbalance see introductory notes), diarrhoea, constipation, anorexia; paraesthesia, dizziness, minor psychiatric or visual disturbances; rash, pruritus; rise in blood urea nitrogen.

Dose: *Oedema, used alone*, by mouth, initially 10 mg daily in 1 or 2 divided doses, adjusted according to response (maximum 20 mg daily). *Combined with a thiazide or a loop diuretic*, by mouth, initially 5 mg daily, increasing to 10 mg if necessary (maximum 20 mg daily).

POM **Amiloride** *(WMF 16.3)*
Tablets, Amiloride hydrochloride 5 mg.

AMILORIDE plus HYDROCHLOROTHIAZIDE

Therapeutic category: Diuretic/ antihypertensive

Indications: Oedema of cardiac origin; hepatic cirrhosis with ascites and oedema; CHF; hypertension.

Contra-indications: Hyperkalaemia, renal insufficiency, potassium supplementation, Diabetes mellitus.

Precautions: Impaired hepatic function, pregnancy, breast-feeding.

Adverse effects: Headache, weakness, nausea, rash, dizziness; orthostatic hypotension, impotence.

Advice to patients: May be taken with food or milk to prevent nausea; take early in the day to avoid nocturia or sleep disturbance; avoid salt substitutes and potassium rich foods such as oranges and bananas unless otherwise ordered by the physician; report any muscle cramps, weakness, nausea, or dizziness; use caution when operating machinery or performing other tasks requiring alertness; photosensitivity reactions may occur with skin rash, redness, itching or sunburn; may increase blood glucose levels in diabetics.

Nursing considerations: •Assess fluid status via daily weights, I & 0 ratios, standing and supine blood pressures.
•Tell patient to check with doctor before taking OTC preparations.
•Advise patient to rise slowly to prevent sudden posture change and orthostatic hypotension; observe for hyperkalaemia.

Dose: Adult, 1-2 tabs daily; up to a max. 4 tabs. daily.
Not recommended for children.

POM **Amiloride plus Hydrochlorothiazide** *(EDL 16)*
Tablet, Amiloride HCl 5mg, hydrochlorothiazide 50 mg.

POM **APO-AMILZIDE®** *(Lahams)*
Tablet, Amiloride HCl 5 mg, hydrochlorothiazide 50 mg; peach, scored tab. marked 'APO 5/50'.
Pack - 1000.

POM **JURETIC®** *(Juhel)*
Tablet, Amiloride HCl 5 mg, Hydrochlorothiazide 50 mg; orange scored diamond-shaped tablet marked '5/50' on one side and 'Juhel' on the reverse.
Pack - 10 x 10's (in blister); 500's (in jars).

POM **MODURETIC®** *(Bolax/BPP)*
Tablet, Amiloride HCl 5 mg, hydrochlorothiazide 50 mg; peach, half-scored, diamond-shaped tab marked 'MSD 917'.
Pack - 30; 500.

POM **NORMORETIC®** *(Neimeth)*
Tablet, Amiloride HCl 5 mg, hydrochlorothiazide 50 mg.
Pack - 10; 100; 200.

SPIRONOLACTONE

Therapeutic category: Potassium Sparing Diuretic; Antihypertensive.

Pharmacology: Spironolactone is a steroid with a structure resembling that of aldosterone. It acts on the distal portion of the renal tubule as a competitive inhibitor of aldosterone increasing sodium and water excretion and reducing potassium excretion.

Indications: Refractory oedema in congestive heart failure; adjunct to ACE inhibitor and diuretic in severe congestive heart failure; nephrotic syndrome; hepatic cirrhosis with ascites and oedema; ascites associated with malignancy; primary hyperaldosteronism.

Contra-indications: Pregnancy (Appendix 2); breastfeeding; hyperkalaemia; hyponatraemia; severe renal impairment; Addison disease.

Precautions: Monitor blood urea nitrogen and plasma electrolytes (discontinue if hyperkalaemia); elderly (reduce dose); diabetes mellitus; renal impairment (Appendix 4); hepatic impairment; porphyria; high doses carcinogenic in rodents; **interactions**: Appendix 1.

Adverse effects: Hyperkalaemia, hyponatraemia, hyperchloraemic acidosis, dehydration (for symptoms of fluid and electrolyte imbalance see introductory notes); transient increase in blood urea nitrogen; diarrhoea; gynaecomastia, menstrual irregularities; impotence, hirsutism, deepening of voice; rash, ataxia, fever, hepatotoxicity.

Advice to patients: Avoid hazardous activities such as driving, until response to drug is known; take with meals or milk, if nausea occurs; avoid excessive ingestion of foods high in potassium or use of salt substitutes.

Nursing considerations: •Give with meals if nausea occurs; may slightly reduce absorption.

•Give in the morning to avoid interference with sleep.

•Diuretic effect may be delayed 2-3 days and maximum hypotensive effect may be delayed 2-3 weeks.

Advise patient to avoid potassium-rich food like oranges, bananas.

•Weigh patient daily and monitor I&O throughout therapy (effect of drug on fluid loss may determine the reduction in the number of times it is administered per day).

Monitor for signs of confusion especially in elderly; may institute safety measures if necessary.

Dose: *Oedema*, by mouth, ADULT 100–200 mg daily, increased if necessary to 400 mg daily in resistant oedema; usual maintenance dose 75–200 mg daily; CHILD initially 3 mg/kg daily in divided doses.

Primary hyperaldosteronism, by mouth, ADULT, *diagnosis*, 400 mg daily for 3–4 weeks (see notes above); *preoperative management*, 100–400 mg daily; if not suitable for surgery, lowest effective dose for long-term maintenance.

Adjunct in severe heart failure, by mouth, ADULT usually 25 mg daily.

POM **Spironolactone** *(WMF 16.3)*
Tablets, Spironolactone 25 mg.

POM **Spironolactone** *(EDL 16)*
Tablets, Spironolactone 25 mg, 50 mg.

POM **ALDACTONE®** *(Morison)*
Tablet, Spironolactone 25 mg; buff f-c tab. marked 'SEARLE 39'.
25 mg - 20; 100.

POM **APO-SPIRO®** *(Lahams)*
Tablet, Spironolactone 25 mg; tan, scored tab. marked 'APO25'.
25 mg - 500.

POM **SPIROTAC®** *(Hovid)*
Tablet, Spironolactone 25 mg.
25 mg - 1000.

TRIAMTERENE plus HYDROCHLOROTHIAZIDE

Therapeutic category: Diuretic/antihypertensive.

Pharmacology: Triamterene is a potassium sparing diuretic that inhibits sodium reabsorption and potassium excretion by direct action on the distal tubule. Hydrochlorothiazide is a thiazide diuretic that increases urine excretion of sodium and water by inhibiting sodium reabsorption at the beginning of the distal convoluted tubule. Traimterene has weak diuretic effect when used on its own. It is used as adjunct with thiazide or loop diuretic instead of giving potassuim supplements.

Indications: Treatment of hypertension, alone or in combination with other antihypertensive drugs; control of oedema in cardiac failure, cirrhosis of the liver or the nephrotic syndrome.

Contra-indications: Hyperkalaemia, progressive renal failure, potassium supplements or other potassium-conserving drugs.

Precautions: Hepatic or renal insufficiency; patients predisposed to gout (both components can elevate uric acid levels); diabetic patients (thiazide diuretics can provoke hyperglycaemia and glycosuria); pregnancy, breast-feeding.

Interactions:

•Lithium (avoid co-administration as thiazides reduce the excretion of lithium).

Adverse effects: Nausea, vomiting, diarrhoea, muscle cramps, weakness, dizziness, headache, dry mouth, rash; rarely, photosensitivity reaction, anaphylaxis.

Advice to patients: May be taken with food or milk to minimise nausea; take early in the day to avoid nocturia; take the last dose of multiple doses early in the evening unless instructed otherwise; increased sensitivity to sunlight may occur with skin rash, redness,

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itching, or sunburn; may increase blood glucose levels in diabetics; notify physician if weakness, headache, joint swelling, or nausea becomes severe or persist; may impart a blue fluorescent colour to urine.

Nursing considerations: •If ordered once daily, dose should be given in the morning.

•Assess weight, I&O reports daily to determine fluid loss.

•Take blood pressure with patient lying down and standing; observe for hypokalaemia.

•See also under Hydrochlorothiazide

Dose: Adult only, *In hypertension*, initially, 1-2 tabs daily; adjust according to the patients needs up to a max. 4 tabs daily. *In Oedema*, initially, 1 tab. twice daily after meals; may be increased to 3 tabs daily, 2 tabs after breakfast and 1 tab. after lunch.
Maintenance dose, 1 tab. daily or 2 tabs on alternate days.
Elderly: As for the adult.

POM **DYAZIDE**® *(GSK)*
Tablet, Triamterene 50 mg, hydrochlorothiazide 25 mg; peach-coloured, half-scored, circular tab. marked 'SKF E93'.

5.2.4 Osmotic diuretics

Osmotic diuretics, such as **mannitol**, are administered in sufficiently large doses to raise the osmolarity of plasma and renal tubular fluid. Osmotic diuretics are used to reduce or prevent cerebral oedema, to reduce raised intraocular pressure or to treat disequilibrium syndrome. Mannitol is also used to control intraocular pressure during acute attacks of glaucoma. Reduction of cerebrospinal and intraocular fluid pressure occurs within 15 minutes of the start of infusion and lasts for 3–8 hours after the infusion has been discontinued; diuresis occurs after 1–3 hours.

Circulatory overload due to expansion of extracellular fluid is a serious adverse effect of mannitol; as a consequence, pulmonary oedema can be precipitated in patients with diminished cardiac reserve, and acute water intoxication may occur in patients with inadequate urine flow.

MANNITOL

Indications: Cerebral oedema; raised intraocular pressure (emergency treatment or before surgery).

Contra-indications: Pulmonary oedema; intracranial bleeding (except during craniotomy); severe congestive heart failure; metabolic oedema with abnormal capillary fragility; severe dehydration; renal failure (unless test dose produces diuresis).

Precautions: Monitor fluid and electrolyte balance; monitor renal function.

Adverse effects: Fluid and electrolyte imbalance (for symptoms see introductory notes); circulatory overload, acidosis; pulmonary oedema particularly in diminished cardiac reserve; chills, fever, chest pain, dizziness, visual disturbances; hypertension; urticaria, hypersensitivity reactions; extravasation may cause oedema, skin necrosis, thrombophlebitis; rarely, acute renal failure (large doses).

Dose: TEST DOSE IF PATIENT OLIGURIC OR RENAL FUNCTION IS INADEQUATE, BY INTRAVENOUS INFUSION, AS A 20% SOLUTION, 200 MG/KG BODY WEIGHT INFUSED OVER 3–5 MINUTES; REPEAT TEST DOSE IF URINE OUTPUT LESS THAN 30–50 ML/HOUR; IF RESPONSE INADEQUATE AFTER SECOND TEST DOSE, RE-EVALUATE PATIENT.

Raised intracranial or intraocular pressure, by intravenous infusion, as a 20% solution infused over 30–60 minutes, 0.25–2 g/kg body weight.
Cerebral oedema, by intravenous infusion, as a 20% solution infused rapidly, 1 g/kg body weight.

PHARMACEUTICAL PRECAUTIONS: SOLUTIONS CONTAINING MORE THAN MANNITOL 15% MAY CRYSTALLIZE DURING STORAGE, CRYSTALS MUST BE REDISSOLVED BY WARMING SOLUTION BEFORE USE AND SOLUTION MUST NOT BE USED IF ANY CRYSTALS REMAIN; INTRAVENOUS ADMINISTRATION SETS MUST HAVE A FILTER; MANNITOL SHOULD NOT BE ADMINISTERED WITH WHOLE BLOOD OR PASSED THROUGH THE SAME TRANSFUSION SET AS BLOOD.

POM **Mannitol** *(WMF 16.4)*
Infusion (Solution for infusion), Mannitol 10%, 20%.

5.3 Antihypertensive drugs

5.3.1 Beta–adrenoceptor blocking drugs
5.3.2 Vasodilators
5.3.3 Alpha-adrenoceptor blocking drugs
5.3.4 Centrally acting antihypertensive drugs
5.3.5 Angiotensin-converting enzyme (ACE) inhibitors
5.3.6 Calcium-channel blockers
5.3.7 Diuretics (see also section 5.2)

Management of hypertension

Treatment of hypertension should be integrated into an overall programme to

manage factors that increase the risk of cardiovascular events (such as stroke and myocardial infarction). Treatment is oftten life-long. Hypertension was formerly classified as mild, moderate or severe, but a grading system is now preferred. Grade 1 hypertension is defined as 140–159 mmHg systolic blood pressure and 90–99 mmHg diastolic blood pressure, Grade 2 hypertension 160–179 mmHg systolic and 100–109 mmHg diastolic and Grade 3 hypertension more than 180 mmHg systolic and more than 110 mmHg diastolic. The goal of treatment is to obtain the maximum tolerated reduction in blood pressure.

Lifestyle changes should be introduced for all patients; they include weight reduction, reduction in alcohol intake, reduction of dietary sodium, stopping tobacco smoking, and reduction in saturated fat intake. The patient should eat a healthy nutritious diet including adequate fruit and vegetables and should exercise regularly. These measures alone may be sufficient in mild hypertension, but patients with moderate to severe hypertension will also require specific antihypertensive therapy.

Drug treatment of hypertension

Three classes of drug are used for first-line treatment of hypertension: thiazide diuretics, beta-adrenoceptor antagonists (beta-blockers), and angiotensin-converting enzyme (ACE) inhibitors. Calcium-channel blockers are considered first-line in specific populations only e.g. Africans or the elderly. Other classes of drugs may be used in certain situations.

Thiazide diuretics, such as **hydrochlorothiazide** (see also section 5.2.1), have been used as first-line antihypertensive therapy, and are particularly indicated in the elderly. They have few adverse effects in low doses, but in large doses they may cause a variety of unwanted metabolic effects (principally potassium depletion), reduced glucose tolerance, ventricular ectopic beats and impotence; they should be avoided in gout. These effects can be reduced by keeping the dose as low as possible; higher doses do not produce an increased reduction in blood pressure. Thiazides are inexpensive and, when used in combination, can enhance the effectiveness of many other classes of antihypertensive drug.

Beta-adrenoceptor antagonists (beta-blockers) such as **atenolol** are effective in all grades of hypertension, and are particularly useful in angina and following myocardial infarction; they should be avoided in asthma, chronic obstructive pulmonary disease, and heart block.

Angiotensin-converting enzyme inhibitors (ACE inhibitors) such as **enalapril** are effective and well tolerated by most patients. They can be used in heart failure, left ventricular dysfunction and diabetic nephropathy, but should be avoided in renovascular disease and in pregnancy. The most common adverse affect is a dry persistent cough.

Dihydropyridine calcium-channel blockers such as **nifedipine** are useful for isolated systolic hypertension, in populations unresponsive to other antihypertensives (e.g. Africans) and in the elderly when thiazides cannot be used. Short-acting formulations of nifedipine should be **avoided** as they may evoke reflex tachycardia and cause large variations in blood pressure.

Drugs acting on the central nervous system are also effective antihypertensive drugs. In particular, **methyldopa** is effective in the treatment of hypertension in pregnancy.

A single antihypertensive drug is often not adequate and other antihypertensive drugs are usually added in a stepwise manner until blood pressure is controlled.

Hypertensive emergencies

In situations where immediate reduction of blood pressure is essential and treatment by mouth is not possible, intravenous infusion of **sodium nitroprusside** is effective. Over-rapid reduction in blood pressure is hazardous and can lead to reduced organ perfusion and cerebral infarction.

Hypertension in pregnancy

This is defined as a sustained diastolic blood pressure of 90 mmHg or more. Drug therapy for chronic hypertension during pregnancy remains controversial. If diastolic blood pressure is greater than 95 mmHg, **methyldopa** is the safest drug. Beta-blockers should be used with caution in early pregnancy, since they may retard fetal growth; they are effective and safe in the third trimester. ACE inhibitors are contraindicated in pregnancy since they may damage fetal and neonatal blood

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pressure control and renal function. Women who are taking these drugs and become pregnant should have their antihypertensive therapy changed immediately.

Pre-eclampsia and eclampsia. If pre-eclampsia or severe hypertension occurs beyond the 36th week of pregnancy, delivery is the treatment of choice. For acute severe hypertension in pre-eclampsia or eclampsia, intravenous hydralazine can be used. Magnesium sulfate (section 11.1) is the treatment of choice to prevent eclamptic convulsions in eclampsia and severe pre-eclampsia.

5.3.1 Beta–adrenoceptor blocking drugs

ATENOLOL

Atenolol is a representative beta-adrenoceptor antagonist. Various drugs can serve as alternatives.

Therapeutic category: Antihypertensive; Antianginal Agent; Beta-adrenergic Blocker.

Pharmacology: Atenolol is a beta-adrenoceptor blocking drug which is $Beta_1$ - Selective (i.e. acts preferentially on $Beta_1$ - adrenergic receptors in the heart). It is without intrinsic sympathomimetic and membrane stabilising activities. It crosses the blood brain barrier only to a negligible extent. Its mechanism of action is probably by reducing the cardiac rate and contractility which makes it effective in eliminating or reducing the symptoms of angina.

Indications: Hypertension; angina (section 5.5); arrhythmias (section 5.4); migraine prophylaxis (section 1.9.2).

Contra-indications: Asthma or history of obstructive airways disease (unless no alternative, then with extreme caution and under specialist supervision); uncontrolled heart failure, Prinzmetal angina, marked bradycardia, hypotension, sick sinus syndrome, second- or third-degree atrioventricular block, cardiogenic shock; metabolic acidosis; severe peripheral arterial disease; phaeochromocytoma (unless used with alpha-blocker).

Precautions: Avoid abrupt withdrawal especially in angina; may precipitate or worsen heart failure; pregnancy (Appendix 2); breastfeeding (Appendix 3); first-degree atrioventricular block; liver function deteriorates in portal hypertension; reduce dose in renal impairment (Appendix 4); diabetes mellitus (small decrease in glucose tolerance, masking of symptoms of hypoglycaemia); history of hypersensitivity (increased reaction to allergens, also reduced response to epinephrine (adrenaline)); myasthenia gravis; **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances (nausea, vomiting, diarrhoea, constipation, abdominal cramp); fatigue; cold hands and feet; exacerbation of intermittent claudication and Raynaud phenomenon; bronchospasm; bradycardia, heart failure, conduction disorders, hypotension; sleep disturbances, including nightmares; depression, confusion; hypoglycaemia or hyperglycaemia; exacerbation of psoriasis; rare reports of rashes and dry eyes (oculomucocutaneous syndrome—reversible on withdrawal).

Advice to patients: See Label 8 in Appendix 6. Avoid abrupt withdrawal of the drug; adhere to dosage regimen; watch for postural hypotension; take at the same time each day; may mask diabetes symptoms; notify physician if any adverse effects occur; use with caution while driving or performing tasks requiring alertness; may be taken without regard to meals.

Nursing considerations: •Administer tablet whole or crushed before meals or at bedtime.

•Counsel that the drug should be withdrawn gradually to prevent worsening of condition; to avoid hazardous activities if dizziness occurs.

•Monitor B.P., apical and radial pulses, fluid I&O,daily weight, respirations, and circulation in extremeties before and during therapy.

•Teach patient take pulse at home and when to report to the doctor.

•Atenolol may mask the sympoms hypoglycaemia.

Dose: *Hypertension*, by mouth, ADULT 50 mg once daily (higher doses rarely necessary).

POM **Atenolol** *(WMF 12.3)*
Tablets, Atenolol 50 mg, 100 mg.

POM **Atenolol** *(EDL 12.3)*
Tablets, Atenodol 50 mg, 100 mg.

POM **APO-ATENOLOL®** *(Lahams)*
Tablet, Atenolol 100 mg; white tab. marked 'APO A100'.
100 mg - 500.

POM **ATELIN®** *(Lahams)*
Tablet, Atenolol BP 50 mg; uncoated tab.
50 mg - 2 x 14's (in blister).

POM **TENOLOL**® *(IPCA)*
Tablets, Atenolol BP 50 mg, 100 mg; f-c tabs. 100 mg - 1000.

POM **TENORMIN**® *(Reals)*
Tablets, Atenolol 50 mg, 100 mg; orange biconvex f-c tab. marked 'TENORMIN and ICI'.

POM **TERNOLOL**® *(Hovid)*
Tablet, Atenolol 100 mg.
50 mg - 10's; 14's.
100 mg - 10's; 14's.

ATENOLOL plus CHLORTALIDONE

Therapeutic category: Antihypertensive/ Diuretic.
Pharmacology: Atenolol is a cardioselective beta–blocker and chlortalidone is a diuretic. The Combination produces a 24–hour antihypertensive effect after a single oral dose.
Indication: Management of hypertension.
Contra-indications, Precautions, etc.: See Atenolol.
Dose: By mouth, one tablet daily.
Not recommended for children.
Dosage may be reduced in the elderly and in renal failure

POM **TENORETIC**® *(Reals)*
Tablet, Atenolol 100 mg, chlortalidone 25 mg; round, biconvex, f–c tab. marked 'TENORETIC' on one side.

BISOPROLOL

Therapeutic category: Antihypertensive; $ß_1$-blocker.
Pharmacology: Bisoprolol is a highly $ß_1$-selective adrenoceptor antagonist with low $ß_2$-receptor affinity. It has nointrinsic sympathomimetic activity nor membrane-stabilising properties. It reduces blood pressure, and by blockade of the cardiac $ß_1$-receptors, it reduces cardiac action, and hence myocardial oxygen demand. The mechanism of action of $ß_1$-adrenergic blocking agents in hypertension is not clear, but it is known that bisoprolol reduces the heart rate and depresses plasma renin levels.
Bisoprolol is rapidly absorbed after oral administration in man and excreted predominantly via the urine as unaltered substance and metabolites. In man 50% of a dose is metabolised in the liver while the other 50% is eliminated unchanged via the kidneys. None of the metabolites found in man has $ß_1$-receptor blocking action. In man, the plasma elimination half life is 0-12 hours, resulting in a duration of action of 24 hours. Because of its moderate hepatic metabolism, it is subject only to a very small hepatic first pass metabolism. Therefore, bisoprolol displays a high bioavailability of 90% after an oral dose.
Indications: Mild to moderate hypertension and angina pectoris.
Contra-indications, Precautions, Adverse effects: See under Atenolol.
Advice to patients: Take on an empty stomach or with breakfast. Do not discontinue medication abruptly; may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease. Discontinuation of therapy should be gradual, and patients should be advised to limit the extent of their physical activity during the period in which the medicine is being discontinued. See also under Atenolol.
Dose: By mouth, *Hypertension and angina*,
initially 5 mg once daily in the morning; increased to 10 mg daily according to individual response. Up to max. 20 mg daily may be needed.
Reduce dose in severe renal or hepatic impairment and in elderly.
Overdosage and Treatment: Symptoms may include bradycardia and severe hypotension; bronchospasm and heart failure may be produced in certain individuals. Bradycardia associated with severe hypotension should be treated with IV Atropine (1-2 mg). If necessary this should be followed up by a slow IV infusion of 25 micrograms Isoprenaline. Bronchospasm should be treated with IV Aminophylline, and heart failure with digitalis and diuretics.

POM **CONCOR**® *(Biofem)*
Tablet (5 mg), Bisoprolol 5 mg; light yellow heart-shaped f-c tab scored on both sides.
5 mg – 30's (in blister)
Tablet (10 mg), Bisoprolol 10 mg; light orange heart-shaped f-c tab scored on both sides.
10 mg – 30's (in blister).

PROPRANOLOL

Therapeutic category: Antihypertensive; Antianginal Agent; Antiarrhythmic Agent; Beta-Adrenergic Blocker.
Pharmacology: Propranolol is a non-selective beta-adrenergic receptor-blocking agent without intrinsic sympathomimetic activity. It abolishes the responsiveness of myocardium and coronary vessels to endogenous and exogenous catecholamines, reduces the impulse-generating activity of sinus node and prolongs

AV conduction time. Increased atrial and ventricular contraction rate is stopped, refraction period is prolonged, myocardial oxygen demand is diminished, arterial blood pressure is reduced.

Indications: Angina pectoris, cardiac arrhythmias, hypertension.

Contra-indications: Bronchial asthma, bronchitis with bronchospasm, allergic hay fever, sinus bradycardia or partial heartblock, diabetes, metabolic acidosis, after prolonged fasting.

Precautions: CHF, late pregnancy, breast-feeding, elderly, liver disease, renal impairment, avoid abrupt withdrawal in angina.

Adverse effects: Bradycardia, AV block, lung oedema, insomnia, tiredness, abdominal pains, allergic reactions, G1 disturbances, CHF, cold extremities, blood disorders, rashes.

Advice to patients: See Label 8 in Appendix A. Do not discontinue abruptly; notify physician if CHF symptoms become worse or side-effects develop; take at the same time each day; may mask diabetes symptoms; consult pharmacist or physician before taking with other adrenergic drugs (e.g., cold medications); use with caution while driving or performing tasks requiring alertness.

Nursing considerations: •Give with a full glass of water on empty stomach; co-administration with aluminium containing antacids may decrease GI absorption.

•Educate the patient about his disease and the importance of taking his drug as prescribed, even when he is feeling well.

•Sudden withdrawal can exacerbate angina and myocardial infarction; inform the outpatient to avoid abrupt withdrawal of the drug but to report any unpleasant reactions to the physician.

•Instruct patient to make positon changes slowly to prevent fainting.

•Patient's therapeutic response may be evaluated by looking at B.P., apical and radial pulses, fluid I&O, daily weight, respirations,and circulation in extremeties before and during therapy.

•Propranolol may mask the sympoms of shock and hypoglycaemia.

Dose: By mouth, Adult, *Hypertension*, initially 80 mg twice a day, increased at weekly intervals according to response; usual dose range is 160–320 mg per day.

Angina, anxiety, migraine, and essential tremor, initially 40 mg 2-3 times daily, increased at weekly intervals according to response; usual dose range is 80-160 mg per day except in angina which is 120-240 mg per day.

Dysrhythmias, anxiety, tachycardia, hypertrophic obstructive cardiomyopathy and thyrotoxicosis, 10-40 mg 3-4 times a day.

Post myocardial infarction, initially 40 mg 4 times a day for 2-3 days starting between days 5 and 21 after the infarction; then, 80 mg twice a day to improve compliance.

Phaechromocytoma (use only with an alpha-adrenoceptor blocker),
Preoperative: 60 mg daily for 3 days.
Non-operable malignant cases, 30 mg daily.

By I.V. injection, Adult, *Emergency treatment of cardiac dysrhythmias and thyrotoxic crisis only*, initially 1 mg (1 ml) injected over one minute; repeated at 2-minute intervals up to a maximum dose of 10 mg in conscious patients or 5 mg in anaesthesised patients.

Child: *Dysrhythmias, phaeochromocytoma, thyrotoxicosis*, by mouth, 0.25-0.5 mg/kg b.wt. 3-4 times daily.

By I.V. injection, 0.025-0.05 mg/kg b.wt. injected slowly under ECG Control; repeated 3-4 times daily.

Migraine, by mouth, under 12 years: 20 mg 2-3 times daily.

Over 12 years: same as adult dose.

POM **Propranolol** *(EDL 12.1)*
Tablets, Propranolol HCl 10 mg, 40 mg, 80 mg
Injection, Propranolol HCl 1 mg per ml; in amp.

POM **APO-PROPRANOLOL®** *(Lahams)*
Tablets, Propranolol HCl 10 mg, orange tab. marked 'APO 10'; 40 mg, green tab. marked 'APO 40'.
10 mg - 1000
40 mg - 1000.

POM **INDERAL®** *(Reals)*
Tablets, Propranolol HCl 10 mg, 40 mg, 80 mg; all pink, round, bi–convex, f–c tabs marked 'ICI' on one side, and tab. name and strength on the reverse.
Injection, Propranolol HCl 1 mg per ml; in 1 ml printed glass amp.

POM **JUNOLOL®** *(Juhel)*
Tablet, Propranolol HCl BP 40 mg; pink scored biconvex tablet marked 'PNL/40' on one side and 'Juhel' on the reverse.
40 mg – 10 x 10's; 500's.

POM **PROP-10®** *(Fidson)*
Tablet, Propranolol HCl 10 mg
10 mg - 1000.

LABETALOL

Synonym: Ibidomide.

Therapeutic category: Antihypertensive

Pharmacology: Labetalol has both beta-adrenoceptor as well as alpha-adrenoceptor blocking properties. The alpha-blocking effect results in decrease in peripheral vascular resistance and a rapid reduction in blood pressure. Concurrent beta-blockade protects the heart from reflex sympathetic drive normally induced by peripheral vasodilation.

Indications: For rapid control of blood pressure in severely hypertensive patients including severe Hypertension of pregnancy and for use in anaesthesia where a hypotensive technique is indicated; also in hypertensive episodes following acute myocardial infarction.

Contra-indications: Second or third degree heart block, cardiogenic shock and other conditions associated with severe and prolonged hypotension or severe bradycardia; asthma or a history of obstructive airways disease; liver dysfunction.

Precautions: Late pregnancy, breast-feeding, use during anaesthesia; stop and do not re-start if liver injury occurs or the patient is jaundiced.

Interactions: Class 1 antiarrhythmic agents, calcium antagonists of the verapamil type; bronchodilators, cardiac glycoside, noradrenaline, adrenaline, tricyclic antidepressants, cimetidine.

Adverse effects: Postural hypotension (if patients are allowed to assume the upright position within 3 hours of receiving the labetalol injection; headache, tiredness, tingling sensation in the scalp, tremor, difficulty in micturition, ejaculatory failure, epigastric pain, nausea, vomiting, liver dysfunction, rash.

Advice to patients: See Label 8 in Appendix 6. Do not stop medication without aid of physician; may mask signs and symptoms of diabetes; dizziness is a common side effect, avoid alcohol.

Nursing considerations: •Administer orally, crush or allow patient to swallow whole; if administered I.V., keep patient recumbent for 3 hours.

•Instruct patient to check with the doctor before using OTC products such as cold remedies or nasal decongestants.

•Inform patient that dizziness may be minimized by rising slowly and avoiding sudden positional changes as well as hazardous activities.

•Monitor B.P (standing and sitting or supine), apical/radial pulse; advise patient not to stop drug abruptly in order not to exacerbate angina and myocardial infarction.

Dose: By mouth, initially 100 mg twice daily with food, increased fortnightly where required to 200 mg twice daily; up to 400 mg twice daily; maximum up to 2400 mg *in severe, refractory hypertension and hypertension of pregnancy*.

Elderly: Initially 50 mg twice daily.

Child: Not recommended.

By intravenous injection (Bolus injection), 50 mg over at least 1 minute; repeated, if necessary, at 5 minute intervals until a satisfactory response occurs; maximum 200 mg.

By Intravenous infusion, 2 mg (2 ml of infusion solution) per minute, until a satisfactory response is obtained; usual effective dose range 50-200 mg, *increased in phaeochromocytoma*.

In hypertension of pregnancy, 20 mg per hour; may be doubled every 30 minutes to a maximum 160 mg per hour.

In hypertensive episodes following acute myocardial infarction, 15 mg per hour; gradually increased to a maximum 120 mg per hour.

Note The Infusion solution is made by diluting the contents of 2 ampoules (200 mg) to 200 ml with Sodium Chloride and Dextrose Injection B.P. or 5% Dextrose Intravenous Infusion B.P. The resultant infusion solution contains 1 mg/1 ml of labetalol.

POM **Labetalol** *(EDL 12.3)*

Tablets, Labetalol HCl 100 mg, 200 mg.

Injection, Labetalol HCl 5 mg per ml; in 20 ml amp.

PINDOLOL plus CLOPAMIDE

Therapeutic category: Antihypertensive; Beta-adrenergic Blocker; Thiazide Diuretic.

Pharmacology: A combination of the beta-adrenoceptor blocking drug pindolol and the thiazide-type diuretic clopamide; both components lower blood pressure, but by different mechanism of action.

Indications: Hypertension.

Contra-indications: Bronchial asthma, marked bradycardia, severe renal or hepatic failure, hypercalcaemia, hypersensitivity to sulphonamides, pregnancy.

Precautions: Heart failure, history of bronchial asthma, general anaesthesia, kidney or liver failure, patients on antidiabetic therapy, breast-feeding.

Adverse effects: Dizziness, tiredness, G1 disturbances, sleep disturbances, skin reactions, psychic symptoms, thrombo-cytopenia, leucopenia.

Advice to patients: See under Atenolol.

Nursing considerations: See under Atenolol.

Dose: By mouth, Adult, ½ tab. daily with breakfast; increased to 2 tabs daily after 2-3 weeks if necessary.

POM **Pindolol plus Clopamide** *(EDL 12.3)*
Tablet, Pindolol 10 mg, clopamide 5 mg.

TIMOLOL

Therapeutic category: Antihypertensive; Antianginal Agent; Beta-adrnergic Blocker.

Indications: Hypertension; angina pectoris due to ischaemic heart disease.

Contra-indications: Bronchospasm or history of bronchospasm; sinus bradycardia, AV block, severe chronic destructive pulmonary disease; hypersensitivity to timolol.

Precautions: CHF, thyrotoxicosis, major surgery, labile diabetes.

Adverse effects: Fatigue, headache, bradycardia, dyspepsia, bronchospasm, tinnitus.

Advice to patients: See Label 8 in Appendix 6.

Nursing considerations: •Administer tablet whole or crushed with or immediately after meals, preferably at bedtime to minimize orthostatic hypotension.
•Advise patient to check with the physician before taking OTC preparations; to avoid abrupt withdrawal of the drug, because angina and myocardial infarction may be exacerbated; to avoid alcohol and smoking, and to reduce sodium intake; to avoid hazardous activities if dizziness occurs.
•Teach patient take pulse at home and when to report to the doctor.
•Timolol may mask common signs of shock and hypoglycaemia.

Dose: *Hypertension*, by mouth, 10 mg daily as a single dose; up to a max. 60 mg daily in divided doses.
Angina, initially 5 mg 2-3 times daily; may be increased to 15 mg 3 times daily.
Migraine prophylaxis, 10-20 mg once daily.

POM **BLOCADREN®** *(Bolax/BPP)*
Tablet, Timolol maleate 10 mg; blue half-scored tab. marked 'MSD 136/ BLOCADREN'.
10 mg - 500.

5.3.2 Vasodilators

HYDRALAZINE

Therapeutic category: Peripheral vasodilator/ antihypertensive.

Pharmacology: Hydralazine directly relaxes arteriolar smooth muscles. It is widely together with a beta-blocker and a diuretic i hypertension not responding to simpler regimens. Hydralazine when used alone causes tachycardia and fluid retention, hence, it is usually used as part of combination therapy e.g. with beta-blockers and/or diuretics.

Indications: In combination therapy in moderate to severe hypertension, hypertensive crises; hypertension associated with pregnancy (including pre-eclampsia or eclampsia); heart failure (section 5.1).

Contra-indications: Idiopathic systemic lupus erythematosus, severe tachycardia, high output heart failure, myocardial insufficiency due to mechanical obstruction, cor pulmonale, dissecting aortic aneurysm, porphyria.

Precautions: Hepatic impairment (Appendix 5); renal impairment (reduce dose, Appendix 4); coronary artery disease (may provoke angina, avoid after myocardial infarction until stabilized); cerebrovascular disease; check acetylator status before increasing dose above 100 mg daily; test for antinuclear factor and for proteinuria every 6 months; pregnancy (Appendix 2); breastfeeding (Appendix 3); occasionally over-rapid blood pressure reduction even with low parenteral doses; **interactions**: Appendix 1.

Adverse effects: Tachycardia, palpitations, postural hypotension; fluid retention; gastrointestinal disturbances including anorexia, nausea, vomiting, diarrhoea, rarely constipation; dizziness, flushing, headache; abnormal liver function, jaundice; systemic lupus erythematosus-like syndrome, particularly in women and slow acetylators; nasal congestion, agitation, anxiety, polyneuritis, peripheral neuritis, rash, fever, paraesthesia, arthralgia, myalgia, increased lacrimation, dyspnoea; raised plasma creatinine, proteinuria, haematuria; blood disorders including haemolytic anaemia, leukopenia, thrombocytopenia.

Advice to patients: Report flu-like symptoms; rise slowly from sitting/lying position; take with meals.

Nursing considerations: •Give oral drug with meals to increase absorption; give IV dose in a recumbent position; keep for i hr after administration.
•Monitor B.P. closely with IV use; check IV site for extravasation.
•Aid with ambulation; rising may cause orthostasis.
•Watch the patient for signs of lupus erythematosus-like syndrome (sore throat, fever, skin rash, muscle and joint aches), and report to doctor immediately.

•Emphasize the need to comply with drug regimen.
•Advise patient not to discontinue drug suddenly but to report adverse reactions to the physician.
•Tell patient to avoid OTC preparations unless prescribed by the doctor.

Dose: *Hypertension*, by mouth, ADULT 25 mg twice daily, increased if necessary to maximum 50 mg twice daily.
Hypertensive crises (including during pregnancy), by slow intravenous injection, ADULT 5–10 mg diluted with 10 ml sodium chloride 0.9%; if necessary may be repeated after 20–30 minutes.
Hypertensive crises (including during pregnancy), by intravenous infusion, ADULT initially 200–300 micrograms/minute; maintenance usually 50–150 micrograms/minute.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Hydralazine** *(WMF 12.3)*
Tablets, Hydralazine HCl 25 mg, 50 mg.
Injection (Powder for solution for injection), Hydralazine HCl, 20-mg ampoule.

POM **Hydralazine** *(EDL 12.3)*
Tablet, Hydralazine HCl 25 mg, 50 mg.
Injection, Hydralazine HCl 20 mg; dry powder in amp.

POM **APRESOLINE**® *(Novartis)*
Tablets, Hydralazine HCl 25 mg (yellow s-c tab. marked 'GF and CIBA'); 50 mg (deep pink s-c tab. marked 'HG and CIBA').
25 mg - 100.
Injection, Hydralazine HCl 20 mg; powder in amp.
Pack - 5.

SODIUM NITROPRUSSIDE

Sodium nitroprusside is a complementary drug for the treatment of hypertensive crisis.

Indications: Hypertensive crisis (when treatment by mouth not possible).

Contra-indications: Severe hepatic impairment; compensatory hypertension; severe vitamin B_{12} deficiency; Leber optic atrophy.

Precautions: Impaired pulmonary function; hypothyroidism; renal impairment (Appendix 4); ischaemic heart disease, impaired cerebral circulation; hyponatraemia; raised intracranial pressure; elderly; hypothermia; monitor blood pressure and blood-cyanide concentration, also blood-thiocyanate concentration if given for more than 3 days; avoid sudden withdrawal (reduce infusion over 15–30 minutes to avoid rebound effects); pregnancy; breastfeeding; **interactions**: Appendix 1.

Adverse effects: Severe hypotension; effects associated with over-rapid reduction in blood pressure include headache, dizziness; retching, abdominal pain; perspiration; palpitations, apprehension, retrosternal discomfort; rarely reduced platelet count, acute transient phlebitis.
Adverse effects associated with excessive concentration of cyanide metabolite include tachycardia, sweating, hyperventilation, arrhythmias, marked metabolic acidosis (discontinue infusion and give antidote, section 19.2.7).

Dose: *Hypertensive crisis*, by intravenous infusion, ADULT initially 0.3 micrograms/kg/minute; usual maintenance dose 0.5–6 micrograms/kg/minute; maximum dose 8 micrograms/kg/minute; stop infusion if response unsatisfactory after 10 minutes at maximum dose; lower doses in patients already being treated with antihypertensives.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Sodium nitroprusside** *(WMF 12.3)*
Infusion (Powder for solution for infusion), Sodium nitroprusside, 50-mg ampoule.

5.3.3 Alpha-adrenoceptor blocking drugs

DOXAZOSIN

Therapeutic category: Alpha adrenergic blocker/ vasodilator.

Pharmacology: Doxazosin mesylate is a quinazoline compund that is a selective inhibitor of the $alpha_1$(post functional) subtype of alpha adrenergic receptors. Doxazosin and Prazosin have similar abilities to antagonise pressor effects of Phenylephrine (an $alpha_1$ agonist). The antihypertensive effect of doxazosin results from a decrease in systemic vascular resistance, with little change in cardiac output. Maximum effect usually occurs 2-6 hours after dosing. Bioavailability is approximately 65%, reflecting first pass metabolism of doxazosin by the liver. Food doesn't have significant effect on doxazosin bioavailability. No major pharmacokinetic differences in the eld-

erly and in renal insufficiency.

Indications: Treatment of hypertension; may be used alone or in combination with diuretics, beta-adrenergic blocking agents, calcium channel blockers or ACE inhibitors. Benign prostatic hyperplasia (BPH) -*see Section 11.4*.

Contra-indications: Sensitivity to quinazolines; liver dysfunction; children below 12 years.

Precautions: To decrease likelihood of excessive hypotension and syncope, initiate therapy with the 1mg dose and adjust dose slowly; other antihypertensive agents; impaired hepatic function or drugs that influence hepatic metabolism; pregnancy and lactation.

Advice to patients: Avoid driving or harzadous tasks for 24 hours after the first dose, after a dosage increase and after interruption of therapy when treatment is resumed.

Sit or lie down if dizziness or other symptoms of lowered B.P. occur. Rise from sitting or lying positon carefully to minimize orthostatic hypertension.

Report to physician if dizziness, lightheadedness or palpitations are bothersome.

Adverse effects: Orthostatic hypotension with syncope and other symptoms of lowered B.P. such as dizziness, lightheadedness or vertigo especially at initiation of therapy or at the time of dose increases; headache, weakness,oedema, somnolence, nausea, rhinitis; less frequently GI symptoms,tremor, rash, pruritus.

Nursing considerations: •Administer first dose at bedtime to minimize effect of orthostatic hypotension; tablet may be crushed or chewed.

•Advise patient not to drive or operate machinery until stabilized on medication; to make position changes slowly.

•Observe patient daily for oedema in feet, legs.

•Monitor pulse, I&O (note fluid retention), daily weight (inform doctor of any increase), B.P. (standing/sitting).

Dose: *Hypertension*, initially 1 mg once daily; increased after 1-2 to weeks to 2 mg once daily, and thereafter if necessary to 4 mg, 8 mg ,and max. 16 mg daily.

Note: Increases in dose beyond 4mg increase the likelihood of excessive postural effects including syncope, postural dizziness/vertigo and postural hypotension. If administration is discontinued for several days, therapy should be restarted using the initial dosing regimen.

POM **CARDURA** ® *(Pfizer)*
Tablets, Doxazosin mesylate 2 mg, 4 mg.
2 mg - 10 (blister)
4 mg -10 (blister).

PRAZOSIN

Synonym: Furazosin.

Therapeutic category: Antihypertensive; Alpha-adrenergic Blocker.

Pharmacology: Prazosin relaxes both arterial and venous smooth muscles probably by blocking postsynaptic alpha receptors. It causes a decrease in total peripheral vascular resistance. The antihypertensive effect is a direct result of peripheral vasodilation. Blood pressure is lowered in both the supine and standing positions. While Prazosin could be used alone in mild hypertension, it is more often employed in combination with beta–blockers or diuretics. It is always started cautiously with low doses because of orthostatic hypotension and syncope which may be severe after the first dose.

Indications: Essential (primary) hypertension and secondary hypertension of varied aetiology.

Contra-indications: Sensitivity to quinazolines.

Precautions: Pregnancy, breast-feeding; not recommended for Children under 12 years; postural hypotension, dizziness, weakness, rarely loss of consciousness; elderly.

Adverse effects: Dizziness, headache, drowsiness, lack of energy, weakness, orthostatic hypotension, nausea.

Advice to patients: See Label 3 in Appendix 6. Rise from sitting/lying carefully; may cause dizziness; report if painful, persistent erection occurs; avoid alcohol.

Nursing considerations: •Administer first dose at bedtime to minimize effect of orthostatic hypotension.

•Instruct patient to sit or lie down if he feels dizzy; to make position changes slowly.

•Advise patient not to drive or operate machinery until stabilized on medication; to avoid OTC products except with doctor's permission.

•Observe patient daily for oedema in feet, legs.

•Monitor pulse, I&O (note fluid retention), daily weight (inform doctor of any increase), B.P. (standing/sitting).

Dose: *Hypertension*, 0.5 mg at bedtime initially; increasing to 0.5 mg 2-3 times daily; then 1 mg 2-3 times daily. Maintenance, 3-20 mg in divided doses. See lit. for details.

POM **Prazosin** *(EDL 12.3)*
Tablets, Prazosin HCl 1 mg, 2 mg, 5 mg.

POM **APO-PRAZO**® *(Lahams)*
Tablet, Prazosin HCl 5 mg; white, scored, diamond-shaped tab. marked 'APO P5'.
5 mg - 100.

POM **MINIPRESS**® *(Pfizer)*
Tablet, Prazosin HCl 1 mg; scored tab.
1 mg - 30; 100.

PRAZOSIN plus POLYTHIAZIDE

Therapeutic category: Antihypertensive/ diuretic

Pharmacology: Prazosin causes a decrease in total peripheral vascular resistance. Its vasodilator effect is related to blockade of postsynaptic alpha-1-adrenoceptors. Unlike non-selective alpha-adrenergic blockers, the antihypertensive action of prazosin is not accompanied by reflex tachycardia. The antihypertensive effect is a direct result of peripheral vasodilation. Blood pressure is lowered in both the supine and standing positions. Polythiazide belongs to the benzothiadiazine family of diuretic/antihypertensive agents. Its mechanism of action results in an interference with the renal tubular mechanism of electrolyte reabsorption.

Indications: Treatment of hypertension.

Contra-indications: Sensitivity to the component drugs; anuria.

Precautions: Postural hypotension; fluid or electrolyte imbalance, hyperuricaemia, latent diabetes mellitus and insulin requirements in diabetics due to the thiazide; pregnancy, breast-feeding.

Adverse effects: GI disturbances such as nausea, jaundice; CNS disturbances such as dizziness; haematological reactions such as agranulocytosis; dermatological reactions such as rashes; CVS disorders such as orthostatic hypotension; others such as alopecia, hyperglycaemia, muscle spasm, weakness.

Advice to patients: See Label 3 in Appendix 6. See also under Prazosin.

Nursing considerations: •Administer with food if nausea occurs and in the morning to prevent nocturia.
•Monitor weight daily to determine fluid loss.
•Observe B.P. standing, sitting and lying because postural hypertension may occur.
•Test urine for glucose in diabetic patients; insulin requirements may be adjusted. Tell diabetic patient that blood sugar may increase.
•Teach patient to eat food rich in potassium viz tomatoes, bananas, citrus fruits, and dates.
•Observe for signs of hypokalaemia such as muscle weakness and cramps.
•See also under Prazosin.

Dose: By mouth, initially one tab. once daily usually in the morning; increase after 2 weeks to 2-4 tabs daily in 2 divided doses if necessary.
See lit. for details.

POM **Prazosin plus Polythiazide** *(EDL 12.3)*
Tablet, Prazosin HCl 0.5 mg, polythiazide 0.25 mg.

POM **MINIZIDE**® *(Pfizer)*
Tablet, Prazosin HCl 0.5 mg, polythiazide 0.25 mg.
Pack - 30; 100; 500.

5.3.4 Centrally acting antihypertensive drugs

Methyldopa (via an active metabolite, methylnoradenaline) and **Clonidine** (directly) act on alpha$_2$-receptors in the brain stem to reduce efferent sympathetic tone and BP. Methyldopa is safe in asthmatics, in heart failure and in pregnancy. Postural hypotension may occur with methyldopa especially in the elderly. Side-effects are minimised if the daily dose is kept below 1 g.

Clonidine has the disadvantage that sudden withdrawal may cause a hypertensive crisis with sweating, anxiety and tremor within 24-36 hours.

Reserpine also acts centrally to reduce BP. However, it is often used in combination with other drugs. The use of central drugs is decreasing as there are alternative drugs of comparative efficacy with fewer adverse effects. Methyldopa may be used as an alternative to beta-blockers or diuretics where the first choice drug is contraindicated or poorly tolerated.

METHYLDOPA

Therapeutic category: Antihypertensive; Alpha-adrenergic Inhibitor.

Indications: Hypertension in pregnancy

Contra-indications: Depression; active liver disease; phaeochromocytoma, porphyria.

Precautions: History of hepatic impairment (Appendix 5); renal impairment (Appendix 4); blood counts and liver-function tests advised; history of depression; positive direct Coomb test in up to 20% of patients (affects blood cross-matching); interference with laboratory tests; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Tend to be transient and reversible, including sedation, dizziness, lightheadedness, postural hypotension, weakness, fatigue, headache, fluid

retention and oedema, sexual dysfunction; impaired concentration and memory, depression, mild psychosis, disturbed sleep and nightmares; drug fever, influenza-like syndrome; nausea, vomiting, constipation, diarrhoea, dry mouth, stomatitis, sialadenitis; liver function impairment, hepatitis, jaundice, rarely fatal hepatic necrosis; bone-marrow depression, haemolytic anaemia, leukopenia, thrombocytopenia, eosinophilia; parkinsonism; rash (including toxic epidermal necrolysis); nasal congestion; black or sore tongue; bradycardia, exacerbation of angina; myalgia, arthralgia, paraesthesia, Bell palsy; pancreatitis; hypersensitivity reactions including lupus erythematosus-like syndrome, myocarditis, pericarditis; gynaecomastia, hyperprolactinaemia, amenorrhoea; urine darkens on standing.

Advice to patients: See Labels 3 and 8 in Appendix 6. May cause urine discolouration; notify physician of unexplained prolonged general tiredness, fever, or jaundice; rise slowly from prolonged sitting or lying position and avoid sudden position changes to minimize orthostatic hypotension.

Nursing considerations: •Administer drug before meals.
•Give I.V. injection by infusion over 30 minutes.
•Transient sedation or depression may be common for first 72 hours of therapy (usually disappears over time); assist with ambulation.
•Dry mouth can be relieved with chewing gum or ice chips.
•Teach patient not to discontinue medication abruptly (this may cause headache, raised B.P., insomnia, tremors, nausea and sweating).
•Advise patient not to drive or operate machinery until stabilized on medication; to make position changes slowly; to avoid OTC preparations unless prescribed by physician.

Dose: *Hypertension in pregnancy*, by mouth, ADULT initially 250 mg 2–3 times daily; if necessary, gradually increased at intervals of 2 or more days, maximum 3 g daily.

POM **Methyldopa** *(WMF 12.3)*
Tablets, Methyldopa 250 mg.

POM **Methyldopa** *(EDL 12.3)*
Tablets, Methyldopa 250 mg, 500 mg.

POM **ALDOMET®** *(Bolax/BPP)*
Tablets, Methyldopa 250 mg, 500 mg; yellow f-c tabs. marked 'ALDOMET' and coded 'MSD 401' or 'MSD 516' respectively.
250 mg - 30; 500.
500 mg - 100.

POM **ALDOXI®** *(Sam)*
Tablet, Methyldopa 250 mg.
250 mg - 10 x 10's; 500's.

POM **AXELDOPA-250®** *(Panvij Biotec)*
Tablet, Methyldopa 250 mg; yellow coloured, f-c tab.
250 mg - 10 x 10.

POM **CHEMDOPA®** *(Chemiron)*
Tablet, Methyldopa 250 mg.

POM **DOPATAB®** *(Hovid)*
Tablet, Methyldopa 250 mg; f-c tab.
250 mg - 1000

POM **FEVADOPA®** *(David)*
Tablet, Methyldopa 250 mg.

POM **KEZZ METHYLDOPA®** *(Kezz)*
Tablets, Methyldopa BP 250 mg; f-c tab.
250 mg - 10 x 10's (in blister).

POM **MDOSAM®** *(Sam)*
Tablet, Methyldopa 250 mg.
250 mg - 500.

RESERPINE plus CLOPAMIDE plus DIHYDROERGOCRISTINE

Therapeutic category: Antihypertensive

Pharmacology: Reserpine exerts its effect through a central action; clopamide is a diuretic of the thiazide type promoting water and sodium excretion; dihydroergocristine inhibits the hypertensive response to stress. The blood pressure is usually reduced after 4-7 days and optimum effect is achieved after 1-4 weeks.

Indications: Essential hypertension of all grades of severity.

Contra-indications: Hypersensitivity to any of the components and to sulphonamides (Clopamide belongs to this group); hypokalaemia resistant to therapy; severe liver or renal disorders; severe cardiovascular disease; history of mental depression; active peptic ulcer; pregnancy, breast-feeding.

Precautions: Diabetes; gout; check serum potassium level regularly; impaired renal function; road users due to fatigue or orthostatic hypotension.

Interactions: Corticosteriods, NSAIDs, lithium, oral anticoagulants, MAOIs, Alcohol, CNS depressants, levodopa.

Adverse effects: GI disturbances, electrolyte disturbances (hypokalaemia); orthostatic

hypotension; fatigue; muscle weakness; nasal congestion; rarely mental depression or thrombocytopenia.

Advice to patients: See Label 2 in Appendix 6.

Nursing considerations: •Give with food or milk.
•Monitor B.P. (standing and sitting/supine); weigh patient daily and notify physician of any weight gain.
•Observe for mental depression and alert family to report symptoms.
•Advise patient to rise slowly from sitting or lying position to minimize orthostatic hypotension.
•Inform patient that drug may cause drowsiness, impair judgement and coordination; impotence, gynaecomastia may occur but is reversible.
•Dry mouth can be relieved by chewing gum or ice cube chips.
•Advise patient to avoid OTC preparations unless on prescription.

Dose: By mouth, initially 1 tab. daily; increased to 2-3 tabs daily in *severe hypertension*. Maintenance, 1 tab daily or every other day. Dosage should not be increased more frequently than once per week.

POM **Reserpine plus Clopamide plus Dihydroergocristine** *(EDL 12.3)*
Tablet, Reserpine 0.1 mg, clopamide 5.0 mg, dihydroergocristine 0.5 mg.

POM **BRINERDIN®** *(Novartis)*
Tablet, Reserpine 0.1 mg, Clopamide 5 mg, dihydroergocristine (as mesilate) 0.5 mg; white s-c tab.

Reserpine plus Dihydroergotoxine plus Hydrochlorothiazide
POM **SINEPRESS®** *(Taylek)*
Tablet, Dihyroergotoxine mesylate 0.6 mg, reserpine 0.1 mg, hydrochlorothiazide 10 mg; coated tab.
Pack - 30; 50; 100; 500.

Dose: By mouth, usually 1-2 tabs daily; increased if necessary to 3 tabs daily.

5.3.5 Angiotensin–converting enzyme (ACE) inhibitors

ACE inhibitors inhibit the conversion of angiotensin I to angiotensin II (a potent vasoconstrictor); this results in lower levels of angiotensin II which causes an increase in plasma renin activity and a reduction in aldosterone secretion. They also prevent the degradation of Bradykinin (a vasodilator). Examples include **Captopril**, **Enalapril**, **Lisinopril**, **Ramipril**, **Perindopril Erbumine**. They are used in hypertension, and in congestive heart failure (usually starting with a low dose e.g. 6.25 mg captopril). Other uses include hypertensive crisis, diabetic nephropathy, myocardial infarction.

These drugs may cause very rapid falls in B.P. in some patients and it is therefore recommended that diuretic therapy should be stopped for a few days, if possible, before initiating treatment with ACE inhibitors. The first dose should preferably be taken at bedtime. Time for onset of hypotensive effect after oral administration is about 1 - 1.5 hours (Captopril); within 6 hours (Lisinopril) and about 1 hour (Enalapril). Enalapril is a prodrug and undergoes biotransformation to **Enalaprilat** in the liver. It is eliminated principally in the urine with some faecal excretion. Captopril is about 50% metabolised and 95% excreted in urine within 24 hours. Lisinopril is well absorbed and is unaffected by food in the stomach. It is almost entirely excreted in urine as unchanged drug.

These drugs may cause impairment of renal function which may progress and become severe. At particular risk are those with pre-existing renal disease or impairment, the elderly, and those with bilateral renal artery stenosis. Concomitant treatment with NSAIDs or potassium-sparing diuretics and use of potassium-containing salt substitutes may increase the risk. Renal function and electrolytes should be checked before starting treatment with an ACE inhibitor, and monitored during treatment.

CAPTOPRIL

Therapeutic category: Antihypertensive

Pharmacology: Captopril is a specific competitive inhibitor of angiotensin 1-converting enzyme, the enzyme responsible for the conversion of angiotensin I to angiotensin II. Angiotensin, an octapeptide, is a potent endogenous vasoconstrictor substance and also stimulates aldosterone secretion from the adrenal cortex, thereby contributing to sodium and fluid retention and potassium loss. Captopril causes a decrease in angiotensin II and an increase in plasma renin activity (PRA). It produces a reduction in peripheral arterial resistance in hypertensive patients.

Indications: Management of hypertension and treatment of CHF; also in hypertensive crisis, diabetic nephropathy, postmyocardial infarction for prevention of ventricular failure.

Contra-indications: Hypertensensivity to captopril and other ACE inhibitors.

Precautions: Renal impairment (reduce

dosage); severe hypotension may occur in patients who are taking diuretics, who are sodium and/or volume depleted and also in elderly (initiate lower doses and monitor closely when starting therapy in these patients).

Interactions:

•NSAIDs especially indomethacin (reduced hypotensive effect).

•Antacids (reduced bioavailability of captopril - separate administration times by 1 to 2 hours).

•Phenothiazines (increased hypotensive effects).

•Potassium preparations or potassium-sparing diuretics (co-administration may result in elevated potassium levels).

Adverse effects: Tachycardia, chest pain, palpitations, insomnia, headache, dizziness, fatigue, malaise, rash, pruritus, alopecia, abdominal pain, vomiting, nausea, diarrhoea, constipation, anorexia, paraesthesias, oliguria, transient cough, hypotension, hyperkalaemia.

Advice to patients: Take 1 hour before meals; do not stop therapy except under prescriber's advice; notify physician if you develop sore throat, fever, swelling, rash, difficult breathing, irregular heart beats, chest pains, or cough. May cause dizziness, fainting, and lightheadedness, especially in first week of therapy (avoid sudden position changes); do not add a salt substitute (potassium) without advice of a physician.

Nursing considerations: •Give 1 hr before meals or 2 hr after meals; food decreases absorption of captopril 30% to 40%. Tablet may be crushed and mixed with food.

•Watch for hypotensive effect within 1-3 hours of first dose or new higher dose; advise patient to make position changes slowly.

•Monitor patient's B.P. and pulse rate frequently, and report excessive perspiration, vomiting and diarrhoea.

•Advise patient to check with doctor before taking any other drug including OTC medications.

Dose: *Mild to moderate hypertension*, by mouth, 12.5 mg twice daily; usual maintenance dose 25 mg twice daily; increased at 2-4 week intervals if necessary up to a maximum 50 mg twice daily.

CHF, initially 6.25-12.5 mg 3 times daily in conjunction with cardiac glycoside and diuretic therapy; initial dose depends upon patient's fluid/electrolyte status. Not recommended for children.

POM **Captopril** *(EDL 12.3)*

Tablets, Captopril 12.5 mg, 25 mg.

POM **APO-CAPTO®** *(Lahams)*

Tablets, Captopril 12.5 mg, white, double-scored, oblong tab. marked 'APO 12.5'; 25 mg, white, double-scored tab. marked 'APO 25'.

12.5 mg - 100

25 mg - 100.

ENALAPRIL

Enalapril is a representative angiotensin-converting enzyme inhibitor. Various drugs can serve as alternatives.

Synonym: Enalaprilat.

Therapeutic category: Antihypertensive.

Pharmacology: Enalapril is an ACE inhibitor. It is a prodrug and undergoes biotransformation to Enalaprilat in the liver. It is eliminated principally in the urine with some faecal excretion. Time for onset of hypotensive effect after oral administration is about about 1 hour.

Indications: Hypertension; heart failure (section 5.1).

Contra-indications: Hypersensitivity to ACE inhibitors (including angioedema); renovascular disease; pregnancy (Appendix 2).

Precautions: Use with diuretics; hypotension with first doses, especially in patients on diuretics, on a low-sodium diet, on dialysis, if dehydrated, or with heart failure; peripheral vascular disease or generalized atherosclerosis (risk of clinically silent renovascular disease); use with great care in severe or symptomatic aortic stenosis; monitor renal function before and during treatment; renal impairment (reduce dose, see also Appendix 4); liver impairment (Appendix 5); possibly increased risk of agranulocytosis in collagen vascular disease; history of idiopathic or hereditary angioedema (use with care or avoid); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Use with Diuretics: Risk of very rapid falls in blood pressure in volume-depleted patients; treatment should therefore be initiated with very low doses. High-dose diuretic therapy (furosemide dose greater than 80 mg) should be discontinued, or dose significantly reduced, at least 24 hours before starting enalapril (may not be possible in heart failure—risk of pulmonary oedema). If high-dose diuretic cannot be stopped, medical supervision advised for at least 2 hours after administration or until blood pressure stable.

Anaphylactoid Reactions: Avoid enalapril during dialysis with high-flux polyacrilonitrile membranes and during low-density lipoprotein apheresis with dextran sulfate; also withhold before desensitization with wasp or bee venom.

Adverse effects: Dizziness, headache; less commonly, nausea, diarrhoea, hypotension (severe in rare cases), dry

cough, fatigue, asthenia, muscle cramps, rash and renal impairment; rarely, vomiting, dyspepsia, abdominal pain, constipation, glossitis, stomatitis, ileus, anorexia, pancreatitis, liver damage, chest pain, palpitations, arrhythmias, angioedema, bronchospasm, rhinorrhoea, sore throat, pulmonary infiltrates, paraesthesia, vertigo, nervousness, depression, confusion, drowsiness or insomnia, pruritus, urticaria, alopecia, sweating, flushing, impotence, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, pemphigus, taste disturbance, tinnitus, blurred vision; electrolyte disturbances and hypersensitivity-like reactions (including fever, myalgia, arthralgia, eosinophilia, and photosensitivity) reported.

Advice to patients: Notify physician if vomiting, diarrhoea, excessive perspiration, or dehydration should occur (these may lead to hypotension); also if swelling of face, lips, tongue, or difficulty in breathing occurs or if persistent cough develops.

Nursing considerations: •Stop any diuretic 2-3 days before beginning enalapril therapy to help reduce the risk of hypotension; a diuretic may be added later if enalapril alone fails to control the B.P.

•Monitor B.P and pulse regularly.

•Advise patient to comply to drug schedule; also not to discontinue drug suddenly but to report adverse reaction to the doctor.

•May cause depression in some patients; discontinue if angioedema of the face, extremities, lips, tongue, or glottis occurs.

•Watch for hypotensive effects within 1-3 hours of first dose or new higher dose. Advise patient to avoid sudden postural changes to minimize orthostatic hypotension.

•Advise patient to check with doctor or pharmacist before taking OTC medications.

•Enalapril is similar to captopril and other ACE inhibitors, but has a longer duration of action.

Dose: *Hypertension*, by mouth, initially 5 mg once daily; if used in addition to diuretic, in elderly patients, or in renal impairment, initially 2.5 mg daily; usual maintenance dose 10–20 mg once daily; in severe hypertension may be increased to maximum 40 mg once daily.

POM **Enalapril** *(WMF 12.3)*
Tablets, Enalapril 2.5 mg.

POM **APO-ENALAPRIL**® *(Lahams)*
Tablets, Enalapril maleate 5 mg, white, scored, barrel-shaped tab. marked 'APO E5'; 10 mg, rust red tab. marked 'APO E 10'.
5 mg - 100
10 mg - 100

POM **ENVAS**® *(Interpharma)*
Tablets, Enalapril maleate 2.5 mg, 5 mg, 10 mg
2.5 mg - 10 x 10's
5 mg - 10 x 10's
10 mg - 10 x 10's

POM **RENITEC**® *(Bolax/BPP)*
Tablet, Enalapril maleate 5 mg, 20 mg.
5 mg - 28.
20 mg - 28.

POM **VASORETEC**® *(Afrab-Chem)*
Tablets, Enalapril maleate 5 mg, 10 mg, 20 mg.
5 mg - 20
10 mg - 20
20 mg - 20.

ENALAPRIL plus HYDROCHLOROTHIAZIDE

Therapeutic category: Antihypertensive/ Diuretic.

Indication: Hypertension.

Contra-indications: Hypersensitivity to the components of the drug and to other sulphonamide-derived drug; anuria.

Precautions: Hepatic disease; surgery/ anaesthesia; metabolic and endocrine effects (dosage of antidiabetic drugs may be adjusted); not recommended for pregnant and nursing women, and children.

Adverse effects: Dizziness, fatigue, muscle cramps, cough, nausea, headache, asthenia.

Advice to patients: See under Enalapril.

Nursing considerations: See under Enalapril.

Dose: *Hypertension*, usually one tablet daily; may be increased to 2 tablets once daily if necessary.
Prior diuretic therapy, discontinue the diuretic 2-3 days prior to initiation of therapy.

POM **CO-RENITEC**® *(Bolax/BPP)*
Tablet, Enalapril maleate 20 mg, hydrochlorothiazide 12.5 mg.
Pack - 10; 30.

POM **ENAZIDE**® *(Titan)*
Tablet, Enalapril 10 mg, hydrochlorothiazide 25 mg.
Pack - 10 x 10.

LISINOPRIL

Therapeutic category: Antihypertensive.

Pharmacology: Lisinopril is an ACE inhibitor. Time for onset of hypotensive effect after oral

administration is within 6 hours. Lisinopril is well absorbed and is unaffected by food in the stomach. It is almost entirely excreted in urine as unchanged drug.

Indications: Essential and renovascular hypertension; congestive heart failure (CHF) as an adjunctive treatment with diuretics and where appropriate digitalis; haemodynamically stable patients within 24 hours of an acute myocardial infarction (AMI); renal complications of diabetes.

Contra-indications: Hypersensitivity to ACE inhibitors; history of angioneurotic oedema either hereditary or idiopathic or associated with previous ACE inhibitors.

Precautions: Volume depleted patients and CHF (symptomatic hypotension may occur); ischaemic heart or cerebrovascular disease; history of angioedema; patients undergoing desensitisation treatment and certain haemodialysis procedures (anaphylactoid reactions may occur); renal impairment (reduce dose or avoid); surgery/anaesthesia (hypotension may occur); pregnancy and breast-feeding.

Interactions:

•Diuretics, other antihypertensives, probenecid (increased hypotensive effects).

•Aspirin, indomethacin (decreased effect of lisinopril).

•Potassium supplements, potassium-sparing diuretics (increased potassium levels).

•Allopurinol (increased hypersensitivity reactions).

Adverse effects: Nausea, headache, fatigue, cough, rash, diarrhoea, orthostatic effects, asthenia, GI irritation; rarely angioneurotic oedema (discontinue); palpitations; abdominal pain, dry mouth, hepatitis, alopecia, cholestatic jaundice; increases (usually reversible) in blood urea, serum creatinine, liver enzymes and serum bilirubin; thrombocytopenia, neutropenia, granulocytosis, hyperkalaemia.

Advice to patients: See under Enalapril.

Nursing considerations: See under Enalapril.

Dose: *Hypertension*, initially 10 mg once daily (lower starting dose required in patients with renal impairment, renovascular hypertension, volume or salt depleted patients, when diuretics cannot be discontinued, and some elderly patients); usual maintenance dose 10-20 mg daily. Adjust dosage according to blood pressure response upto a max. 80 mg daily.

CHF, initially 2.5 mg once daily; usual maintenance dose 5-20 mg daily. To be used together with diuretics and appropriate digitalis.

Acute myocardial infarction (within 24 hours in haemodynamically stable patients), initially 5 mg, followed by 5 mg after 24 hours; then 10 mg after 48 hours and 10 mg once daily thereafter.

Renal complications, 10-20 mg once daily.

POM **ACEPRIL**® *(Korlyns)*

Tablet (5 mg), Lisinopril 5 mg; white oblong tab. marked 'DUO 861'.
Pack – 100's; 250's; 500's.
Tablet (10 mg), Lisinopril 10 mg; light green oblong tab. marked 'DUO 861'.
Pack – 100's; 250's; 500's.
Tablet (20 mg), Lisinopril 20 mg; orange oblong tab. marked 'DUO 861'.
Pack – 100's; 250's; 500's.

POM **RANOPRIL**® *(Ranbaxy)*

Tablets, Lisinopril (as dihydrate) Ph. Eur. 5 mg, 10 mg, 20 mg.
5 mg - 10 x 10's (in blister)
10 mg - 10 x 10's (in blister)
20 mg - 10 x 10's (in blister).

POM **ZESTRIL**® *(Reals)*

Tablets, Lisinopril 5 mg, 10 mg, 20 mg.
5 mg - 28
10 mg - 28
20 mg - 28.

LISINOPRIL plus HYDROCHLOROTHIAZIDE

Therapeutic category: Antihypertensive/ Diuretic.

Indications: Treatment of essential hypertension for patients in whom combination therapy is appropriate.

Contra-indications: Hypersensitivity to any component of the preparation; anuria; history of angioedema relating to ACE inhibitor, hereditary or idiopathic angioedema; hypersensitivity to sulphonamide derived drugs; pregnancy and lactation.

Precautions: Symptomatic hypotension especially in the presence of fluid or electrolytes imbalance, e.g. volume depletion (monitor serum electrolytes periodically); avoid in renal insufficiency; impaired hepatic function or progressive liver disease (alterations of fluid and electrolyte balance may precipitate hepatic coma); surgery/anaesthesia (hypotension may occur); thiazides may impair glucose tolerance (dosage of insulin and other antidiabetic agents may be adjusted); thiazides

may precipitate hyperuricaemia and/or gout.
Interactions:
•Potassium supplements, potassium-sparing agents, or potassium-containing salt substitutes (may cause increased serum potassium).
•Lithium (co-administration reduces the renal clearance of lithium).
•Indomethacin, ohter NSAIDs, tubocurarine.
Adverse effects: Dizziness, headache, non-productive and persistent cough, fatigue, hypotension including orthostatic hypotension, diarrhoea, nausea, vomiting, dry mouth, rash, gout, palpitations, chest discomfort, muscle cramps and weakness, paraesthesia, asthenia and impotence; rarely, hypersensitivity/ angioedema.
Advice to patients: See under Enalapril.
Nursing considerations: See under Enalapril.
Dose: *Hypertension*, usually one tablet once daily; may be increased to two tablets once daily if the desired therapeutic effect is not achieved after 2 to 4 weeks.
Note: To be taken at approximately the same time each day as with all other medications taken once daily. Not recommended for children.

POM **ZESTORETIC**® *(Reals)*
Tablet, Lisinopril 20 mg, hydrochlorothiazide 12.5 mg.
Pack - 20 x 28.

5.3.6 Calcium–channel blockers

These agents **(Amlodipine, Isradipine, Nifedipine, Lacidipine)** interfere with the action of intracellular calcium on both smooth and cardiac muscles. They are also used in the treatment of Angina. The common adverse effects which result from reflex responses to peripheral vasodilation, can be countered by beta-blockers (flushing, headache) or diuretics (fluid retention).
Nifedipine has more influence on vessels and less on the myocardium, and has no antiarrhythmic properties when compared with **Verapamil**.

AMLODIPINE

Therapeutic category: Antihypertensive/anti-angina.
Pharmacology: Amlodipine is a calcium ion influx inhibitor (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and smooth muscle. The antihypertensive action is due to a relaxant effect on vascular smooth muscle. The antianginal effect is believed to be due to a reduction in the total ischaemic burden either by dilating the peripheral arterioles and thus, reducing the total peripheral resistance (afterload) against which the heart works or by dilating the main coronary arteries and coronary arterioles thereby increasing myocardial oxygen delivery in patients with coronary artery spasm (or Prinzmetal's or variant angina).
Indications: Hypertension; myocardial ischaemia whether due to fixed obstruction (stable angina) and/or vasospasm/vasoconstriction (Prinzmetal's or variant angina) of coronary vasculature; alone or in combination with other antianginal drugs in patients with angina that is refractory to nitrates and/or beta-blockers.
Precautions: Impaired hepatic function, pregnancy, breast-feeding.
Adverse effects: Headache, oedema, fatigue, nausea, flushing and dizziness.
Advice to patients: Do not discontinue abruptly; report any dizziness, shortness of breath; palpitations, or oedema.
•Administer once daily with or without food.
•Advise patient not to drive or operate machinery until stabilized on medication; to make position changes slowly to prevent orthostatic hypotension.
•Advise patient to avoid OTC preparations unless on prescription.
•Teach patient to observe and report irregular heartbeat, shortness of breath, swelling of feet and hands, severe dizziness, constipation, nausea, hypotension.
•Monitor pulse, I&O (note fluid retention), daily weight (inform doctor of any increase), B.P., respiration.
Dose: By mouth, *Hypertension or angina*, initially 2.5 to 5 mg once daily; increase if necessary to a max. 10 mg daily depending on the individual patient's response.
Note: Adjust dosage according to the patient's need over 7 to 14 days. Small, fragile or elderly individuals, or patients with hepatic insufficiency should be started 2.5 mg once daily and this dose may be used when adding amlodipine to other antihypertensive therapy.

POM **NORVASC**® *(Pfizer)*
Tablets, Amlodipine besylate 5 mg, 10 mg; white scored emerald-shaped tab.
5 mg - 10; 100
10 mg - 10; 100.

FELODIPINE

Therapeutic category: Antihypertensive/Anti-

angina.

Pharmacology: Felodipine is a highly vascular selective calcium antagonist, which in therapeutic doses has no direct effect on cardiac contractility or condition. As a result of arterior dilatation, it lowers systemic vascular resistance and arterial blood pressure. Coronary blood flow is increased due to dilatation of both epicardial arteries and arterioles.

Indications: Management of hypertension; prophylaxis of chronic stable angina.

Contra-indications: Pregnancy; hypersensitivity to felodipine or the ingredient; uncompensated heart failure; acute myocardial infarction; unstable angina pectoris.

Precautions: May precipitate significant hypotension which may result in myocardial ischaemia (withdraw if ischaemic pain or cardiogenic shock occurs after initiating therapy). Avoid co-administration with grapefruit juice (may inhibit metabolism of felodipine leading to increased plasma concentration). Breast-feeding; hepatic impairment.

Interactions:

•Co-administration with substances which interfere with the cytochrome P450 3A4 enzyme system may affect plasma concentrations of dihydropyridine calcium antagonists such as felodipine.

•Enzyme inhibitors (e.g. cimetidine, erythromycin, itraconazole, ketoconazole and certain flavonoids present in grapefruit juice) may increase plasma concentration of felodipine.

•Enzyme inducers (e.g. phenytoin, carbamazepine, rifampicin and barbiturates) may decrease plasma concentrations of felodipine.

Adverse effects: Flushing, headache, palpitations, dizziness, fatigue, gravitational oedema, rash and pruritus, gum hyperplasia, angiodema, aggravation of angina on initiation of therapy.

Advice to patients: See Label 25 in Appendix 6.

Nursing considerations: See under Amlodipine.

Dose: *Hypertension*, initially 5 mg (elderly 2.5 mg) once daily in the morning; the dose may be increased or another antihypertensive agent added if necessary. Maintenance: 5-10 mg once daily. Doses higher than 20 mg generally not required.

Angina pectoris, initially 5 mg once daily in the morning; increased if needed to 10 mg once daily.

Note: Tablets should be swallowed whole with water, administered in the morning. Not indicated for use in children.

POM **PLENDIL®** *(Reals)*
Tablets, Felodipine 2.5 mg, 5 mg, 10 mg.

ISRADIPINE

Therapeutic category: Antihypertensive.

Pharmacology: Isradipine is a potent dihydropyridine calcium antagonist with a higher affinity for calcium channels in arterial smooth muscle than for those in the myocardium. It thus dilates arterial vascular beds, in particular those of the heart, brain and skeletal muscle without depressing cardiac function. As a result of peripheral vasodilation, arterial blood pressure is lowered. At blood pressure lowering doses, isradipine possesses a moderate but significant natriuretic activity in animals and man.

Indications: Hypertension.

Precautions: Renal or hepatic dysfunction, chronic heart failure, elderly; tight aortic stenosis; hypersensitivity reactions (discontinue); pregnancy, breast feeding, children.

Interactions:

•Propranolol, anticoagulants, anticonvulsants, cimetidine; rifampicin or other enzyme-inducing drugs e.g. phenobarbital (avoid concomitant administration).

Adverse effects: Dizziness, headache, flushing, tachycardia and palpitation, localised oedema of non–cardiac origin; rarely orthostatic hypotension, fatigue, abdominal discomfort, skin rash; elevation of serum transaminases.

Advice to patients: Do not discontinue abruptly; report any dizziness, shortness of breath, palpitations, or oedema.

Nursing considerations: See under Amlodipine.

Dose: By mouth, Adult: *mild to moderate hypertension*, 2.5 mg twice daily; may be increased if necessary to 5 mg twice daily after 4 weeks.

Elderly or in impaired hepatic or renal function, 1.25 mg twice daily.

POM **LOMIR®** *(Novartis)*
Tablet, Isradipine 2.5 mg; angle-scored tab.
Capsules (SRO), Isradipine 2.5 mg, 5 mg.

NIFEDIPINE

Nifedipine is a representative dihydropyridine calcium-channel blocker. Various drugs can serve as alternatives.

Therapeutic category: Antihypertensive.

Pharmacology: Nifedipine is a calcium ion antagonist, acting by inhibition of calcium ion flow through low channels towards contractile fibers. It also decreases heart work and myocardial oxygen demand and relaxes vascular smooth muscle, thereby reducing peripheral vascular resistance.

Indications: Hypertension.

Contra-indications: Cardiogenic shock; advanced aortic stenosis; within 1 month of myocardial infarction; unstable or acute attacks of angina; porphyria.

Precautions: Stop if ischaemic pain occurs or existing pain worsens shortly after starting treatment; poor cardiac reserve; heart failure or significantly impaired left ventricular function; reduce dose in hepatic impairment (Appendix 5); diabetes mellitus; may inhibit labour; pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid grapefruit juice (may affect metabolism); **interactions**: Appendix 1.

Adverse effects: Headache, flushing, dizziness, lethargy; tachycardia, palpitations; gravitational oedema (only partly responsive to diuretics); rash (erythema multiforme reported), pruritus, urticaria; nausea, constipation or diarrhoea; increased frequency of micturition; eye pain, visual disturbances; gum hyperplasia; paraesthesia, myalgia, tremor; impotence, gynaecomastia; depression; telangiectasis; cholestasis, jaundice.

Advice to patients: See Label 21 and (label 25 for sustained release preparations) in Appendix 6.

Nursing considerations: •Administer with or without meals.

•Sustained release products should be given with food and not crushed or chewed.

•Advise patient not to drive or operate machinery until stabilized on medication; to make position changes slowly to prevent orthostatic hypotension.

•Advise patient to limit caffeine intake and to avoid alcohol and OTC drugs.

•Patient should notify physician if angina pain is not reduced when taking this drug, and if irregular heartbeat, shortness of breath, swelling, dizziness, constipation, nausea, or hypotension occurs.

•Advise patient not to stop therapy without physician's advice.

•May cause some patients to urinate frequently at night; may cause inflamed gums - teach good oral hygiene.

•Capsule may be punctured and drug solution administered sublingually or orally to reduce B.P. in recumbent patient.

Dose: *Hypertension*, by mouth (as sustained-release tablets), ADULT usual range 20–100 mg daily in 1–2 divided doses, according to manufacturer's directions.

NOTE: PRESCRIBERS SHOULD BE AWARE THAT DIFFERENT FORMULATIONS OF SUSTAINED-RELEASE TABLETS MAY NOT HAVE THE SAME CLINICAL EFFECT; IF POSSIBLE, THE PATIENT SHOULD BE MAINTAINED ON THE SAME BRAND. SHORT-ACTING FORMULATIONS OF NIFEDIPINE SHOULD BE AVOIDED IN HYPERTENSION, PARTICULARLY IN PATIENTS WHO ALSO HAVE ANGINA, SINCE THEIR USE MAY BE ASSOCIATED WITH LARGE VARIATIONS IN BLOOD PRESSURE AND REFLEX TACHYCARDIA, POSSIBLY LEADING TO MYOCARDIAL OR CEREBROVASCULAR ISCHAEMIA.

POM **Nifedipine** *(WMF 12.3)*
Sustained-release tablets (Modified-release tablets), Nifedipine 10 mg.
NOTE: SUSTAINED-RELEASE (PROLONGED-RELEASE) TABLETS ARE AVAILABLE FOR ONCE DAILY ADMINISTRATION. A PROPOSAL TO INCLUDE SUCH A PRODUCT IN A NATIONAL LIST OF ESSENTIAL DRUGS SHOULD BE SUPPORTED BY ADEQUATE DOCUMENTATION.

POM **Nifedipine** *(EDL 12.3)*
Tablet or Capsule, Nifedipine 10 mg, 20 mg.

POM **ARCONIFED®** *(Strides Vital)*
Capsule, Nifedipine 10 mg.
10 mg - 10 x 10's

POM **APO-NIFED-PA®** *(Lahams)*
Tablet (prolonged action), Nifedipine 20 mg; greyish-pink, f-c tab. marked '20'.
20 mg - 60.

POM **CALRIF®** *(Interpharma)*
Tablet, Nifedipine 20 mg.
20 mg - 10 x 10's.

POM **CORACTEN®** *(GSK)*
Capsule, (spansule), Nifedipine 20 mg; s-r, opaque light-brown capsules, with opaque red cap, containing yellow pellets.

POM **NIFECARD®** *(Taylek)*
Tablet, Nifedipine 10 mg.
10 mg - 50.
Retard tablet, Nifedipine 20 mg.
20 mg - 50.

POM **NIFECARD XL®** *(Taylek)*
Tablets, Nifedipine 30 mg, 60 mg; extended release tablets.
30 mg - 20; 30; 100.
60 mg - 20; 30; 100; 400.

Indications: Arterial hypertension; coronary disease (stable or vasospastic angina pectoris).

Dose: By mouth, Adult, initially 30 mg or 60 mg once daily; adjust according to

patient's needs. Do not exceed 90mg daily.

Note: To be swallowed whole, not divided, crushed or chewed. Discontinue therapy gradually.

POM **NIFEGEM RETARD**® *(Gemini)*
Tablet, Nifedipine 20 mg.
20 mg - 20; 56; 100.

Indications: Treatment of coronary heart disease due to insufficient myocardial oxygen supply, chronic stable angina pectoris, angina pectoris after cardiac infarction (except for the 8 days after acute myocardial infarction. Treatment of hypertension.

Dose: *Coronary heart disease, chronic stable angina pectoris (stress-induced angina), angina pectoris after cardiac infarction*, 10 mg twice a day.
Dose should be given according to the need of the individual, severity of the disease and patient's responsiveness.
In some further cases, an increase in the dose to 2 x 40 mg may be necessary.

Administration - Long term treatment: It should be taken with a little liquid, independent of mealtime and at a recommended interval doses of about 12 hrs and should not be less than 4 hrs.

Note: If an adequate antiangina effect is not achieved after about 14 days of treatment of angina pectoris, the patient should be changed over to the fast acting Nifegem capsules (10 mg), as advised by the doctor. The drug contains a light-sensitive active substance protected from light inside its packaging; nevertheless, the tablets should only be removed from foil immediately before use. The tablets should not be divided due to its light-sensitive active substance thereby destroying its protections.

POM **NIFFEX RETARD**® *(Titan)*
Tablet, Nifedipine 20 mg; s-r tab.
20 mg - 10 x 2 x 10.

POM **RETARDIN**® *(Fidson)*
Tablet, Nifedipine 20 mg; s-r tab.
20 mg - 50.

LACIDIPINE

Therapeutic category: Antihypertensive.

Pharmacology: Lacidipine is a specific and potent calcium antagonist, with a predominant selectivity for calcium channels in the vascular smooth muscle. Its main action is to dilate peripheral arterioles, reducing peripheral vascular resistance and lowering blood pressure. Lacidipine is rapidly but poorly absorbed from the GIT following oral dosing. It undergoes extensive first pass metabolism in the liver. Peak plasma concentrations are reached between 30 and 150 minutes. The drug is eliminated primarily by hepatic metabolism and it is not associated with either induction or inhibition of hepatic enzymes. Approximately 70% of the administered dose is eliminated as metabolites in the faeces and the remainder as metabolites in the urine.

Indications: Treatment of hypertension either alone or in combination with other antihypertensive agents e.g. Beta-blockers and diuretics.

Contra-indication: Hypersensitivity to lacidipine.

Precautions: Liver failure (antihypertensive effect may be increased); Cardiac abnormalities; pregnancy, breast-feeding.

Interactions: •Other antihypertensive agents e.g. diuretics and beta-blockers (co-administration may have additive hypotensive effect).
•Cimetidine (co-administration may increase plasma level of lacidipine).

Adverse effects: Headache, flushing, oedema, dizziness and palpitation; less commonly, asthenia, skin rash (including erythema and itching), gastric upset, nausea and polyuria; few cases of chest pain and gingival hyperplasia which are common with other calcium antagonists.

Dose: By mouth, Adult, initially 4 mg once daily; increased if necessary to 6 mg once daily after about 3–4 weeks (i.e. enough time for full pharmacological effect to be realised).
In liver disease, reduce dose to 2 mg once daily.
In renal disease, no dosage modification required (not excreted by the kidneys).
In the elderly, initially 2 mg once daily; increased to 4-6 mg daily if necessary as above.

Note: Lacidipine should be taken at the same time each day, preferably in the morning. It can be taken at any time relative to food.

POM **LACIPIL**® *(GSK)*
Tablets, Lacidipine 2 mg, white, circular, f–c tab. marked '2' on one side; 4 mg, white, f–c, oval, biconvex tab. scored on both sides.

VERAPAMIL

Therapeutic category: Antianginal Agent;

Antiarrhythmic Agent,Class IV; Antihypertensive; Calcium Channel Blocker.

Pharmacology: Verapamil inhibits calcium ion influx across cardiac and smooth muscle cells, thus decreasing myocardial contractility and oxygen demand, and dilates coronary arteries and arterioles.

Indications: Angina pectoris (vasospastic ,chronic stable, unstable), hypertension, supraventricular tachyarrhythmias.

Contra-indications: Sinus bradycardia; ventricular tachycardia; 2nd or 3rd degree AV block; cardiogenic shock; artrial fibrillation or flutter associated with accessory conduction pathways; hypersensitivity to verapamil or any component.

Precautions: I.V. administration should be done with ECG and B.P. monitoring plus facilities for resustation and cardioversion. Pregnancy (avoid during the Ist half), breast-feeding; hepatic or renal impairment; hypotension; avoid abrupt withdrawal .

Adverse effects: Constipation, headache, dizziness, orthostatic hypotension, peripheral oedema; impairment of liver or kidney function especially in high doses; bradycardia; Ist, 2nd or 3rd degree A-V block..

Advice to patients: Sustained release products should be taken with food and not crushed; limit caffeine intake; notify physician if angina pain is not reduced when taking this drug ,or if irregular heartbeat or shortness of breath occurs.

Nursing considerations: •Give before meals, at bedtime.

•Taking sustained-release tablets with food may decrease rate and extent of absorption, but allows smaller fluctuations of peak and trough blood levels. Do not crush sustained-release drug product; administer around-the-clock to promote less variation in peak and trough serum levels;

•Give I.V. dose slowly over at least 3 minutes to minimize the risk of adverse reactions.

•Advise patient not to drive or operate machinery until stabilized on medication; to make position changes slowly to prevent orthostatic hypotension.

•Advise patient to limit caffeine intake and to avoid alcohol and OTC drugs unless prescribed.

•Signs of CHF such as swelling of hands and feet or shortness of breath should be reported to the physician.

•Monitor B.P. closely.

Dose: By mouth, *Angina*, 80-120 mg 3 times daily;

Hypertension, 240-480 mg daily in 2-3 divided doses;

Supraventricular tachyarrhythmias, 40-120 mg 3 times daily.

By slow I .V.injection over 2 mins (3 mins in elderly), *Supraventricular tachyarrhythmias*, 5-10 mg; a second dose of 10 mg may be given 15-30 mins after the initial dose if patient tolerates, but does not respond to initial dose.

Note: I.V. administration should preferably be done with close B.P. and ECG monitoring.

POM **Verapamil** *(Sanofi)*

Tablets, Verapamil HCl 40 mg, 80 mg; coated tabs.

40 mg – 100; 1000.

80 mg – 100; 1000.

Injection, Verapamil HCl 2.5 mg per ml; in 2 ml amp.

Pack - 5; 25.

5.3.7 Diuretics

See also section 5.2

HYDROCHLOROTHIAZIDE

Hydrochlorothiazide is a representative thiazide diuretic. Various drugs can serve as alternatives.

Indications: Alone in mild hypertension, and in combination with other drugs in moderate to severe hypertension; heart failure (section 5.1); oedema (section 5.2.1).

Contra-indications: Severe renal or severe hepatic impairment; hyponatraemia, hypercalcaemia, refractory hypokalaemia, symptomatic hyperuricaemia; Addison disease.

Precautions: Renal and hepatic impairment (Appendices 4 and 5); pregnancy and breastfeeding (Appendices 2 and 3); elderly (reduce dose); may cause hypokalaemia; may aggravate diabetes mellitus and gout; may exacerbate systemic lupus erythematosus; porphyria; **interactions**: Appendix 1.

Adverse effects: Fluid and electrolyte imbalance leading to dry mouth, thirst, gastrointestinal disturbances (including nausea, vomiting), weakness, lethargy, drowsiness, seizures, headache, muscle pains or cramps, hypotension (including postural hypotension), oliguria, arrhythmias; hypokalaemia, hypomagnesaemia, hyponatraemia, hypochloraemic alkalosis, hypercalcaemia; hyperglycaemia, hyperuricaemia, gout; rash, photosensitivity; altered plasma lipid concentration; rarely impotence (reversible); blood disorders (including neutropenia, thrombocytopenia); pancreatitis, intrahepatic cholestasis; acute renal failure;

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hypersensitivity reactions (pneumonitis, pulmonary oedema, severe skin reactions).
Dose: *Hypertension*, by mouth, ADULT 12.5–25 mg daily; ELDERLY initially 12.5 mg daily.

POM **Hydrochlorothiazide** *(WMF 12.3)*
Tablets, Hydrochlorothiazide 25 mg.

5.4 Antiarrhythmic drugs

Treatment of arrhythmias requires precise diagnosis of the type of arrhythmia, and electrocardiography is essential; underlying causes such as heart failure require appropriate treatment.

Antiarrhythmic drugs must be used cautiously since most drugs that are effective in treating arrhythmias can provoke them in some circumstances; this arrhythmogenic effect is often enhanced by hypokalaemia. When antiarrhythmic drugs are used in combination, their cumulative negative inotropic effects may be significant, particularly if myocardial function is impaired.

Atrial fibrillation

The increased ventricular rate in atrial fibrillation can be controlled with a **beta-adrenoceptor antagonist** (beta-blocker) or **verapamil**. **Digoxin** is often effective for controlling the rate at rest; it is also appropriate if atrial fibrillation is accompanied by congestive heart failure. Intravenous digoxin is occasionally required if the ventricular rate needs rapid control. If adequate control at rest or during exercise cannot be achieved readily verapamil may be introduced with digoxin, but it should be used with caution if ventricular function is impaired. **Anticoagulants** are indicated especially in valvular or myocardial disease, and in the elderly. **Warfarin** is preferred to acetylsalicylic acid in preventing emboli. If atrial fibrillation began within the previous 48 hours and there does not appear to be a danger of thromboembolism, antiarrhythmic drugs, such as **procainamide** or **quinidine**, may be used to terminate the fibrillation or to maintain sinus rhythm after cardioversion.

Atrial flutter

Digoxin will sometimes slow the ventricular rate at rest. Reversion to sinus rhythm is best achieved by direct current electrical shock. If the arrhythmia is long-standing, treatment with an anticoagulant should be considered before cardioversion to prevent emboli. Intravenous verapamil reduces ventricular fibrillation during paroxysmal (sudden onset and intermittent) attacks of atrial flutter. An initial intravenous dose may be followed by oral treatment; hypotension may occur with high doses. It should not be used for tachyarrhythmias where the QRS complex is wide unless a supraventricular origin has been established beyond doubt. If the flutter cannot be restored to sinus rhythm, antiarrhythmics such as **quinidine** can be used.

Paroxysmal supraventricular tachycardia

In most patients this remits spontaneously or can revert to sinus rhythm by reflex vagal stimulation. Failing this, intravenous injection of a beta-adrenoceptor antagonist (beta-blocker) or verapamil may be effective. Verapamil and a beta-blocker should **never** be administered concomitantly because of the risk of hypotension and asystole.

Ventricular tachycardia

Very rapid ventricular fibrillation causes profound circulatory collapse and must be treated immediately with direct current shock. In more stable patients intravenous **lidocaine** or **procainamide** may be used. After sinus rhythm is restored, drug therapy to prevent recurrence of ventricular tachycardia should be considered; a beta-adrenoceptor antagonist (beta-blocker) or verapamil may be effective.

Torsades de pointes is a special form of ventricular tachycardia associated with prolongation of the QT interval. Initial treatment with intravenous infusion of **magnesium sulfate** (usual dose 2 g over 10–15 minutes, repeated once if necessary) together with temporary pacing is usually effective; alternatively, isoprenaline infusion may be given with extreme caution until pacing can be instituted. **Isoprenaline** is an inotropic sympathomimetic; it increases the heart rate and therefore shortens the QT interval, but given alone it may induce arrhythmias.

Bradyarrhythmias

Sinus bradycardia (less than 50 beats/minute) associated with acute myocardial infarction may be treated with atropine.

Temporary pacing may be required in unresponsive patients. Drugs are of limited value for increasing the sinus rate long term in the presence of intrinsic sinus node disease and permanent pacing is usually required.

Cardiac arrest

In cardiac arrest, **epinephrine** (adrenaline) is given by intravenous injection in a dose of 1 mg (10 ml of 1 in 10 000 solution) as part of the procedure for cardiopulmonary resuscitation.

AMIODARONE

Therapeutic category: Antiarrhythmic Agent, Class III.

Pharmacology: Amiodarone is a Class III antiarrhythmic that inhibits adrenergic stimulation, prolongs the action potential and refractory period in myocardial tissue; decreases A-V conduction and sinus node function. It is administered orally or by I.V. infusion.Unlike oral amiodarone, I.V. amiodarone may act relatively rapidly. Amiodarone has a very long half - life (extending to several weeks) and only needs to be given once daily (but high doses may cause nausea unless divided).It is not considered a first - line antiarrhythamic due to high incidence of adverse reactions.

Indications: Treatment of arrhythmias particularly those refractory to other therapy or when other drugs are contra-indicated; may be used for paroxysmal supraventricular, nodal and ventricular tachycardias, atrial fibrillation and flutter, ventricular fibrillation.

Contra-indications: Hypersensitivity to amiodarone; severe sinus node dysfunction; marked sinus bradycardia except if pacemaker is fitted; thyroid disease; avoid I.V. use in severe respiratory failure; iodine sensitivity; sino-atrial heart block; pregnancy and breast-feeding; circulatory collapse; severe arterial hypotension.

Precautions: Hospitalize patients while initiating therapy; perform liver-function and thyroid-function tests before therapy and then every 6 months; elderly are predisposed to toxic effects; due to extensive tissue distribution and long half-life, the time arrhythmia will reocccur following discontinued therapy or interaction with subsequent therapy is unpredictable; avoid rapid I.V. administration or overdose (may precipitate circulatory collapse); perform chest X-ray before treatment; renal impairment; heart failure.

Interactions: •Due to long half-life of amiodarone, interaction may still occur several weeks after discontinuation of therapy.
•Oral anticoagulant (enhanced anticoagulant effect due to inhibition of its metabolism).
•Antiepileptics (metabolism of phenytoin inhibited with possible symptoms of phenytoin toxicity).
•Avoid co-administration with TCAs, antihistamines (astemizole and terfenadine), antimalarials (chloroquine, halofantrine, quinine, mefloquine, hydroxychloroquine), antipsychotics (phenothiazines, haloperidol, pimozide), and cisapride due to increased risk of ventricular arrhythmias.
•Beta-blockers and calcium-channel blockers (increased risk of bradycardia, AV block and myocardial depression).
•Lithium (increased risk of hypothyroidism).
•Cimetidine (increased plasma concentration of amiodarone).
•Cardiac glycosides (increased plasma concentration of digoxin).

Adverse effects: Phototoxicity, skin reactions, visual disturbances, anaphylaxis on rapid injection, pulmonary fibrosis, interstitial pneumonitis, hypotension, hypothyroidism or hyperthyroidism; GI, haematologic, neurological, hepatic, cardiac, CNS, and respiratory effects.

Advice to patients: See Label 11 in Appendix 6. Take with food; use sunscreen or stay out of sun to prevent burns; may wear sunglasses if photophobia occurs; do not discontinue abruptly; notify physician if persistent dry cough or shortness of breath occurs (may be signs of respiratory failure).

Nursing considerations: •Divide oral loading dose into three equal doses and give with meals to minimize GI upset. Maintenance dose may be given once daily, but may be divided into two doses and given with meals if GI upset occurs.
•Monitor liver-function and thyroid-function tests, B.P. and heart rate; report any significant changes to the physician.
•Observe closely for adverse reactions including pulmonary toxicity.
•Advise patient to use a sunscreen to prevent photosensitivity.

Dose: By mouth, 200 mg 3 times daily for 1 week reduced to 200 mg twice daily for a further week; maintenance, usually 200 mg daily or the minimum required to control the arrhythmia.
By I.V. infusion via caval catheter, 5 mg/kg over 20-120 minutes with ECG monitoring; max. 1.2 g in 24 hours.

POM **CORDARONE**® *(Sanofi)*
Tablet, Amiodarone 200 mg; white scored tab.

200 mg - 30; 50.

ATENOLOL

Atenolol is a representative beta-adrenoceptor antagonist. Various drugs can serve as alternatives.

Indications: Arrhythmias; angina (section 5.5); hypertension (section 5.3); migraine prophylaxis (section 1.9.2)

Contra-indications: Asthma or history of obstructive airways disease (unless no alternative, then with extreme caution and under specialist supervision); uncontrolled heart failure, Prinzmetal angina, marked bradycardia, hypotension, sick sinus syndrome, second- and third-degree atrioventricular block, cardiogenic shock; metabolic acidosis; severe peripheral arterial disease; phaeochromocytoma (unless used with alpha-blocker).

Precautions: Avoid abrupt withdrawal especially in angina; may precipitate or worsen heart failure; pregnancy (Appendix 2); breastfeeding (Appendix 3); first-degree atrioventricular block; liver function deteriorates in portal hypertension; reduce dose in renal impairment (Appendix 4); diabetes mellitus (small decrease in glucose tolerance, masking of symptoms of hypoglycaemia); history of hypersensitivity (increased reaction to allergens, also reduced response to epinephrine (adrenaline)); myasthenia gravis; **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances (nausea, vomiting, diarrhoea, constipation, abdominal cramp); fatigue; cold hands and feet; exacerbation of intermittent claudication and Raynaud phenomenon; bronchospasm; bradycardia, heart failure, conduction disorders, hypotension; sleep disturbances, including nightmares; depression, confusion; hypoglycaemia or hyperglycaemia; exacerbation of psoriasis; rare reports of rashes and dry eyes (oculomucocutaneous syndrome—reversible on withdrawal).

Dose: *Arrhythmias*, by mouth, ADULT 50 mg once daily, increased if necessary to 50 mg twice daily or 100 mg once daily.

POM **Atenolol** *(WMF 12.2)*

Tablets, Atenolol 50 mg, 100 mg.

DIGOXIN

Indications: Supraventricular arrhythmias, particularly atrial fibrillation; heart failure (section 5.1).

Contra-indications: Hypertrophic obstructive cardiomyopathy (unless also atrial fibrillation and heart failure); Wolff-Parkinson-White syndrome or other accessory pathway, particularly if accompanied by atrial fibrillation; intermittent complete heart block; second-degree atrioventricular block.

Precautions: Recent myocardial infarction; sick sinus syndrome; severe pulmonary disease; thyroid disease; elderly (reduce dose); renal impairment (Appendix 4); avoid hypokalaemia; avoid rapid intravenous administration (nausea and risk of arrhythmias); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Usually associated with excessive dosage and include anorexia, nausea, vomiting, diarrhoea, abdominal pain; visual disturbances, headache, fatigue, drowsiness, confusion, delirium, hallucinations, depression; arrhythmias, heart block; rarely rash, intestinal ischaemia; gynaecomastia on long-term use; thrombocytopenia reported.

Dose: *Atrial fibrillation*, by mouth, ADULT 1–1.5 mg in divided doses over 24 hours for rapid digitalization or 250 micrograms 1–2 times daily if digitalization less urgent; maintenance 62.5–500 micrograms daily (higher dose may be divided), according to renal function and heart rate response; usual range 125–250 micrograms daily (lower dose more appropriate in elderly)

Emergency control of atrial fibrillation, by intravenous infusion over at least 2 hours, ADULT 0.75–1 mg.

NOTE: INFUSION DOSE MAY NEED TO BE REDUCED IF DIGOXIN OR OTHER CARDIAC GLYCOSIDE GIVEN IN PREVIOUS 2 WEEKS.

POM **Digoxin** *(WMF 12.2)*

Tablets, Digoxin 62.5 micrograms, 250 micrograms.

Oral solution, Digoxin 50 micrograms/ml

Injection (Solution for injection), Digoxin 250 micrograms/ml; in 2-ml ampoule.

DISOPYRAMIDE

Therapeutic category: Class I-A antiarrhythmic agent.
Indications: Treatment and prevention of ventricular arrhythmias.
Contra-indications: Complete heart block.
Precautions: Cardiac failure, partial heart block, renal or hepatic impairment, glaucoma, urinary retention, myasthenia gravis.
Adverse effects: Anticholinergic effects, GI upset, skin rashes, CNS disturbances, muscle ache and weakness, hypoglycaemia, hypokalaemia.
Nursing considerations: •Administer around-the-clock rather than 4 times/day (i.e, 12-6-12-6, not 9-1-5-9) to promote less variation in peak and trough serum levels.
•Do not crush controlled release capsules; constipation can be managed with proper diet or bulk laxatives or water; give chewing gum or hard candy to relieve the discomfort of dry mouth.
•Advise patient to avoid alcohol, and OTC drugs (unless on prescription).
•Instruct patient to make position changes gradually and to avoid hazardous activities if drowsiness or blurred vision occurs.
•Monitor pulse, I&O (note fluid retention), daily weight (inform doctor of rapid increase), B.P., respiration.
•Notify physician of urinary retention or worsening CHF.
•Notify the physician if pulse rate is below 60 beats/minute or above 120 beats/minute.
Dose: By mouth, 300-800 mg in divided doses.

POM **Disopyramide** *(EDL 12.2)*
Tablet or Capsule, Disopyramide 100 mg, 150 mg.

POM **NORPACE®** *(Morison)*
Capsule, Disopyramide phosphate 100 mg, 150 mg.
Pack - 20.

EPINEPHRINE

Synonym: Adrenaline.
Indications: Cardiac arrest; anaphylaxis (section 8.2).
Precautions: Heart disease, hypertension, arrhythmias, cerebrovascular disease; hyperthyroidism, diabetes mellitus; angle-closure glaucoma; second stage of labour; **interactions**: Appendix 1.
Adverse effects: Anxiety, tremor, tachycardia, headache, cold extremities; nausea, vomiting, sweating, weakness, dizziness, hyperglycaemia also reported; in overdosage arrhythmias, cerebral haemorrhage, pulmonary oedema.
Dose: CAUTION: DIFFERENT DILUTIONS OF EPINEPHRINE INJECTION ARE USED FOR DIFFERENT ROUTES OF ADMINISTRATION.

Cardiac arrest, by intravenous injection through a central line using epinephrine injection 1 in 10 000 (100 micrograms/ml), ADULT 1 mg (10 ml), repeated at 3-minute intervals if necessary.

NOTE: IF CENTRAL LINE NOT IN PLACE, SAME DOSE IS GIVEN VIA PERIPHERAL VEIN, THEN FLUSHED THROUGH WITH AT LEAST 20 ML SODIUM CHLORIDE 0.9% INJECTION (TO EXPEDITE ENTRY INTO CIRCULATION).

POM **Epinephrine** *(WMF 12.2)*
Injection (Solution for injection), Epinephrine HCl 100 micrograms/ml (1 in 10 000); in 10-ml ampoule.

ISOPRENALINE

Isoprenaline is a complementary antiarrhythmic for use in rare disorders or in exceptional circumstances.
Indications: Severe bradycardia, unresponsive to atropine; short-term emergency treatment of heart block; ventricular arrhythmias secondary to atrioventricular nodal block.
Precautions: Ischaemic heart disease, diabetes mellitus or hyperthyroidism; **interactions**: Appendix 1.
Adverse effects: Arrhythmias, hypotension, sweating, tremor, headache, palpitations, tachycardia, nervousness, excitability, insomnia.
Dose: *Cardiac disorders*, by slow intravenous injection, ADULT 20–60 micrograms (1–3 ml of solution containing 20 micrograms/ml); subsequent doses adjusted according to ventricular rate.
Bradycardia, by intravenous infusion, ADULT 1–4 micrograms/minute
Heart block (acute Stokes-Adams attack), by intravenous infusion, ADULT 4–8 micrograms/minute.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Isoprenaline** *(WMF 12.2)*
Injection (Solution for injection), isoprenaline HCl 20 micrograms/ml; in 10-ml ampoule.

LIDOCAINE

Indications: Ventricular arrhythmias (especially after myocardial infarction); local anaesthesia (section 3.4).

Contra-indications: Sino-atrial disorder, any grade of atrioventricular block or any other type of conduction disturbances, severe myocardial depression, acute porphyria or hypovolaemia.

Precautions: Lower dosage in congestive heart failure, bradycardia, hepatic impairment (Appendix 5), marked hypoxia, severe respiratory depression, following cardiac surgery and in elderly; pregnancy (Appendix 2), breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Dizziness, paraesthesia, drowsiness, confusion, apnoea, respiratory depression, coma, seizures, and convulsions, hypotension, arrhythmias, heart block, cardiovascular collapse and bradycardia (may lead to cardiac arrest); nystagmus often an early sign of lidocaine overdosage.

Nursing considerations: •Administer I.M. injection in deltoid muscle; aspirate to avoid intravascular administration. Check site regularly for infiltration or extravasation.

•Local thrombophlebitis may occur in patients receiving prolonged I.V. infusions; check I.V. site regularly for infiltration or extravasation.

•Monitor patient's response, especially B.P. and serum electrolytes, BUN, and creatinine and notify physician of any abnormalities.

•Discontinue drug and notify physician immediately if toxic signs such as dizziness, confusion occur; continued infusion may lead to seizures and coma.

Dose: *Ventricular arrhythmias*, by intravenous injection, ADULT, loading dose of 50–100 mg (or 1–1.5 mg/kg) at a rate of 25–50 mg/minute, followed immediately by intravenous infusion of 1–4 mg/minute, with ECG monitoring of all patients (reduce infusion dose if required for longer than 24 hours).

IMPORTANT: FOLLOWING INTRAVENOUS INJECTION LIDOCAINE HAS A SHORT DURATION OF ACTION (OF 15–20 MINUTES). IF IT CANNOT BE GIVEN BY INTRAVENOUS INFUSION IMMEDIATELY, THE INITIAL INTRAVENOUS INJECTION OF 50–100 MG CAN BE REPEATED IF NECESSARY ONCE OR TWICE AT INTERVALS OF NOT LESS THAN 10 MINUTES.

POM **Lidocaine** *(WMF 12.2)*

Injection (Solution for injection), Lidocaine HCl 20 mg/ml; in 5-ml ampoule.

POM **Lignocaine** *(EDL 12.2)*

Injection, Lignocaine HCl 20 mg per ml; 5 ml amp.

PROCAINAMIDE

Procainamide HCl is a representative antiarrhythmic drug. Various drugs can serve as alternatives. Procainamide hydrochloride is also a complementary drug for use when drugs in the core list are known to be ineffective or inappropriate for a given patient.

Synonym: Procaine Amide Hydrochloride.

Therapeutic category: Class I-A anti-arrhythmic agent.

Indications: Severe ventricular arrhythmias, especially those resistant to lidocaine or those appearing after myocardial infarction; atrial tachycardia, atrial fibrillation; maintenance of sinus rhythm after cardioversion of atrial fibrillation.

Contra-indications: Asymptomatic ventricular premature contractions, torsades de pointes, systemic lupus erythematosus, heart block, heart failure, hypotension.

Precautions: Elderly, renal and hepatic impairment (Appendices 4 and 5), asthma, myasthenia gravis, pregnancy; breastfeeding (Appendix 3); use only under specialist supervision; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, diarrhoea, anorexia, rashes, pruritus, urticaria, flushing, fever, myocardial depression, heart failure, angioedema, depression, dizziness, psychosis; blood disorders include leukopenia, haemolytic anaemia and agranulocytosis after prolonged treatment; lupus erythematosus-like syndrome; high plasma procainamide concentration may impair cardiac conduction.

Advice to patients: Do not discontinue therapy unless instructed by physician; notify physician or pharmacist if soreness of mouth, throat or gums, unexplained fever, or symptoms of upper respiratory tract infection occur; do not chew sustained release tablets.

Nursing considerations: •Do not crush sustained release drug product.

•Administer I.M. injection in deltoid muscle; aspirate to avoid intravascular administration.

•Give I.V. slowly as rapid injection can cause hypotension; check I.V. site regularly for infiltration or extravasation. Keep patient supine for I.V. administration if hypotension occurs.

•Monitor B.P., pulse, respiration (observe for respiratory depression).

•Monitor serum electrolytes especially potassium as hypokalaemia predisposes patients to arrhythmias.

•Monitor B.P closely in the elderly as they may experience hypotension more readily.

Dose: *Ventricular arrhythmias*, by mouth, adult up to 50 mg/kg daily in divided doses every 3–6 hours, preferably

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controlled by monitoring plasma-procainamide concentration (therapeutic concentration usually within range 3–10 micrograms/ml)
Atrial arrhythmias, higher doses may be required.
Ventricular arrhythmias, by slow intravenous injection, ADULT 100 mg at rate not exceeding 50 mg/minute, with ECG monitoring; may be repeated at 5-minute intervals until arrhythmia controlled; maximum 1 g.
Ventricular arrhythmias, by intravenous infusion, ADULT 500–600 mg over 25–30 minutes with ECG monitoring, reduced to maintenance dose of 2–6 mg/minute; if further treatment by mouth required, allow interval of 3–4 hours after infusion.

POM **Procainamide** *(WMF 12.2)*
Tablets, Procainamide HCl 250 mg, 500 mg [not included on WHO Model List].
Injection (Solution for injection), Procainamide HCl 100 mg/ml; in 10-ml ampoule.

POM **Procainamide** *(EDL 12.2)*
Tablet, Procainamide HCl 250 mg.
Injection, Procainamide HCl 100 mg per ml; in 10 ml amp.

QUINIDINE

Quinidine is a representative antiarrhythmic drug. Various drugs can serve as alternatives.
Quinidine sulfate is also a complementary antiarrhythmic drug for use when drugs in the core list cannot be made available.

Indications: Suppression of supraventricular arrhythmias and ventricular arrhythmias; maintenance of sinus rhythm after cardioversion of atrial fibrillation.

Contra-indications: Complete heart block.

Precautions: Partial heart block; extreme care in uncompensated heart failure, myocarditis, severe myocardial damage; myasthenia gravis; acute infections or fever (symptoms may mask hypersensitivity reaction to quinidine); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Hypersensitivity reactions, nausea, vomiting, diarrhoea, rashes, anaphylaxis, purpura, pruritus, urticaria, fever, thrombocytopenia, agranulocytosis after prolonged treatment, psychosis, angioedema, hepatotoxicity, respiratory difficulties; cardiac effects include myocardial depression, heart failure, ventricular arrhythmias and hypotension; cinchonism including tinnitus, impaired hearing, vertigo, headache, visual disturbances, abdominal pain, and confusion; lupus erythematosus-like syndrome.

Dose: Initial test dose of 200 mg to detect hypersensitivity to quinidine.
Arrhythmias, by mouth, ADULT 200–400 mg 3–4 times daily; increased if necessary in supraventricular tachycardia to 600 mg every 2–4 hours (maximum 3–4 g daily); frequent ECG monitoring required.

POM **Quinidine** *(WMF 12.2)*
Tablets, Quinidine sulfate 200 mg.
NOTE: QUINIDINE SULFATE 200 MG = QUINIDINE BISULFATE 250 MG.

VERAPAMIL

Indications: Supraventricular arrhythmias; angina (section 5.5).

Contra-indications: Hypotension, bradycardia, second- and third-degree atrioventricular block, sinoatrial block, sick sinus syndrome; cardiogenic shock; history of heart failure or significantly impaired left ventricular function (even if controlled by therapy); atrial flutter or fibrillation complicating Wolff-Parkinson-White syndrome; porphyria.

Precautions: First-degree atrioventricular block; acute phase of myocardial infarction (avoid if bradycardia, hypotension, left ventricular failure); hepatic impairment (Appendix 5); children (specialist advice only); pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid grapefruit juice (may affect metabolism); **interactions**: Appendix 1.
VERAPAMIL AND BETA-BLOCKERS: BOTH VERAPAMIL AND BETA-BLOCKERS HAVE CARDIODEPRESSANT ACTIVITY, AND THEIR USE TOGETHER MAY LEAD TO BRADYCARDIA, HEART BLOCK AND LEFT VENTRICULAR FAILURE, PARTICULARLY IN PATIENTS WITH MYOCARDIAL INSUFFICIENCY. TREATMENT WITH BETA-BLOCKERS SHOULD BE DISCONTINUED AT LEAST 24 HOURS BEFORE INTRAVENOUS ADMINISTRATION OF VERAPAMIL.

Adverse effects: Constipation; less commonly nausea, vomiting, flushing, headache, dizziness, fatigue, ankle oedema; rarely allergic reactions (erythema, pruritus, urticaria, angioedema,

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Stevens-Johnson syndrome); myalgia, arthralgia, paraesthesia, erythromelalgia; increased prolactin concentration; gynaecomastia and gingival hyperplasia on long-term treatment; with high doses, hypotension, heart failure, bradycardia, heart block, and asystole (due to negative inotropic effect).

Dose: *Supraventricular arrhythmias*, by mouth, ADULT 40–120 mg 3 times daily.

Supraventricular arrhythmias, by intravenous injection, ADULT 5–10 mg over 2 minutes (preferably with ECG monitoring); ELDERLY 5–10 mg over 3 minutes; in *paroxysmal tachyarrhythmias*, further 5 mg may be given after 5–10 minutes if required.

POM **Verapamil** *(WMF 12.2)*

Tablets, Verapamil HCl 40 mg, 80 mg.

NOTE: SUSTAINED-RELEASE (PROLONGED-RELEASE) TABLETS ARE AVAILABLE. A PROPOSAL TO INCLUDE SUCH A PRODUCT IN A NATIONAL LIST OF ESSENTIAL DRUGS SHOULD BE SUPPORTED BY ADEQUATE DOCUMENTATION.

Injection (Solution for injection), Verapamil HCl 2.5 mg/ml; in 2-ml ampoule.

5.5 Antianginal drugs

The three main types of angina are:

- *stable angina* (angina of effort), where atherosclerosis restricts blood flow in the coronary vessels; attacks are usually caused by exertion and relieved by rest
- *unstable angina* (acute coronary insufficiency), which is considered to be an intermediate stage between stable angina and myocardial infarction
- *Prinzmetal angina* (variant angina), caused by coronary vasospasm, in which attacks occur at rest.

Management depends on the type of angina and may include drug treatment, coronary artery bypass surgery, or percutaneous transluminal coronary angioplasty.

Stable angina

Drugs are used both for the relief of acute pain and for prophylaxis to reduce further attacks; they include organic nitrates, beta-adrenoceptor antagonists (beta-blockers), and calcium-channel blockers.

NITRATES

Organic nitrates have a vasodilating effect; they are sometimes used alone, especially in elderly patients with infrequent symptoms. Tolerance leading to reduced antianginal effect is often seen in patients taking prolonged-action nitrate formulations. Evidence suggests that patients should have a 'nitrate-free' interval to prevent the development of tolerance. Adverse effects such as flushing, headache, and postural hypotension may limit nitrate therapy but tolerance to these effects also soon develops. The short-acting sublingual formulation of **glyceryl trinitrate** is used both for prevention of angina before exercise or other stress and for rapid treatment of chest pain. A sublingual tablet of **isosorbide dinitrate** is more stable in storage than glyceryl trinitrate and is useful in patients who require nitrates infrequently; it has a slower onset of action, but effects persist for several hours.

BETA-BLOCKERS

Beta-adrenoceptor antagonists (beta-blockers), such as **atenolol**, block beta-adrenergic receptors in the heart, and thereby decrease heart rate and myocardial contractility and oxygen consumption, particularly during exercise. Beta-blockers are first-line therapy for patients with effort-induced chronic stable angina; they improve exercise tolerance, relieve symptoms, reduce the severity and frequency of angina attacks, and increase the anginal threshold.

Beta-blockers should be withdrawn gradually to avoid precipitating an anginal attack; they should not be used in patients with underlying coronary vasospasm (Prinzmetal angina).

Beta-blockers may precipitate asthma and should not be used in patients with asthma or a history of obstructive airways disease. Some, including atenolol, have less effect on $beta_2$ (bronchial) receptors and are therefore relatively cardioselective. Although they have less effect on airways resistance they are not free of this effect and should be avoided.

Beta-blockers slow the heart and may induce myocardial depression, rarely precipitating heart failure. They should not be given to patients who have incipient ventricular failure, second- or third-degree atrioventricular block, or peripheral vascular disease.

Beta-blockers should be used with caution in diabetes since they may mask the

symptoms of hypoglycaemia, such as rapid heart rate. Beta-blockers enhance the hypoglycaemic effect of insulin and may precipitate hypoglycaemia.

CALCIUM-CHANNEL BLOCKERS

A calcium-channel blocker, such as **verapamil**, is used as an alternative to a beta-blocker to treat stable angina. Calcium-channel blockers interfere with the inward movement of calcium ions through the slow channels in heart and vascular smooth muscle cell membranes, leading to relaxation of vascular smooth muscle. Myocardial contractility may be reduced, the formation and propagation of electrical impulses within the heart may be depressed and coronary or systemic vascular tone may be diminished. Calcium-channel blockers are used to improve exercise tolerance in patients with chronic stable angina due to coronary atherosclerosis or with abnormally small coronary arteries and limited vasodilator reserve.

Calcium-channel blockers can also be used in patients with unstable angina with a vasospastic origin, such as Prinzmetal angina, and in patients in whom alterations in cardiac tone may influence the angina threshold.

Unstable angina

Unstable angina requires prompt aggressive treatment to prevent progression to myocardial infarction.

Initial treatment is with acetylsalicylic acid to inhibit platelet aggregation, followed by heparin. Nitrates and beta-blockers are given to relieve ischaemia; if beta-blockers are contraindicated, verapamil is an alternative, provided left ventricular function is adequate.

Prinzmetal angina

Treatment is similar to that for unstable angina, except that a calcium-channel blocker is used instead of a beta-blocker.

Nursing Considerations:- Antianginals

•Monitor orthostatic B/P, pulse. Headache, light-headedness, decreased B/P may indicate a need for decreased dosage.

•Advise patient to avoid OTC products (unless prescribed by doctor), alcohol, smoking, sodium intake and to make position changes slowly to prevent fainting. To adhere to non-drug measures such as weight control, diet and exerxise.

ATENOLOL

Atenolol is a representative beta-adrenoceptor antagonist. Various drugs can serve as alternatives.

Indications: Angina and myocardial infarction; arrhythmias (section 5.4); hypertension (section 5.3); migraine prophylaxis (section 1.9.2).

Contra-indications: Asthma or history of obstructive airways disease (unless no alternative, then with extreme caution and under specialist supervision); uncontrolled heart failure, Prinzmetal angina, marked bradycardia, hypotension, sick sinus syndrome, second- and third-degree atrioventricular block, cardiogenic shock; metabolic acidosis; severe peripheral arterial disease; phaeochromocytoma (unless used with alpha-blocker).

Precautions: Avoid abrupt withdrawal in angina; may precipitate or worsen heart failure; pregnancy (Appendix 2); breastfeeding (Appendix 3); first-degree atrioventricular block; liver function deteriorates in portal hypertension; reduce dose in renal impairment (Appendix 4); diabetes mellitus (small decrease in glucose tolerance, masking of symptoms of hypoglycaemia); history of hypersensitivity (increased reaction to allergens, also reduced response to epinephrine (adrenaline)); myasthenia gravis; **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances (nausea, vomiting, diarrhoea, constipation, abdominal cramp); fatigue; cold hands and feet; exacerbation of intermittent claudication and Raynaud phenomenon; bronchospasm; bradycardia, heart failure, conduction disorders, hypotension; sleep disturbances, including nightmares; depression, confusion; hypoglycaemia or hyperglycaemia; exacerbation of psoriasis; rare reports of rashes and dry eyes (oculomucocutaneous syndrome—reversible on withdrawal).

Dose: *Angina*, by mouth, ADULT 50 mg once daily, increased if necessary to 50 mg twice daily or 100 mg once daily.

Myocardial infarction (early intervention within 12 hours), by intravenous injection over 5 minutes, ADULT 5 mg, then by mouth 50 mg after 15 minutes, followed by 50 mg after 12 hours, then 100 mg daily.

POM **Atenolol** *(WMF 12.1)*

Tablets, Atenolol 50 mg, 100 mg.
Injection (Solution for injection), Atenolol 500 micrograms/ml; in 10-ml ampoule [not included on WHO Model List].

DILTIAZEM

Therapeutic category: Antianginal agent; antihypertensive; calcium channel blocker.
Pharmacology: Diltiazem inhibits calcium ion from entering the "slow channel" of vascular smooth muscle and myocardium during depolarisation, producing a relaxation of coronary vascular smooth muscle and coronary vasodilation; it increases myocardial oxygen delivery in patients with vasospastic angina.
Indications: Chronic stable angina or angina from coronary artery spasm.
Contra-indications: Severe hypotension (less than 90mm Hg systolic) or second and third degree heart block; hypersensitivity to other calcium channel blockers, adenosine; atrial and ventricular arrhythmias, acute myocardial infarction and pulmonary congestion; pregnancy, lactation; hypersensitivity to the drug.
Precautions: Impaired renal or hepatic function (titrate dosage); CHF, severe left ventricular dysfunction, obstructive cardiomyopathy, oedema, concomitant therapy with beta-blockers or digoxin, or increased intracranial pressure with cranial tumors; do not abruptly withdraw (may cause chest pain); elderly may experience hypotension and constipation more readily.
Interactions: H_2 blockers, beta-blockers, digitalis, carbamazepine, cyclosporine, fentanyl, quinidine, theophylline.
Adverse effects: Headache, bradycardia, vasodilation (flushing), A-V block (first degree), oedema, ECG abnormality, dizziness, asthenia, nausea, vomiting; less commonly angina, amnesia, insomnia, nervousness, depression, urticaria, alopecia, purpura, GIT disturbances, blood disorders, tremor, retinopathy, pharyngitis, cough increase, flu syndrome, acute hepatic injury.
Advice to patients: Avoid alcohol; notify physician if angina pain is not reduced when taking this drug, or if irregular heartbeat, shortness of breath, swelling, dizziness, constipation, nausea, or hypotension occurs; do not stop therapy without advice of physician; limit caffeine consumption.
Nursing considerations: •Administer tablet before meals, preferably at bedtime.
•Monitor B.P. during initiation of therapy and dosage adjustment.
•Assist patient with ambulation as dizziness may oocur.
•Withhold drug and notify physician if systolic pressure is below 90 mm Hg, or heart rate is below 60 beats/minute.
•Advise patient to limit caffeine intake; to avoid OTC drugs unless prescribed; to avoid hazardous activities until stabilized on medication.
Dose: Adult, *Chronic stable angina or vasospastic angina*, by mouth, initially 30 mg 4 times daily, before meals and at bedtime; dosage should be gradually increased (given in 3-4 equally divided doses) at 1- to 2-day intervals until optimum response is obtained.
Dosage must be adjusted to each patient's needs.
Unstable angina pectoris (ICU use), titrate rapidly, upto 360 mg daily in 3-4 equally divided doses with consideration of concomitant therapy.
Maximum dose for all indications: 360 mg daily.

POM **APO-DILTIAZ®** *(Lahams)*
Tablet, Diltiazem HCl 30 mg; light green tab. marked 'APO D30'.
30 mg - 100.

GLYCERYL TRINITRATE

Synonym: Nitroglycerine; Nitroglycerol; NTG.
Therapeutic category: Anti-anginal.
Pharmacology: Glyceryl trinitrate relaxes smooth muscle, including vascular smooth muscle, and reduces systolic B.P. Its anti-anginal effect mainly depends on reducing myocardial oxygen demand by means of peripheral vasodilation which causes decreased venous return, permitting a reduction in left ventricular volume and energy expenditure.
Indications: Prophylaxis and treatment of angina.
Contra-indications: Hypersensitivity to nitrates; hypotension; hypovolaemia; hypertrophic obstructive cardiomyopathy, aortic stenosis, cardiac tamponade, constrictive pericarditis, mitral stenosis; marked anaemia; head trauma; cerebral haemorrhage; angle-closure glaucoma.
Precautions: Severe hepatic or renal impairment; hypothyroidism; malnutrition; hypothermia; recent history of myocardial infarction; **interactions**: Appendix 1.
Adverse effects: Throbbing headache; flushing; dizziness, postural hypotension; tachycardia (paradoxical bradycardia also reported).
Advice to patients: See Label 26 in Appendix 6. Notify physician if no relief after 3 sublingual

doses; do not swallow or chew sublingual form; do not change brands without notifying your physician or pharmacist; take oral nitrate on an empty stomach with a full glass of water.

Nursing considerations: •Teach paient to take sublingual tablet at first sign of attack. He should wet the tablet with saliva, place it under the tongue until completely absorbed, and sit down and rest.

•8- to 12-hour nitrate-free interval is needed each day to prevent tolerance.

•Advise patient to report to the physician if symptoms are not relieved 15 minutes after taking sublingual dosage form; also to take drug before stressful activities such as exercise, sexual activities.

•Tell patient to avoid hazardous activities if dizziness occurs and to make position changes slowly to prevent fainting.

•Instruct patient to avoid alcohol as it may cause increased hypotension.

•Drug may cause headche which can be relieved with aspirin or paracetamol.

Dose: *Angina*, sublingually, ADULT 0.5–1 mg; repeated as required.

POM **Glyceryl trinitrate** *(WMF 12.1)*
Sublingual tablets, Glyceryl trinitrate 500 micrograms.

NOTE: GLYCERYL TRINITRATE TABLETS ARE UNSTABLE. THEY SHOULD THEREFORE BE DISPENSED IN GLASS OR STAINLESS STEEL CONTAINERS, AND CLOSED WITH A FOIL-LINED CAP WHICH CONTAINS NO WADDING. NO MORE THAN 100 TABLETS SHOULD BE DISPENSED AT ONE TIME, AND ANY UNUSED TABLETS SHOULD BE DISCARDED 8 WEEKS AFTER OPENING THE CONTAINER.

POM **Glyceryl Trinitrate** *(EDL 12.1)*
Tablet, (Sublingual), Glyceryl trinitrate 0.5 mg.

ISOSORBIDE DINITRATE

Isosorbide dinitrate is a representative nitrate vasodilator. Various drugs can serve as alternatives.

Synonym: ISD; ISDN.

Therapeutic category: Anti-anginal.

Indications: Prophylaxis and treatment of angina; heart failure (section 5.1).

Contra-indications: Hypersensitivity to nitrates; hypotension; hypovolaemia; hypertrophic obstructive cardiomyopathy, aortic stenosis, cardiac tamponade, constrictive pericarditis, mitral stenosis; marked anaemia; head trauma; cerebral haemorrhage; angle-closure glaucoma.

Precautions: Severe hepatic or renal impairment; hypothyroidism; malnutrition; hypothermia; recent history of myocardial infarction; **interactions**: Appendix 1.

TOLERANCE: PATIENTS TAKING ISOSORBIDE DINITRATE FOR THE LONG-TERM MANAGEMENT OF ANGINA MAY OFTEN DEVELOP TOLERANCE TO THE ANTIANGINAL EFFECT; THIS CAN BE AVOIDED BY GIVING THE SECOND OF 2 DAILY DOSES OF LONGER-ACTING ORAL PRESENTATIONS AFTER AN 8-HOUR RATHER THAN A 12-HOUR INTERVAL, THUS ENSURING A NITRATE-FREE INTERVAL EACH DAY.

Adverse effects: Throbbing headache; flushing; dizziness, postural hypotension; tachycardia (paradoxical bradycardia also reported).

Advice to patients: See Label 26 in Appendix 6. Do not chew or crush sublingual or sustained release dosage form; notify physician if no relief from sublingual tablets after 15 minutes; do not change brands without consulting your pharmacist or physician.

Nursing considerations: •Administer oral form with plenty of water on an empty stomach, either 30 min before or 1 to 2 hours after meals; oral tablet should be swallowed whole while chewable tablet should be chewed thoroughly before swallowing.

•8- to 12-hour nitrate-free interval is needed each day to prevent tolerance.

•Ensure that patient does not confuse sublingual with oral form.

•Headache can be relieved with aspirin or paracetamol; advise patient to take drug before stressful activities; also not to discontinue drug abruptly to prevent vasospasm, and to make position changes slowly to prevent fainting.

•Advise patient to avoid alcohol; to avoid hazardous activities since dizziness or orthostatic hypotension may occur.

Dose: *Angina (acute attack)*, sublingually, ADULT 5–10 mg; repeated as required.
Angina prophylaxis, by mouth, ADULT 30–120 mg daily in divided doses (*see* advice on Tolerance above).

POM **Isosorbide dinitrate** *(WMF 12.1)*
Sublingual tablets, Isosorbide dinitrate 5 mg
Sustained-release (prolonged-release) tablets or capsules, Isosorbide dinitrate 20 mg, 40 mg [not included on WHO Model List].

POM **Isosorbide Dinitrate** *(EDL 12.1)*
Tablet, Isosorbide dinitrate 10 mg.
Tablet, (Sublingual), Isosorbide dinitrate 5 mg.

POM **APO-ISDN®** *(Lahams)*
Tablet (Sublingual), Isosorbide dinitrate 5 mg; pink tab. marked '5'
5 mg - 500.
Tablet, Isosorbide dinitrate 10 mg; white, scored tab. marked 'APO 10'.
10 mg - 1000.

POM **ISOBID®** *(Hovid)*
Tablet, Isosorbide dinitrate 10 mg.
10 mg - 1000.

RETURN

POM **ISORDIL**® *(Wyeth/Delpitano)*
Tablet, (Sublingual), Isosorbide dinitrate 5 mg; pink tab.
Tablets, Isosorbide dinitrate 10 mg, 30 mg; white scored tabs marked with tab. name and strength.
Pack - 500.
Capsule, Isosorbide dinitrate 40 mg; blue/clear s-r cap.
40 mg - 100.

VERAPAMIL

Indications: Angina, including stable, unstable, and Prinzmetal; arrhythmias (section 5.4).

Contra-indications: Hypotension, bradycardia, second- and third-degree atrioventricular block, sinoatrial block, sick sinus syndrome; cardiogenic shock; history of heart failure or significantly impaired left ventricular function (even if controlled by therapy); atrial flutter or fibrillation complicating Wolff-Parkinson-White syndrome; porphyria.

Precautions: First-degree atrioventricular block; acute phase of myocardial infarction (avoid if bradycardia, hypotension, left ventricular failure); hepatic impairment (Appendix 5); children (specialist advice only); pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid grapefruit juice; **interactions**: Appendix 1.

Adverse effects: Constipation; less commonly nausea, vomiting, flushing, headache, dizziness, fatigue, ankle oedema; rarely allergic reactions (erythema, pruritus, urticaria, angioedema, Stevens-Johnson syndrome); myalgia, arthralgia, paraesthesia, erythromelalgia; increased prolactin concentration; gynaecomastia and gingival hyperplasia on long-term treatment; with high doses, hypotension, heart failure, bradycardia, heart block, and asystole (due to negative inotropic effect).

Dose: *Angina*, by mouth, ADULT 80–120 mg 3 times daily (120 mg 3 times daily usually required in Prinzmetal angina).

POM **Verapamil** *(WMF 12.1)*
Tablets, Verapamil HCl 40 mg, 80 mg.
NOTE: SUSTAINED-RELEASE (PROLONGED-RELEASE) TABLETS ARE AVAILABLE. A PROPOSAL TO INCLUDE SUCH A PRODUCT IN A NATIONAL LIST OF ESSENTIAL DRUGS SHOULD BE SUPPORTED BY ADEQUATE DOCUMENTATION.

5.6 Antithrombotic drugs and myocardial infarction

Anticoagulants prevent thrombus formation or the extension of an existing thrombus. For further details see section 6.2 (drugs affecting coagulation).

Antiplatelet drugs also help to inhibit thrombus formation by decreasing platelet aggregation.

Thrombolytics (fibrinolytics) such as **streptokinase** are used to break up thrombi; they are used to treat acute myocardial infarction, extensive deep vein thrombosis, major pulmonary embolism and acute arterial occlusion.

Myocardial infarction

Management of myocardial infarction includes two phases:

- initial management of the acute attack
- long-term management, including prevention of further attacks.

Initial management

Oxygen (section 3.1.3) should be given to all patients, except those with severe chronic obstructive pulmonary disease.

Pain and anxiety are relieved by slow intravenous injection of an opioid analgesic such as **morphine** (section 1.8.2).

Metoclopramide (section 4.5) may also be given by intramuscular injection to prevent and treat nausea and vomiting caused by morphine.

Acetylsalicylic acid 150–300 mg by mouth (preferably chewed or dispersed in water) is given immediately for its antiplatelet effect.

Thrombolytic drugs such as **streptokinase** help to restore perfusion and thus relieve myocardial ischaemia; they should ideally be given within 1 hour of infarction (use after 12 hours requires specialist advice).

Nitrates (section 5.5) may also be given to relieve ischaemic pain.

Early administration of beta-blockers such as **atenolol** (section 5.5) have been shown to reduce both early mortality and the recurrence rate of myocardial infarction; initial intravenous administration is followed by long-term oral treatment (unless the patient has contraindications).

ACE inhibitors (section 5.1) have also been shown to be beneficial in initial management (unless patient has contraindications) when given within 24

hours, and if possible continued for 5–6 weeks.

If arrhythmias occur, they should be treated aggressively, but the likelihood decreases rapidly over the first 24 hours after infarction. Ventricular fibrillation should be treated immediately with a defibrillator; if this is ineffective alone, the antiarrhythmic drug **lidocaine** (section 5.4) should be given.

All patients should be closely monitored for hyperglycaemia; those with diabetes mellitus or raised blood-glucose concentration should receive **insulin**.

Long-term management

Acetylsalicylic acid should be given to all patients in a dose of 75–150 mg daily by mouth, unless it is contraindicated. The prolonged antiplatelet effect has been shown to reduce the rate of reinfarction.

Treatment with **beta-blockers** should be continued for at least 1 year, and possibly for up to 3 years.

ACE inhibitors such as **enalapril** (section 5.1) should also be used since they reduce mortality, particularly in patients with left ventricular dysfunction.

Nitrates (section 5.5) may be required for patients with angina.

The use of **statins** (section 5.7) may also be considered in patients with high risk of recurrence.

Stroke

Stroke (cerebrovascular accident) may be ischaemic or haemorrhagic; precise diagnosis is essential, as management for the two types of stroke is quite different.

Primary prevention of both types of stroke includes reduction of high blood pressure, stopping smoking, weight reduction, and cholesterol reduction. Atrial fibrillation, acute myocardial infarction, and valvular disease may produce embolism and ischaemic stroke. Prophylaxis in patients at risk of ischaemic stroke includes oral anticoagulants such as warfarin (section 6.2) and antiplatelet drugs such as acetylsalicylic acid. Treatment of acute ischaemic stroke includes use of **acetylsalicylic acid**, anticoagulants such as heparin, and of thrombolytics, such as streptokinase. Streptokinase must be used with extreme caution due to risk of bleeding. Long-term therapy with acetylsalicylic acid reduces the risk of having another stroke.

Antiplatelet and thrombolytic drugs are **not** used in the management of haemorrhagic stroke, as they may exacerbate bleeding. The main treatment is to normalize blood pressure.

Acetylsalicylic acid is normally given for at least one year after coronary artery bypass surgery. It is also given to patients with prosthetic heart valves who have had cerebral embolism despite warfarin treatment.

ACETYLSALICYLIC ACID

Indications: Prophylaxis of cerebrovascular disease or myocardial infarction; pyrexia, pain, inflammation (section 1.8.1); migraine (section 1.9.1).

Contra-indications: Hypersensitivity (including asthma, angioedema, urticaria or rhinitis) to acetylsalicylic acid or any other NSAID; children and adolescents under 16 years (Reye syndrome, see section 1.8.1); active peptic ulceration; haemophilia and other bleeding disorders

Precautions: Asthma; uncontrolled hypertension; pregnancy (Appendix 2); breastfeeding (Appendix 3); see also section 1.8.1; **interactions**: Appendix 1.

Adverse effects: Bronchospasm; gastrointestinal haemorrhage (rarely major), also other haemorrhage (for example subconjunctival); see also section 1.8.1.

Dose: *Prophylaxis of cerebrovascular disease or myocardial infarction*, by mouth, ADULT 75–100 mg daily.

POM **Acetylsalicylic acid** *(WMF 12.5)*
Tablets, Acetylsalicylic acid 100 mg.
Dispersible tablets (Soluble tablets), Acetylsalicylic acid 75 mg [not included on WHO Model List].

STREPTOKINASE

Streptokinase is a complementary drug; it is used in the management of myocardial infarction and thromboembolism.

Indications: Life-threatening deep-vein thrombosis, pulmonary embolism, acute arterial thromboembolism; thrombosed arteriovenous shunts; acute myocardial infarction.

Contra-indications: Recent haemorrhage, surgery (including dental), parturition, trauma; heavy vaginal bleeding; haemorrhagic stroke, history of

cerebrovascular disease (especially recent or if residual disability); coma; severe hypertension; coagulation defects; bleeding diatheses, aortic dissection; risk of gastrointestinal bleeding such as recent history of peptic ulcer, oesophageal varices, ulcerative colitis; acute pancreatitis; sever liver disease; acute pulmonary disease with cavitation; previous allergic reactions.

Precautions: Risk of bleeding from any invasive procedure, including injection; external chest compression; pregnancy (Appendix 2); abdominal aneurysm or where thrombolysis may give rise to embolic complications such as enlarged left atrium with atrial fibrillation (risk of dissolution of clot and subsequent embolization); diabetic retinopathy (small risk of retinal haemorrhage); recent or concurrent anticoagulant treatment.

Adverse effects: Nausea and vomiting; bleeding, usually limited to site of injection but internal bleeding including intracranial haemorrhage may occur (if serious bleeding occurs, discontinue infusion—coagulation factors may be required); hypotension, arrhythmias (particularly in myocardial infarction); allergic reactions including rash, flushing, uveitis, anaphylaxis; fever, chills, back or abdominal pain; Guillain-Barré syndrome reported rarely.

Dose: *Thrombosis*, by intravenous infusion, ADULT 250 000 units over 30 minutes, followed by 100 000 units every hour for 12–72 hours according to condition with monitoring of clotting parameters.

Myocardial infarction, by intravenous infusion, ADULT 1 500 000 units over 60 minutes.

Thrombosed arteriovenous shunts, consult manufacturer's literature.

POM **Streptokinase** *(WMF 12.5)*

Injection (Powder for solution for injection), Streptokinase 1.5 million-unit vial.

5.7 Lipid-regulating drugs

The primary aim of therapy is to reduce progression of atherosclerosis and to improve survival in patients with established cardiovascular disease, to reduce premature cardiac morbidity and mortality in people at high risk of cardiovascular events and to prevent pancreatitis due to hypertriglyceridaemia. Before starting drug therapy dietary measures, reduction of blood pressure and cessation of smoking should be tried. The WHO Expert Committee on the Selection and Use of Essential Medicines recognizes the value of lipid-lowering drugs in treating patients with hyperlipidaemia. Beta-hydroxy-beta-methylglutaryl-coenzyme A (HMG Co A) reductase inhibitors, often referred to as 'statins', are potent and effective lipid-lowering drugs with a good tolerability profile. Several of these drugs have been shown to reduce the incidence of fatal and non-fatal myocardial infarction, stroke and mortality (all causes), as well as the need for coronary bypass surgery. All remain very costly, but may be cost-effective for secondary prevention of cardiovascular disease as well as for primary prevention in some very high-risk patients. Since no single drug has been shown to be significantly more effective or less expensive than others in the group, none is included in the WHO Model List; the choice of drug for use in patients at highest risk should be decided at national level.

ATORVASTATIN

Pharmacology: Atorvastatin calcium is a synthetic lipid-lowering agent. Atorvastatin is an inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate-limiting step in cholesterol biosynthesis.

Atorvastatin is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl-coenzyme A to mevalonate, a precursor of sterols, including cholesterol. Pharmacologic inhibition of HMG-CoA reductase blocks the synthesis of endogenous cholesterol in the liver, causing a compensatory increase in the activity of hepatic LDL receptors leading to enhanced clearance of LDL-cholesterol from the blood. These two mechanisms lead to reduction in circulating LDL-C and total cholesterol.

Pharmacokinetcs - Atorvastatin is rapidily absorbed after oral administration; maximum plasma concentrations occur within 1-2 hours. The absolute bioavailability of atorvastatin is 14% and the systemic bioavailability of HMG-CoA reductase inhbitory activity is approximately 30%. It undergoes extensive

first-pass metabolism. The metabolism of atorvastatin is by cytochrome P450 (CYP) 3A4 and 70% of its inhibitory activity has been attributed to its active metabolites. Mean volume of distribution of atorvastatin is approximately 381 liters. Atorvastatin and its metabolites are eliminated primarily in bile following hepatic and/or extra-hepatic metabolism, however, the drug does not undergo enterohepatic recirculation. The half-life of atorvastatin in humans is about 14 hours, but the half-life of inhibitory activity for HMG-CoA reductase is 20-30 hours due to the contribution of active metabolites.

Use in special patient groups - Elderly: LDL-C reduction in elderly patients is comparable to that seen in younger populations given equal doses of atorvastatin. However, plasma concentrations are higher in healthy elderly subjects than in young adults.

Pediatrics: No available pharmacokinetic data in the pediatric population.

Renal insufficiency: Dose adjustments in patients with renal dysfunction is not necessary.

Hepatic insufficiency: Plasma concentration of atorvastatin are markedly increased, hence, atorvastatin should not be used in active liver disease or unexplained persistent elevations of serum transaminases.

Indications: Atorvastatin is indicated as an adjunct to diet to reduce elevated total cholesterol, low-density lipoprotein cholesterol, apo-lipoprotein and triglycerides in patients with primary hypercholesterolemia and mixed dyslipidemia.

Contra-indications: Active liver disease or unexplained persistent elevations of serum transaminases; hypersensitivity to any component of this medication; pregnancy and lactation.

Precautions: With any statin, patients should promptly report muscle pain, tenderness, or weakness. Discontinue drug if myopathy is suspected, if creatinine phosphokinase (CPK) levels rise markedly, or if the patient has risk factors for rhabdomyolysis.

Interactions: The risk of myopathy during treatment with drugs of this class is increased with concurrent administration of cyclosporine, fibric acid derivatives, niacin (nicotinic acid), erythromycin, and azole antifungals.

Adverse effects: The most frequent adverse events related to atorvastatin were constipation, flatulence, dyspepsia and abdominal pain.

Advice to patients: Patient should report promptly unexplained muscle pain, tenderness, or weakness.

Dose: By mouth, 10 mg once daily; may be increased up to 80 mg once daily depending on goal of therapy and response.
To be given as a single dose at any time of the day, with or without food. .

POM **LIPITOR** *(Pfizer)*
Tablets, Atorvastatin calcium 10 mg, 20 mg; white, elliptical, film-coated tablets.
10 mg - 30's (in blister)
20 mg - 30's (in blister)

CLOFIBRATE

Therapeutic category: Antilipemic Agent.

Pharmacology: Clofibrate lowers serum cholesterol and triglyceride levels by reducing very low density lipoprotein (VLDL) and low density Lipoprotein (LDL). It also increases high density Lipoprotein (HDL). Clofibrate is readily absorbed following oral dosage and is hydrolysed to the active acid. The plasma half-life is approximately 16 hours (which may increase to 60-190 hours in renal failure) and the drug is excreted via the kidneys. Some 91-97% is bound to serum albumin, and may displace other similarly bound drugs. The volume of distribution is 5-9 litres; non enters the CSF. Concimitant administration of cholestyramine does not impair absorption of Clofibrate.

Indications: Management of severe hyperlipo-proteinaemia when diet alone has failed; exudative diabetic retinopathy and the hyperlipoproteinaemia accompanying diabetes; xanthomata associated with hyperlipoproteinamia; chronic hyperfibrinogenaemia associated with occlusive vascular disease.

Contra-indications: Acute impairment of renal, bilary or hepatic function; patients with a history of, or existing, gall blader disease or stones (it may increase the lithogenicity of bile and raise the frequency of gallstone formation); pregnancy and breast feeding.

Precautions: In patients with low serum albumin levels, for example those with nephrotic syndrome, high levels of unbound clofibrate may give rise to myalgia and raised serum creatinine kinase levels.

Interactions:
•Anticoagulants (halve the dose of the anticoagulant when administered concomitantly).
•Clofibrate may displace other acidic drugs such as phenytoin or sulphonylureas e.g. tolbutamine, from protein binding sites and

thereby potentiate the effect of such drugs.

Adverse effects: Transient slight abdominal discomfort, nausea and looseness of the bowels, and impotence, headache, drowsiness, skin rashes, pruritus; rarely cardiac arrhythmias and myositis-like syndrome comprising myalgia, myopathy, muscle cramps and sometimes rhabdomyolysis.

Advice to patients: See Label 21 in Appendix 6. If GI upset occurs, may be taken with food; notify physician of chest pain, shortness of breath, irregular heart beat, severe stomach pain with nausea and vomiting, persistent fever, sore throat, or unusual bleeding or bruising; adhere to prescribed diet.

Dose: Adult (including the elderly), by mouth, 20-30 mg/kg b.wt daily in 2 or 3 divided doses after meals as follows:
Over 65 kg, 2 g daily;
50-65 kg, 1.5 g daily;
Child: not usually recommended for children but where necessary, by mouth 20-30 mg/kg b.wt.

Note: Clofibrate should not be used until diet alone has failed and should be given together with an appropriate diet. Patient's adherence and response to treatment should be monitored regularly and in some patients, it may take several months before a reduction in blood cholesterol is seen. If, however, an adequate response has not been observed after 3 months, Clofibrate should be discontinued.

POM **ATROMID-S®** *(Reals)*
Capsule, Clofibrate 500 mg; red cap.

FLUVASTATIN

Therapeutic category: Antilipemic Agent; HMG-CoA Reductase Inhibitor.

Pharmacology: Fluvastatin, a fully synthetic Cholesterol - lowering agent, is a competitive inhibitor of HMG-CoA reductase, which is responsible for the conversion of HMG-CoA to mevalonate, a precursor of sterols, including cholesterol. Fluvastatin exerts its main effect in the liver, which is also the main organ for its metabolism. The inhibition of cholesterol biosynthesis reduces the cholesterol in hepatic cells, which stimulates the synthesis of low density lipoprotein (LDL) receptors and thereby increases the uptake of LDL particles. The ultimate result of these mechanisms is a reduction of the plasma cholesterol concentration. Fluvastatin is absorbed rapidly and completely (98%) after oral administration to fasted volunteers. In a fed state, the drug is absorbed at a reduced rate. More than 98% of the circulating drug is bound to plasma proteins, and this binding is unaffected by drug concentration. Food does not affect its absorption and its plasma concentration is neither affected by age nor gender. Hepatic insufficiency can cause accumulation of the drug since it is metabolised in the liver and eliminated primarily via the biliary route.

Indications: Primary hypercholesterolaemia in patients who do not respond to dietary control.

Contra-indications: Hypersensitivity to fluvastatin; active liver disease or unexplained, persistent elevations in serum transaminases; pregnancy, breast feeding and in women of childbearing potential unless they are using effective contraception during the therapy period.

Precautions: See under Simvastatin.

Interactions: •Food (no significant interaction).
•Cholestyramine and other bile-acid-sequestering agents (clinically significant additive effect, the two drugs should be administered at least 4 hours apart).
•Rifampicin (reduction in the bioavailability of fluvastatin by about 50%).

Adverse effects: Dyspepsia, insomnia, nausea, abdominal pain, headache.

Advice to patients: Avoid prolonged exposure to the sun other ultraviolet light; report unexplained muscle pain or weakness, especially if accompanied by fever or malaise.

Nursing considerations: •Administer without regard to meals.
•See also under Simvastatin.

Dose: By mouth, 20-40 mg once daily to be taken in the evening or at bedtime; adjusted according to patient's response at an interval of not less than 4 weeks up to a maximum 40 mg twice daily at very high cholesterol levels.

Note: Patient should be placed on standard Cholesterol-lowering diet before and during treatment with fluvastatin; may be taken without regard to meals; adjust dosage as needed in response to periodic lipid determinations during the first 4 weeks after a dosge change; lipid lowering effects are additive when fluvastatin is combined with a bile acid binding resin or niacin, however, it must be administered at least 2 hours following these drugs.

POM **LESCOL®** *(Novartis)*
Capsules, Fluvastatin 20 mg, 40 mg.

SIMVASTATIN

Therapeutic category: Antilipemic Agent; HMG-CoA Reductase Inhibitor.

Pharmacology: Simvastatin is a cholesterol-lowering agent derived synthetically from a fermentation product to *Aspergillus terreus*. After oral ingestion, simvastatin is converted to the active N-hydroxyacid form which competitively inhibits 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, an enzyme which catalyzes an early and rate-limiting step in the biosynthesis of cholesterol. This results in the reduction of total plasma cholesterol, low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) - cholesterol concentrations. In addition, simvastatin moderately lowers HDL-cholesterol and reduces plasma triglycerides.

Indications: Reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolaemia, when the response to diet and other non-pharmacological measures alone has been inadequate; reduction of elevated cholesterol levels in patients with combined hypercholesterolaemia and hypertriglyceridaemia, when the hypercholesterolaemia is the abnormality of most concern.

Contra-indications: Active liver disease or unexplained persistent elevations of serum transaminases; pregnancy, breast–feeding, children.

Precautions: Perform liver function tests before commencement of therapy and periodically thereafter in all patients (discontinue treatment if the serum transaminase levels rise three times the upper limit of normal and are persistent); alcoholics especially those with a past history of liver diseases; markedly elevated CPK levels or myopathy (discontinue).

Interactions: •Coumarin anticoagulants (monitor prothrombin time before treatment and thereafter).
•Immunosuppressants.

Adverse effects: Abdominal pain, constipation, flatulence and nausea, less frequently asthenia, acid regurgitation, dyspepsia, headache, insomnia, diarrhoea and rash; rarely myopathy.

Advice to patients: Promptly report any unexplained muscle pain, tenderness or weakness, especially if accompanied by malaise or fever; follow prescribed diet; take with meals.

Nursing considerations: •Administer as a single dose in the evening with meals.
•Liver enzyme elevations may be observed during simvastatin therapy.
•Combination with other hypolipidemic agents may be required to achieve optimal reductions of LDL cholesterol.
•Diet, weight reduction, and exercise should be attempted to control hypercholesterolemia before the institution of simvastatin therapy.
•Advise patient to continue with the diet and exercise regimen during therapy.

Dose: By mouth, initially 10 mg daily given as a single dose in the evening; adjusted if required at an interval of not less than 4 weeks up to maximum 40 mg daily given as a single dose in the evening. Patient should be placed on standard cholesterol-lowering diet before and during treatment with simvastatin.

POM **SIMVOR®** *(Ranbaxy)*
Tablets, Simvastatin USP 5 mg, 10 mg, 20 mg; f-c tablets.
5 mg - 5 x 10's (in blister)
10 mg - 5 x 10's (in blister)
20 mg - 5 x 10's (in blister).

POM **ZOCOR®** *(Bolax/BPP)*
Tablet, Simvastatin 10 mg; peach coloured f-c tab.

6. Drugs affecting blood and nutrition

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6.1 Antianaemia drugs

6.1.1 Drugs used in iron-deficiency and megaloblastic anaemias
6.1.2 Drugs used in neutropenia
6.1.3 Drugs used in hypoplastic, haemolytic, and renal anaemias

IRON-DEFICIENCY ANAEMIA

Anaemia has many different aetiologies. It occurs when the haemoglobin concentration falls below the normal range for the age and sex of the individual. It is essential that a correct diagnosis is made before initiating therapy.

Any serious underlying cause of iron-deficiency anaemia, including gastric erosion and colonic carcinoma, should be excluded before giving iron replacement. Prophylaxis with iron salts in pregnancy should be given to women who have additional factors for iron-deficiency; low-dose iron and folic acid preparations are used for the prophylaxis of megaloblastic anaemia in pregnancy.

Ferrous salts should be given orally wherever possible. They differ only marginally in efficiency of absorption and thus the choice of preparation is usually decided by incidence of adverse effects and cost. Ferric salts are much less well absorbed. The oral dose of elemental iron for treatment of iron-deficiency anaemia in adults should be 100–200 mg daily with meals.

The approximate elemental iron content of various ferrous salts is ferrous fumarate 200 mg (65 mg iron), ferrous gluconate 300 mg (35 mg iron), ferrous succinate 100 mg (35 mg iron), ferrous sulfate 300 mg (60 mg iron), and dried ferrous sulfate 200 mg (65 mg iron).

The haemoglobin concentration should rise by about 100–200 mg/100 ml per day or 2 g/100 ml over 3–4 weeks. After the haemoglobin has risen to normal, treatment should be continued for a further

3 months to replenish the iron stores.

Iron intake in the evening has been reported to improve its absorption. Iron intake with meals may reduce bioavailability but improve tolerability and adherence.

If adverse effects arise with one salt, dosage can be reduced or a change made to an alternative iron salt but an improvement in tolerance may be due to lower content of elemental iron. Gastrointestinal irritation may occur with iron salts. Nausea and epigastric pain are dose-related. Iron preparations taken orally may be constipating, particularly in the elderly, occasionally leading to faecal impaction. Oral iron may exacerbate diarrhoea in patients with inflammatory bowel disease but care is also needed in patients with intestinal strictures and diverticula. Iron as **iron dextran** (a complex of ferric hydroxide with dextrans) [not included on WHO Model List] should be given parenterally only if the patient cannot tolerate oral iron, or does not take it reliably or there is continuing severe blood loss or malabsorption. Many patients with chronic renal failure who are receiving haemodialysis (and some on peritoneal dialysis) require intravenous iron on a regular basis. Parenteral iron may cause more harm than benefit. With the exception of patients on haemodialysis the haemoglobin response is not significantly faster with the parenteral route than the oral route.

MEGALOBLASTIC ANAEMIAS

Megaloblastic anaemias result from a lack of either vitamin B_{12} (hydroxocobalamin) or folate or both. The clinical features of folate-deficient megaloblastic anaemia are similar to those of vitamin B_{12} deficiency except that the accompanying severe neuropathy does not occur; it is essential to establish the underlying cause in every case. **Hydroxocobalamin** is used to treat vitamin B_{12} deficiency whether due to dietary deficiency or malabsorption including pernicious anaemia (due to a lack of intrinsic factor, which is essential for vitamin B_{12} absorption).

Folate deficiency due to poor nutrition, pregnancy, antiepileptics or malabsorption is treated with **folic acid** but this should never be administered without vitamin B_{12} in undiagnosed megaloblastic anaemia because of the risk of precipitating neurological changes due to vitamin B_{12} deficiency.

Preparations containing a **ferrous salt and folic acid** are used for the prevention of megaloblastic anaemia in pregnancy. The low doses of folic acid in these preparations are inadequate for the treatment of megaloblastic anaemias.

PREVENTION OF NEURAL TUBE DEFECTS

An adequate intake of **folic acid** before conception and during early pregnancy reduces the risk of neural tube defects in babies. Therefore, women planning a pregnancy should receive sufficient folic acid before conception and in the first 12 weeks of pregnancy; folic acid may be given as a food or a medicinal supplement in a dose of 400–500 micrograms daily. A woman who has not received supplementary folic acid and suspects that she might be pregnant should start taking folic acid at once and continue until week 12 of pregnancy.

Women at increased risk of giving birth to a baby with neural tube defects (for example history of neural tube defect in a previous child) should receive a higher dose of folic acid of approximately 5 mg daily, starting before conception and continuing for 12 weeks after conception. Women taking antiepileptic medication should be counselled by their doctor before starting folic acid.

6.1.1 Drugs used in iron-deficiency and megaloblastic anaemias

CYANOCOBALAMIN

Synonym: Vitamin B_{12}

Therapeutic category: Water Soluble Vitamin.

Indications: Treatment of pernicious anaemia and other vitamin B_{12} deficiency states; increased vitamin B_{12} requirements due to pregnancy, thyrotoxicosis, haemorrhage, liver or kidney disease.

Contra-indications: Hypersensitivity to cyanocobalamin or any component, cobalt; patients with hereditary optic nerve atrophy.

Adverse effects: Itching, diarrhoea, peripheral vascular thrombosis.

Advice to patients: Pernicious anaemia will require treatment for life.

Nursing considerations: •Administer with fruit juice to disguise taste and with food for better absorption. •Oral therapy is markedly inferior to parenteral therapy due to poor absorption; I.V. is not

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recommended due to problem of rapid elimination (Hydroxocobalamin is retained in the body longer than Cyanocobalamin and is generally preferred).
•Monitor potassium concentrations during early therapy.
•Encourage diet rich in vitamin B_{12} viz egg, yolk, fish, organ meat.

Dose: By mouth, *Vitamin B_{12} deficiency due to inadequate diet*, Adult, 50-150 mcg or more daily; to be taken between meals.
Child: 30-50 mcg twice daily
By I.M. injection, initially 1 mg repeated 10 times at intervals of 2-3 days.
Maintanance: 1 mg every month.

Note: Hydroxocobalamin is now preferred to cyanocobalamin because it is retained in the body longer and for maintenance therapy, it can be given at intervals of up to 3 months.

POM **Cyanocobalamin** *(EDL 11.1)*
Tablet, Cyanocobalamin 50 mcg.
Injections, Cyanocobalamin 250 mcg, 1 mg per ml.

POM **BINOX-12®** *(Beta Drugs)*
Injection, Vitamin B_{12} 1 mg per 2 ml; sterile solution in 2-ml ampoule.
Pack – 2-ml x 10's; 2-ml x 100's.

Vitamin B_{12} + Haemoglobin
OTC **DE-DEON'S B.12®** *(Daily Need)*
Syrup, Haemoglobin, Vitamin B_{12}.
Pack - 60 ml.
Dose: By mouth, Adult, 10 ml twice daily; Child, 5 ml daily. May be taken pure or mixed with water to form a pleasant taste.

FERROUS SALTS

Synonym: Oral iron; Ferrous Fumarate, Ferrous Gluconate, Ferrous Sulfate, Ferrous Succinate; Ferric Ammonium Citrate.
Indications: Iron-deficiency anaemia.
Contra-indications: Haemosiderosis, haemochromatosis; any form of anaemia not caused by iron deficiency; patients receiving repeated blood transfusions; parenteral iron therapy.
Precautions: Should not be administered for longer than 6 months; pregnancy; peptic ulcer, regional enteritis, ulcerative colitis, intestinal strictures, diverticula; overdosage: see section 4.2.4; **interactions**: Appendix 1.
Adverse effects: Constipation, diarrhoea, dark stools, nausea, epigastric pain, gastrointestinal irritation; long-term or excessive administration may cause haemosiderosis.
Advice to patients: May colour stool black; take between meals for maximum absorption; may take with food if GI upset occurs; do not take with milk or antacids; keep out of reach of children.
Nursing considerations: •Administer between meals but may give with food because of GI upset; for best absorption give with fruit juice.
•Tell patient not to crush tablets but to take it whole.
•Give oral liquid preparation with straw to prevent discolouration of tooth enamel.
•Teach patient to avoid reclining position for 15-30 minutes after drug to avoid oesophageal corrosion; to take medication at least 1 hr before bedtime to avoid corrosion in the stomach.
•Do not give antacids, eggs, milk; if these have been eaten, delay administration for an hour.
•Teach patient dietary measures for preventing constipation namely increased bulk and fluid in the diet.

Dose: *Iron-deficiency anaemia*, by mouth, ADULT elemental iron 100–200 mg daily in divided doses.
Prevention of iron deficiency anaemia (in those at particular risk), by mouth, adult (woman) elemental iron 60 mg daily; child under 5 years elemental iron 2 mg/kg (maximum 30 mg) daily, over 5 years elemental iron 30 mg daily; in women and children over 5 years, folic acid may also be given.
See also under the proprietary preparations below

PATIENT ADVICE: ALTHOUGH IRON PREPARATIONS ARE BEST ABSORBED ON AN EMPTY STOMACH THEY MAY BE TAKEN AFTER FOOD TO REDUCE GASTROINTESTINAL ADVERSE EFFECTS; THEY MAY DISCOLOUR STOOLS. LIQUID PREPARATIONS CONTAINING IRON SALTS SHOULD BE WELL DILUTED WITH WATER (AND IF POSSIBLE SWALLOWED THROUGH A DRINKING STRAW TO PREVENT DISCOLORATION OF THE TEETH).

OTC **Ferrous salts** *(WMF 10.1)*
Tablets, Dried ferrous sulfate 200 mg (65 mg iron); Ferrous sulfate 300 mg (60 mg iron); Ferrous fumarate 210 mg (68 mg iron); Ferrous gluconate 300 mg (35 mg iron).
Oral solution, Ferrous sulfate (25 mg iron)/mL.

OTC **Ferrous Salts** *(EDL 11.1)*
Tablets or Mixture, Ferrous fumarate, gluconate, sulphate or succinate equivalent to 60 mg iron.

OTC **Ferric Ammonium Citrate** *(EDL 11.1)*
Mixture, Ferric ammonium citrate 400 mg per 5 ml.

OTC **CHEMOTONE**® *(Chemo-Pharma)*
Mixture, Ferric ammonium citrate 200 mg, vitamin B_{12} 5 mcg, folic acid 0.5 mg per 5 ml.
Pack - 200 ml.

OTC **DETONIC**® *(Afrab-Chem)*
Mixture, Ferrous Gluconate 120 mg, Folic acid 0.3 mg, Vitamin B_1 2.0 mg, Vitamin B_2 1.0 mg, Vitamin B_6 2.0 mg, Vitamin B_{12} 5.0 mcg per 5 ml.
Pack - 200 ml.
Dose: Adult and Child above 12 years, 5-10 ml twice daily.
Child (6-12 yrs), 5 ml twice daily.

OTC **EMZORON**® *(Emzor)*
Mixture, Ferric ammonium citrate 200 mg, folic acid 0.5 mg, Vitamin B_{12} 5 mcg, vitamin B_1 2 mg, Vitamin B_2 1.5 mg per 5 ml.
Pack - 200 ml.
Dose: By mouth, Adult, 15ml 3 times daily
Child, 5ml 3 times daily.

OTC **EPITONE**® *(BCN)*
Mixture, Ferrous gluconate 225 mg, calcium gluconate 200 mg, manganese glycerophosphate 6 mg, vitamin B_1 0.7 mg, vitamin B_2 0.4 mg, nicotinamide 6 mg per 10 ml.
Pack - 200 ml.
Dose: Adult and child over 12 years, 10ml 3 times daily; 5-12 years, 5ml 3 times daily. To be taken after meals.
Not recommended for children below 5 years.

OTC **FERBELAN**® *(Evans)*
Syrup, Ferric ammonium citrate 200 mg and vitamins B_1 2 mg, B_2 500 mcg, B_{12} 2500 ng, nicotinamide 5 mg; dark-brown pleasantly flavoured syrup.
Pack - 100 ml; 200 ml.
Dose: Adult, 5-10 ml 3 times daily.
Child (2-12 years), 5-10 ml 1-2 times daily depending on age and weight.

OTC **FERILEX**® **Junior** *(Therapeutic)*
Syrup, Ferric ammonium citrate 30 mg, folic acid 200 mcg, vitamin B_{12} 5 mcg per 5 ml; dark red syrup.
Pack - 100 ml; 200 ml; 750 ml.

OTC **FERIPLUS**® *(Food & Pharma)*
Mixture, Ferric ammonium citrate 200 mg (equiv. to 40 mg elemental iron), vitamin B_{12} 20 mcg, folic acid 0.5 mg per 5 ml.
Pack - 200 ml
Dose: Adult, Treatment, 10 ml twice daily after meals; Prophylaxis, 5 ml 1-2 times daily.
Child, 2.5-5 ml 1-2 times daily after meals. To be well diluted with water.

OTC **FERITAN**® *(Diamond Remedies)*
Capsule, Ferrous fumarate 300 mg; red cap. marked 'FERITAN'.
300 mg - 3 x 10.

OTC **FEROTAL**® *(Farmex-Meyer)*
Mixture, Ferric ammonium citrate BPC 200 mg (equiv. 40 mg elemental iron), vitamin B_{12} 3 mcg, folic acid 200 mcg, zinc (as sulphate) 2 mg per 5 ml.
Pack - 200 ml; 300 ml; 1 L.
Dose: Adults, 5 ml daily; *In pregnancy*, 5 ml twice daily. Child, 2.5 ml twice daily.
May be used for up to 30 days.

OTC **FERRODAN**® *(Dana)*
Capsule, Ferrous fumarate BP 300 mg.
300 mg - 3 x 10's; 1000's.
Dose: By mouth, 300-600 mg daily in divided doses.

OTC **FERROL**® *(Strides Vital)*
Tablet, Ferrous sulfate.
Pack – 1000's.

OTC **FERRON-6**® *(Justeen)*
Tablet, Ferrous sulfate BP 200 mg.
Pack – 1 x 1000's.

OTC **FEROVITA**® *(Strides Vital)*
Tablet, Ferrous sulfate.
Pack – 3 x 10's.

OTC **Ferrous Gluconate** *(Emzor)*
Tablet, Ferrous gluconate 300 mg; red s-c biconvex tab.
300 mg - 100; 1000.

OTC **Ferrous Sulphate** (*Phamatex*)
Tablet, Ferrous sulphate 200 mg
200 mg - 1000

OTC **Ferrous Sulphate** *(Sam)*
Tablet, Ferrous sulphate 200 mg.
200 mg - 1000

OTC **FERSOLATE**® *(Evans)*
Tablet, Dried ferrous sulphate 200 mg, copper sulphate 2.5 mg, manganese sulphate 2.5 mg; dark red s-c biconvex tab.
Pack - 100; 1000.
Dose: Adult, one tablet 3 times a day during or immediately after meals.

OTC **FESULF**® *(Therapeutic)*
Tablet, Ferrous sulphate (dried) 200 mg (equiv. 60 mg iron); bright red and brown tab.
200 mg - 100; 1000.

POM **HAEMARON**® *(Unique)*
Capsule, Ferrous Fumarate B.P. 150 mg, Vitamin B_1 B.P 1 mg, Vitamin B_6 B.P. 1 mg, Folic Acid B.P. 2 mg, Zinc Sulphate Monohydrate USP 15 mg.
Pack - 3 x 10; 12 x 10 (in blisters).
Dose: One capsule a day.
Mixture, Ferrous Gluconate BP 120 mg, Vitamin B_1 BP 1.0 mg, Vitamin B_2 BP 1.0 mg, Vitamin B_6 BP 2.0 mg, Vitamin B_{12} BP 1.0 mcg, Nicotinamide BP 5.0 mg, Zinc Sulphate BP 15.0 mg per 5 ml.
Pack - 100 ml; 200 ml; 750 ml.
Dose: Adults: 15-30 ml 2 times daily.
Children (6-12 years): 5 ml 2 times daily.

OTC **HAEMATONE**® *(Mopson)*
Mixture, Ferric ammonium citrate 200 mg, riboflavin 0.5 mg, pyridoxine 1.0 mg.
Pack - 200 ml, 2 L.

OTC **HAEM-F**® *(Interpharma)*
Capsule, Ferrous fumarate, cyanocobalamin, folic acid, zinc sulfate.
Pack - 30's.
Syrup, Ferric ammonium citrate 200 mg, cyanocobalamin 5 mg, folic acid 1 mg per 15 ml.
Pack - 200 ml.
Dose: Adult 15 ml 1-2 times daily.

OTC **HAEM UP**® *(Interpharma)*
Capsules, Haemoglobin powder (equiv. to 175 mg protein) 190 mg, ferrous fumerate 150 mg, cupric sulphate 2.5 mg, manganese sulphate 2.5 mg, zinc sulphate 15 mg.
Pack - 30; 100.
Liquid, Glycerinated haemoglobin 1 g, ferric ammonium citrate 100 mg, cupric sulphate 30 mcg, manganese sulphate 30 mcg, zinc sulphate 30 mcg, alcohol 0.87 ml per 15 ml.

OTC **HEMAFOLIN**® *(Neimeth)*
Capsule, Iron (as sulphate) 18 mg, vitamin B_1 1.5 mg, vitamin B_2 2 mg, vitamin B_6 2 mg, vitamin C 75 mg, vitamin B_{12} 3 mcg, niacinamide 20 mg, folic acid 400 mg.
Pack - 30; 90.
Dose: One capsule to be taken once daily.

OTC **HEMFERON-400**® *(Ranbaxy)*
Mixture, Ferric ammonium citrate 400 mg per 5 ml.
Pack - 180 ml.

OTC **JAWARON**® *(Jawa)*
Capsule, Ferrous fumarate 150 mg, vitamin A 1500 i.u., vitamin C 30 mg, vitamin E 3 mg, vitamin B_1 2 mg, vitamin B_2 2 mg, vitamin B_6 2 mg, vitamin B_{12} 5 mcg, nicotinamide 10 mg, folic acid 2 mg, lysine monohydrochloride 100 mg, zinc sulphate 5 mg, copper sulphate 1.5 mg, manganese sulphate 1.5 mg, calcium phosphate 75 mg, magnesium oxide 60 mg, potassium iodide 0.05 mg.
Pack - 20; 30; 120; 250.
Dose: Prophylaxis, 1 capsule daily.
Treatment, 1 capsule 2 times daily.
Mixture, Ferrous gluconate 120 mg, vitamin B_1 1 mg, vitamin B_2 1 mg, vitamin B_6 2 mg, vitamin B_{12} 1 mcg, nicotinamide 5 mg, zinc sulphate 15 mg, lysine monohydrochloride 200 mg per 5 ml.
Pack - 100 ml; 200 ml.
Dose: Adult, 10-20 ml twice daily.
Child (6-12 years), 5ml twice daily.

OTC **JEFERON**® *(Juhel)*
Syrup, Ferric ammonium citrate BP 200 mg, Folic acid 0.5 mg, Vitamins B_{12} 5.0 mcg per 5 ml.
Pack – 200 ml.

OTC **KING TONIC**® *(SKG)*
Mixture, Ferrous succinate 50 mg, vitamin B_1 1 mg, vitamin B_2 1 mg, nicotinamide 10 mg per 5 ml.
Pack - 100 ml; 200 ml.
Dose: Adult and child (over 12 years), 15 ml twice daily; under 7 years, 5 ml twice daily; 7-12 years, 10 ml twice daily.

OTC **MAXIRON**® *(Sam)*
Capsule, Ferrous fumarate 200 mg, folic acid 1 mg, vitamin B_{12} 10 mcg.
Pack - 30's.

POM **OROFER**® *(Fill Pharma)*
Syrup, Iron (111) polymaltose complex equiv. to elemental iron 50 mg per 5 ml.
Pack – 150 ml bottle.
Dose: *Adults*: 5 ml 2-3 times daily
Children: 5 ml 1-2 times daily
Infants: Initially 2.5 ml 1-2 times daily; may be increased to 5 ml 1-2 times daily if necessary.
Note: Orofer syrup may be mixed with fruit or vegetable juices or other liquids if desired.

OTC **RANFERON-12**® *(Ranbaxy)*

Capsule, Ferrous fumarate BP 305 mg (equiv. elemental iron 100 mg), folic acid BP 0.75 mg, cyanocobalamin USP 5 mcg, ascorbic acid USP 75 mg, zinc sulfate 5 mg.
Pack - 30's; 120's.
Syrup, Ferric ammonium citrate BP 200 mg (equiv. to elemental iron 41 mg), vitamin B_{12} BP 5 mcg, folic acid 0.50 mg, sorbitol solution USP 1.75 g per 5 ml.
Pack - 100 ml; 200 ml.
Dose: Adult, Treatment, 10 ml 3 times a day; prophylaxis, 5 ml 1-2 times daily.
Child (5-12 years), 5 ml 1-2 times daily.

OTC **REVITONE®** *(Pharma–Deko)*
Syrup, Ferrous gluconate 200 mg, Vitamin B_1 0.2 mg, Vitamin B_2 0.16 mg, Cyanocobalamin 0.25 mg.
Pack - 200 ml.

OTC **ROYAL TONIC®** (*Doyin*)
Mixture, Ferric ammonium citrate 400 mg per 5 ml.
Pack - 200 ml.
Dose: Adult, 15 ml 3 times daily.
Child (6-12 years), 5 ml 3 times daily.

OTC **RUBYRON®** (*KRSNA*)
Mixture, Ferric ammonium citrate 200 mg, folic acid 0.52 mg, vitamin B_{12} 5 mg per 5 ml.
Pack - 200 ml.
Dose: Adult, 10-15 ml 3 times daily.
Child (6-12 years), 5 ml 2 times daily.

OTC **SULFETONE®** *(Fill Pharma)*
Tablet, Ferrous sulfate (dried) BP 200 mg (equiv. 60 mg iron); sugar-coated tab.
200 mg - 100; 1000.

OTC **VITAFERON®** *(Leady)*
Capsules, Ferrous fumarate, multivitamin, minerals.
Mixtures, Ferric ammonium citrate 400 mg per 5 ml; dark-brown liquid.
Pack - 200 ml.

FERROUS SALT plus FOLIC ACID

Indications: Prevention of iron and folic acid deficiencies in pregnancy.
Precautions: Low doses of folic acid in the combination preparations above are inadequate for treatment of megaloblastic anaemia; overdosage: see section 19.2.4; **interactions**: Appendix 1.
Adverse effects: see Ferrous salts.
Dose: *Severe anaemia*, by mouth, adult elemental iron 120 mg daily with folic acid 400 micrograms daily for 3 months; child under 2 years elemental iron 25 mg daily with folic acid 100–400 micrograms daily for 3 months, 2–12 years elemental iron 60 mg daily with folic acid 400 micrograms daily for 3 months.
Prevention of iron and folic acid deficiencies in pregnancy, by mouth ADULT the equivalent of about 100 mg elemental iron with 350–400 micrograms folic acid daily throughout pregnancy.

OTC **Ferrous salt plus Folic acid** *(WMF 10.1)*
Tablets, Dried ferrous sulfate 325 mg (105 mg iron), folic acid 350 micrograms; dried ferrous sulfate 160 mg (50 mg iron), folic acid 400 micrograms; ferrous fumarate 322 mg (105 mg iron), folic acid 350 micrograms.

FOLIC ACID

Synonym: Vitamin B_9; Folacin; Pteroylglutamic Acid; Folate.
Therapeutic category: Water Soluble Vitamin.
Indications: Treatment of folate-deficiency megaloblastic anaemia; prevention of neural tube defect in pregnancy (see notes above).
Contra-indications: Should never be given without vitamin B_{12} in undiagnosed megaloblastic anaemia or other vitamin B_{12} deficiency states because risk of precipitating subacute combined degeneration of the spinal cord; folate-dependent malignant disease.
Precautions: Women receiving antiepileptic therapy need counselling before starting folic acid; **interactions**: Appendix 1.
Nursing considerations: •Teach patient dietary sources of folic acid: beans, nuts, fruits, fresh vegetable, organ meats.
•Co-administration with oral contraceptives, alcohol may cause increased folic acid demand.
•Inform patient that urine may turn bright yellow.
Dose: *Treatment of folate-deficiency, megaloblastic anaemia*, by mouth, ADULT 5 mg daily for 4 months; up to 15 mg daily may be necessary in malabsorption states.
Prevention of first occurrence of neural tube defect, by mouth , ADULT 400–500 micrograms daily before conception and during the first twelve weeks of pregnancy

RETURN

Prevention of recurrence of neural tube defect, by mouth , ADULT 5 mg daily (reduced to 4 mg daily, if suitable preparation available) from at least 4 weeks before conception until twelfth week of pregnancy.

OTC **Folic acid** *(WMF 10.1)*
Tablets, Folic acid 1 mg, 5 mg.

OTC **Folic acid** *(EDL 11.1)*
Tablet, Folic acid 5 mg.

OTC **Folic Acid** *(Dizpharm)*
Tablet, Folic acid 5 mg.
5 mg - 1000.

OTC **Folic Acid** *(Emzor)*
Tablet, Folic acid 5 mg; yellow biconvex tab. marked EMZOR.
5 mg - 1000.

OTC **Folic Acid** *(Evans)*
Tablet, Folic acid 5 mg; deep yellow biconvex tab.
5 mg - 100; 1000.

OTC **Folic Acid** *(Juhel)*
Tablet, Folic acid 5 mg.
5 mg - 1000.

OTC **Folic Acid** *(Mopson)*
Tablet, Folic acid 5 mg.
Pack - 1000.
Folic acid, Folic acid 2.5 mg per 5 ml.
Pack - 100 ml.

OTC **Folic Acid** *(Novel)*
Tablet, Folic acid 5 mg; yellow tab. marked NDL.
5 mg - 1000.

OTC **Folic Acid** *(Rajrab)*
Tablet, Folic acid 5 mg ; yellow scored tab.
5 mg - 1000.

OTC **Folic Acid** *(Ulticare-Lyka)*
Tablet, Folic acid 5 mg.
5 mg - 100; 1000.

OTC **Folic Acid** *(Vitabiotics)*
Tablets, Folic acid 5 mg.
5 mg - 1000's

POM **Folic acid + B_{12}** *(Vitabiotics)*
Tablet, Folic acid 5 mg, vitamin B_{12}
Pack - 100's

OTC **FOLISAM®** *(Sam)*
Tablet, Folic acid 5 mg
5 mg - 1000.

OTC **FOLTABS®** *(Ranbaxy)*
Tablet, Folic acid 5 mg.
5 mg - 100; 1000.

HYDROXOCOBALAMIN

Synonym: Vitamin B_{12}.
Therapeutic category: Water Soluble Vitamin.
Indications: Megaloblastic anaemia due to vitamin B_{12} deficiency.
Precautions: Except in emergencies, should not be given before diagnosis confirmed; monitor serum potassium levels—arrhythmias secondary to hypokalaemia in early therapy.
Adverse effects: Itching, exanthema, fever, chills, hot flushes, nausea, dizziness; rarely acneiform and bullous eruptions, anaphylaxis.
Dose: *Megaloblastic anaemia without neurological involvement*, by intramuscular injection , ADULT and CHILD initially 1 mg 3 times a week for 2 weeks, then 1 mg every 3 months.
Megaloblastic anaemia with neurological involvement, by intramuscular injection , ADULT and CHILD initially 1 mg on alternate days until no further improvement occurs, then 1 mg every 2 months
Prophylaxis of macrocytic anaemias, by intramuscular injection , ADULT and CHILD 1 mg every 2–3 months.
Tobacco amblyopia and Leber optic atrophy, by intramuscular injection , ADULT and CHILD 1 mg daily for 2 weeks, then 1 mg twice weekly until no further improvement, then 1 mg every 1–3 months.

POM **Hydroxocobalamin** *(WMF 10.1)*
Injection (Solution for injection), Hydroxocobalamin 1 mg/ml; in 1-ml ampoule.

POM **Hydroxocobalamin** *(EDL 11.1)*
Injections, Hydrocobalamin 250 mcg, 1 mg per ml.

IRON DEXTRAN

Therapeutic category: Iron salt.
Indications: Treatment of microcytic hypochromic anaemia resulting from iron

deficiency in whom oral administration is infeasible or ineffective.

Contra-indications: Hypersensitivity to iron dextran, all anaemias not related with iron deficiency, haemochromatosis, haemolytic anaemia.

Precautions: History of allergy, asthma, hepatic impairment, rheumatoid arthritis; not recommended in children below 4 months of age; test dose should be given; elderly.

Interactions:

•Decreased effect with chloramphenicol.

Adverse effects: Anaphylaxis with respiratory difficulties and cardiovascular collapse (give test dose); urticaria, leukocytosis, dizziness, fever, headache, pain, sweating; GI disturbances including metallic taste; staining of skin at the site of I.M. injection, phlebitis; discolouration of urine; arthralgia.

Nursing considerations: •Administer a test dose of 0.5 ml I.V. or I.M. and observe the patient for at least 1 hour before giving the remaining portion; keep adrenaline ready.

•Inject deeply into the upper outer quadrant of the buttock (do not give into arm or other areas); use the Z-track technique to avoid leakage into the subcutaneous tissue and staining of the skin; skin staining may also be minimised by using a separate needle to withdraw the drug from the ampoule.

•I.V. injection should be handled by an experienced clinician and patient should be allowed to rest in a recumbent position for about 15-30 minutes after I.V. administration to prevent orthostatic hypotension.

•Encourage improved nutrition in rich dietary iron sources viz meat, dark green leafy vegetables, beans, eggs.

Dose: By I.M., I.V., a test dose of 0.5 ml (0.25 ml in infants) should be given prior to starting iron dextran therapy. See lit. for details.

Note: Administration - Use Z-track technique for I.M. administration (deep into the upper outer quadrant of buttock); may be administered I.V. bolus at rate not exceeding 50mg/minute or diluted in 250-1000 ml NS and infused over 1-6 hours; infuse initial 25 ml slowly, observe for allergic reactions; have adrenaline ready.

POM **Iron Dextran** *(EDL 11.1)*

Injection, Iron dextran equivalent to 50 mg iron per ml; in 2 ml amp.

6.1.2 Drugs used in neutropenia

Filgrastim (recombinant human granulocyte - colony stimulating factor) is indicated for the reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients treated with established cytotoxic chemotherapy for non-myeloid malignancy and the reduction in the duration of neutropenia and its clinical sequelae in patients undergoing myeloblastic therapy followed by bone marrow transplantation.

In patients, children or adults, with severe congenital cyclic or idiopathic neutropenia with AUC of less than or equal to 0.5 x 10 a/L and a history of severe or recurrent infections, long-term administration of filgrastim is indicated to increase neutrophil counts and to reduce the incidence and duration of infection related incidents.

FILGRASTIM

Synonym: G-CSF; Granulocyte Colony Stmulating Factor.

Therapeutic category: Colony Stimulating Factor.

Indications: See the notes above.

Contra-indications: Hypersensitivity to filgrastim. Avoid in patients with severe congenital neutropenia (kostmen's syndrome) with abnormal cytogenetics. Not to be used to increase the dose of cytotoxic chemotherapy beyond established dosage regimen.

PRECAUTIONS: Pregnancy and breast-feeding; monitor leucocyte count, platelet count and haemoglobin.

Adverse effects: Musculoskeletal pain (usually controlled with standard analgesics); urinary abnormalities predominantly mild to moderate dysuria; reversible and dose-dependent elevations of liver enzymes and serum uric acid; rarely, allergic-type reactions; transient decreases in blood pressure (not requiring clinical treatment).

Advice to patients: Possible bone pain.

Nursing considerations: •Do not shake vial; not to be mixed with sodium chloride solutions.

•Give paracetamol to relieve bone pain

Dose: By s.c. injection or i.v. infusion, 5 mcg (500,000 units)/kg daily started at least 24 hours after cytotoxic chemotherapy, continued until neutrophil count is in normal range, usually for up to 14 days.

Note: It should only be administered by those experienced in its use.

POM **NEUPOGEN®** *(Swipha)*

Injection, Filgrastim 300 mcg (30 million units) per ml; 480 mcg (48 million units) per 1.6 ml.
300 mcg/ml in 1ml vial.
480 mcg/1.6 ml in 1.6 ml vial.

6.1.3 Drugs used in hypoplastic, haemolytic, and renal anaemias

EPOETIN ALFA

Synonym: EPO; Erythropoietin; r-HuEPO.
Therapeutic category: Recombinant human erythropoietin.
Indications: Anaemia associated with erythropoietin deficiency in chronic renal failure; to increase the yield of autologous blood in normal individuals and to shorten the period of anaemia in cancer patients on chemotherapy.
Contra-indications: Hypersensitivity to albumin (human) or mammalian cell-derived products; uncontrolled hypertension.
Precautions: Porphyria, hypertension, history of seizures; prior to and during therapy, other causes of anaemia such as iron or folate deficiency must be evaluated and corrected if necessary; sudden stabbing migraine-like pain is a warning of hypertensive crisis; ischaemic heart disease; thrombocytosis; malignant disease; chronic liver failure; dialysis heparin requirements may increase; pregnancy, breast-feeding.
Interactions:
•ACE inhibitors (antagonism of hypotensive effect and increased risk of hyperkalaemia).
Adverse effects: Dose-dependent increase in B.P. or aggravation of hypertension; flu-like symptoms such as muscular aches from 60-90 mins after I.V. injection (may be reduced by giving I.V. injection over 5mins.); headache, seizures, rash, oedema; hyperkalaemia; hypersensitivity reactions.
Advice to patients: Notify physician if any severe headache develops.
Nursing considerations: •Do not shake vial.
•Advise patient to avoid hazardous activities until stabilized on medication.
Dose: See under the preparations below.

POM **EPREX®** (*Janssen-Cilag*)
Injection(Vials), Epoetin alfa 2000 units, 4000 units per ml; in 1 ml vials.
Dose: *Anaemia associated with chronic renal failure*, by S.C. injection (max. 1 ml per injection site) or I.V. injection over 1-5 minutes, initially 50 units/kg 3 times per week; adjusted according to Hb response and urgency of anaemia correction in steps of 25 units/kg at 4-week intervals; max. dose 240 units/kg 3 times per week.
Maintenance dose: The dose has to be adjusted individually to maintain a packed cell volume of 30-35 volume % (i.e., Hb level of 10-12 g /100 ml). The maintenance dose is approximately half the dose administered in the correction phase.
Cancer patients on Chemotherapy, by S.C. injection (max.1 ml per injection site), initially 150 units/kg 3 times per week for up to 3 months. Monitor haematocrit weekly when adjusting dose. **Withhold dose** if haematocrit rises above 40% until it falls to 36%; then reduce dose by 25% when treatment is resumed and adjust to maintain the desired haematocrit.
Reduce dose if the initial dose of r-HuEPO includes a very rapid rise in haematocrit (more than 4% in any 2-week period).
Doses in excess of 150 units/kg 3 times daily not recommended.
Note: The subcutaneous maintenance dose is approximately 20-35% lower than the intravenous dose. When changing from one route of administration to the other, the same dose should be used and then adjust according to weekly haemglobin measurements to keep the Hb within the target range.
See lit. for more detailed information.

6.2 Drugs affecting coagulation

6.2.1 Anticoagulants
6.2.2 Reversal of anticoagulation

Anticoagulants are used to prevent thrombus formation or extension of an existing thrombus in the slower-moving venous side of the circulation, where the thrombus consists of a fibrin web enmeshed with platelets and red cells. They are therefore used widely in the prevention and treatment of deep-vein thrombosis in the legs, prophylaxis of embolization in rheumatic heart disease and atrial fibrillation and to prevent thrombi forming on prosthetic heart valves.

Heparin is a parenteral anticoagulant that initiates anticoagulation rapidly but has a short duration of action. The low molecular weight heparins have a longer duration of action.

For the treatment of deep venous thrombosis and pulmonary embolism heparin is given as an intravenous loading dose followed by continuous intravenous infusion (using an infusion pump) or by intermittent subcutaneous injection. An oral anticoagulant is started at the same time as heparin. The heparin needs to be continued for at least 5 days, until the oral anticoagulant has taken effect and the INR

(international normalized ratio) has been in the therapeutic range for 2 consecutive days. Laboratory monitoring is essential, on a daily basis. Heparin is also used in regimens for the management of myocardial infarction, the management of unstable angina, acute peripheral arterial occlusion and in dialysis.

In patients undergoing general surgery, low-dose heparin by subcutaneous injection is used to prevent postoperative deep-vein thrombosis and pulmonary embolism in high risk patients (those with obesity, malignant disease, history of deep-vein thrombosis or pulmonary embolism, patients over 40 years, those with an established thrombophilic disorder or those undergoing major or complicated surgery). It is also of value in high-risk medical patients, for example obesity, heart failure, when confined to bed.

If haemorrhage occurs it is usually sufficient to withdraw heparin, but if rapid reversal of the effects of heparin is required, **protamine sulfate** is a specific antidote.

Oral anticoagulants take at least 48–72 hours for the anticoagulant effect to develop fully; if an immediate effect is needed, heparin must be given concomitantly. Warfarin is indicated in deep-vein thrombosis, pulmonary embolism, for patients with atrial fibrillation who are at risk of embolization and for those with mechanical prosthetic heart valves (to prevent emboli developing on the valves); oral anticoagulants should not be used in cerebral thrombosis or peripheral arterial occlusion as first-line therapy. The main adverse effect of oral anticoagulants is haemorrhage. Prothrombin time (usually reported as INR, international normalized ratio) should be checked on a daily basis initially then at longer intervals depending on response.

If severe haemorrhage occurs, stop warfarin and give **phytomenadione** (vitamin K) by slow intravenous injection.

ANTICOAGULANTS IN PREGNANCY

Oral anticoagulants are teratogenic and should not be given in the first trimester of pregnancy. Women at risk of pregnancy should be warned of this danger since stopping warfarin before the sixth week of gestation may largely avoid the risk of fetal abnormality. Oral anticoagulants cross the placenta with the risk of placental or fetal haemorrhage, especially during the last few weeks of pregnancy and at delivery. Therefore, if at all possible, oral anticoagulants should be avoided in pregnancy, especially in the first and third trimester. Difficult decisions may have to be made, particularly in women with prosthetic heart valves or with a history of recurrent venous thrombosis or pulmonary embolism.

HAEMOPHILIA

Desmopressin [not included on WHO Model List] by injection may aid haemostasis and be useful in mild forms of haemophilia. For minor procedures including dental surgery, it may circumvent the need for factor VIII. For the use of factor VIII and factor IX in haemophilia, see section 6.6.

6.2.1 Anticoagulants

Nursing Considerations:- Anticoagulants

•Give at same time each day to maintain steady blood levels.
•Do not massage area or aspirate when giving SC injection; give in abdomen between pelvic bone, rotate sites; do not pull back on plunger; leave in for 10 sec; apply gentle pressure for 1 min.
•Avoid all IM injections that may cause bleeding.
•May withhold drug during active bleeding e.g. menstruation, depending on condition.
•Monitor patient's blood parameters: Hct, platelets, occult blood in stools, prothrombin time.
•Watch for signs of increasing B/P; bleeding gums, petechiae, ecchymosis; black, tarry stools; haematuria; fever, skin rash, urticaria.
•Tell patient to report any signs of bleeding: gums, under skin, urine, stools.
•Advise patient to avoid OTC medications due to adverse drug interactions, except on doctor's prescription.
•Instruct patient to use soft-bristle toothbrush to avoid bleeding gums, avoid contact sports and use electric razor.

ENOXAPARIN

Therapeutic category: Anticoagulant.
Indications: Prevention of various thrombo-embolic diseases following orthopaedic and general surgery; treatment of deep-vein thrombosis; prevention of clotting in extracorporeal circulation during haemodialysis.
Contra-indications: Hypersensitivity to either enoxaparin, heparin or its derivatives;acute septic endocarditis, haemorrhagic stroke, conditions with a high risk of uncontrolled haemorrhage.
Precautions: Renal or hepatic insufficiency,

history of peptic ulcer, arterial hypertension, diabetic retinopathy, recent CNS or ophthalmologic surgery, spinal anaesthesia and epidural block; history of heparin-induced thrombocytopenia; avoid using low molecular weight heparins
interchangeably; avoid use in lactation and during the first trimester of pregnancy. Do not administer I.M.

Interactions: •Avoid co-administration with substances that enhance the risk of haemorrhage such as systemic salicylates, aspirin, systemic NSAIDs, ticlopidine.
•Use caustiously with oral anticoagulants, systemic glucocorticoids , dextran 40.

Adverse effects: Heamorrhage, thrombocytopenia, haematoma, irritation at injection site, erythema, ecchymosis; rarely allergic reactions which may require stopping therapy.

Nursing considerations: •Administer by deep S.C. injection; avoid I.M. injection which may cause bleeding.
•The prefilled syringe is ready for immediate use. Injection should be made preferably when the patient is lying down, in the subcutaneous cellular tissue of the abdomen.
•Instruct patient to avoid use of aspirin containing products due to increased risk of bleeding.
•Advise patient to use soft toothbrush to avoid bleeding gums; to report any signs of bleeding.

Dose: By S.C. injection, *Prevention of deep-vein thrombosis, patients with moderate risk of thrombo-embolism,* 20 mg (0.2 ml) 2 hours before surgery, then 20 mg (0.2 ml) every 24 hours for 7-10 days;
Patients with high risk of thromboembolism, 40 mg (0.4 ml) 12 hours before surgery, then 40 mg (0.4 ml) every 24 hours for 7-10 days.
Treatment of deep-vein thrombosis, 1 mg/kg every 12 hours and during 10 days.
Prevention of clotting in extracorporeal circulation during haemodialysis, usually 1 mg/kg; to be introduced in the arterial line of the circuit at the beginning of the dialysis session. This is usually sufficient for a four hour session but if fibrin rings are found for example after a longer than normal session, a further dose of 0.5 mg - 1 mg/kg may be given.

Note: How to administer:

1. Hold syringe with needle pointing away, slightly raised.
2. Rotate syringe until numbers are clearly visible.
3. Remove needle cap.
4. Depress plunger until edge of black plunger is level with marking corresponding to recommended dose.
5. Insert whole lenght of the needle vertically into a skin fold (of the abdomen) held between the thumb and index finger.
6. Do not release the skin fold until the injection is complete.
7. Do not rub the injection site.

POM **CLEXANE®** *(May & Baker)*
Injection, Enoxaparin 100 mg per ml; in 0.4 ml (40 mg) ready-to-use prefilled syringe. Pack - 40 mg x 10.

POM **CUTENOX®** *(Fidson)*
Injection, Enoxaparin sodium 100 mg per ml; in 0.2 ml (20 mg), 0.4 ml (40 mg), 0.6 ml (60 mg) and 0.8 ml (80 mg) ready-to-use prefilled syringes.

HEPARIN SODIUM

Indications: Treatment and prophylaxis of deep-vein thrombosis and pulmonary embolism.

Contra-indications: Hypersensitivity to heparin; haemophilia and other haemorrhagic disorders, thrombocytopenia, peptic ulcer, recent cerebral haemorrhage, severe hypertension, severe liver or renal disease, after major trauma or recent surgery (especially to eye or nervous system).

Precautions: Hepatic impairment (Appendix 5) and renal failure (Appendix 4); hypersensitivity to low molecular weight heparins; spinal or epidural anaesthesia—risk of spinal haematoma; pregnancy (Appendix 2); diabetes mellitus, acidosis, concomitant potassium-sparing drugs—increased risk of hyperkalaemia; **interactions**: Appendix 1.

Adverse effects: Immune-mediated thrombocytopenia usually developing 6 to 10 days after commencement of therapy (requires immediate withdrawal of heparin); haemorrhage, skin necrosis, hypersensitivity reactions including urticaria, angioedema and anaphylaxis; osteoporosis after prolonged use and rarely alopecia.

Nursing considerations: •Do not massage area or aspirate when giving S.C. injection; avoid I.M. injection which may cause bleeding.
•Inspect the patient's gum for bleeding regularly; notify physician immediately of petechiae, epistaxis, bruises on arms or legs, malaena stools, haematuria, haematemesis.
•Tell patient to avoid OTC medications containing aspirin and other salicylates.
•Ensure that laboratory personnel apply pressure dressing after taking blood.

•Withhold drug during active bleeding as in menstruation.
•Advise patient to use soft toothbrush to avoid bleeding gums; to report any signs of bleeding.

Dose: *Treatment of deep-vein thrombosis and pulmonary embolism*: by intravenous injection, ADULT loading dose of 5000 units (10 000 units in severe pulmonary embolism) followed by continuous intravenous infusion of 15–25 units/kg/hour or by subcutaneous injection of 15 000 units every 12 hours; laboratory monitoring is essential, preferably on a daily basis and dose adjusted accordingly; by intravenous injection, SMALL ADULT and CHILD , lower loading dose, then by continuous intravenous infusion, 15–25 units/kg/hour or by subcutaneous injection, 250 units/kg every 12 hours
Prophylaxis in general surgery, by subcutaneous injection, ADULT 5000 units 2 hours before surgery, then every 8–12 hours for 7 days or until patient is ambulant (monitoring not needed); during pregnancy (with monitoring) 5000–10 000 units every 12 hours (**important**: not intended to cover prosthetic heart valve management in pregnancy, which requires specialist management).

POM **Heparin sodium** *(WMF 10.2)*
Injection (Solution for injection), heparin sodium 1000 units/ml, 1-ml ampoule; 5000 units/ml, 1-ml ampoule; 25 000 units/ml, 1-ml ampoule.

POM **Heparin sodium** *(EDL 11.2)*
Injections, Heparin sodium 1000 units, 25,000 units per ml; in amps.

NADROPARIN

Therapeutic category: Anticoagulant.
Indications: Nadroparin calcium is a low-molecular weight heparin used in prevention and treatment of venous thrombosis; also for prevention of coagulation during haemodialysis.
Contra-indications: Hypersensitivity to the drug or any component; major blood coagulation disorders; history of low blood platelet count; gastric or duodenal ulcer; acute infections; endocarditis; severe renal insufficiency, haemorrhagic CVA, high B.P. or co-administration with inhibitor of platelet aggregation such as aspirin.
Precautions: Avoid I.M. administration; regular blood platelet count; history of liver or renal disease ,ulcer; pregnancy.
Dose: *Prevention of venous thrombosis*, by S.C. injection, 2850 I.U. (0.3 ml) once daily for less than 10 days.
In high risk surgery, 38 I.U./kg once daily; then one daily injection of 57 I.U./kg from the 4th day after the intervention.
Treatment of Venous thrombosis, by S.C. injection, 85 I.U. / kg 12 hourly for a period not exceeding 10 days.
Haemodialysis, by I.V. injection, 65 I.U./kg as a single dose; to be given at the beginning of each haemodialysis session.

POM **FRAXIPARINE®** *(Sanofi)*
Injection, Nadroparin calcium 2850 I.U. per 0.3 ml; solution for injection in a pre-filled syringe. Pack - 2; 6; 10 .

WARFARIN SODIUM

Warfarin is a representative oral anticoagulant. Various drugs can serve as alternatives.
Indications: Prophylaxis of embolization in rheumatic heart disease and atrial fibrillation; prophylaxis after insertion of prosthetic heart valve; prophylaxis and treatment of venous thrombosis and pulmonary embolism; transient ischaemic attacks.
Contra-indications: Pregnancy (see notes above and Appendix 2); peptic ulcer, severe hypertension, bacterial endocarditis.
Precautions: Hepatic impairment (Appendix 5) or renal failure (Appendix 4), recent surgery, breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Haemorrhage; hypersensitivity, rash, alopecia, diarrhoea, unexplained drop in haematocrit, 'purple toes', skin necrosis, jaundice, hepatic dysfunction, nausea, vomiting and pancreatitis.
Advice to patients: Do not take with food; report any signs of bleeding; avoid hazardous activities; use soft tooth brush; urine may turn red/orange; be sure of other drugs and foods to avoid. Notify physician if urine turns dark brown or if red or tar black stools occur.
Nursing considerations: •Give alone and not with food (food and enteral feeding that contain vitamin k may cause inadequate anticoagulation due to the neutralizing effect of vitamin k on warfarin); may give tablet whole or crushed.
•Avoid I.M. injection that may cause bleeding; also

avoid ear-piercing, circumcision; do not give during active bleeding e.g. menstruation.
•Advise patient to use soft toothbrush to avoid bleeding gums; to report any signs of bleeding namely bleeding gums, bruises on arms or legs, petechiae, nosebleeds, melena, tarrystools, haematuria, haematemesis. Female patient should report if menses is heavier than usual.
•Watch for skin rash and fever; may indicate adverse reaction.
•Advise patient to avoid the use of other drugs except on prescription; to avoid hazardous activities.

Dose: NOTE: WHEREVER POSSIBLE, THE BASE-LINE PROTHROMBIN TIME SHOULD BE DETERMINED BEFORE THE INITIAL DOSE IS GIVEN.

Prophylaxis and treatment of thromboembolic disorders, by mouth, ADULT usual induction dose is 10 mg daily for 2 days, according to the individual patient; the subsequent dose depends upon the prothrombin time; the usual daily maintenance dose is 3–9 mg taken at the same time each day.

POM **Warfarin sodium** *(WMF 10.2)*
Tablets, Warfarin sodium 1 mg, 2 mg, 5 mg.

POM **Warfarin sodium** *(EDL 11.2)*
Tablets, Warfarin sodium 1 mg, 5 mg.

6.2.2 Reversal of anticoagulation

PROTAMINE SULFATE

Indications: antidote to overdosage with heparin.

Precautions: If used in excess protamine has an anticoagulant effect; allergic reactions increased in persons at risk including previous treatment with protamine or protamine insulin, fish allergies, men who are infertile or who have had a vasectomy.

Adverse effects: Nausea, vomiting, lassitude, flushing, hypotension, bradycardia, dyspnoea, allergic reactions (including angioedema, anaphylaxis).

Nursing considerations: •For IV use only; administer slowly because rapid IV infusion causes hypotension.
•Monitor vital signs continually.
•Protamine sulfate may act as anticoagulant in very high doses.
•Observe for heparin rebound associated with anticoagulation and bleeding.

Dose: *Heparin overdose*, by intravenous injection over approximately 10 minutes, 1 mg neutralizes 80–100 units heparin when given within 15 minutes; if longer time, less protamine needed as heparin is rapidly excreted.

POM **Protamine sulfate** *(WMF 10.2)*
Injection (Solution for injection), Protamine sulfate 10 mg/ml, 5-ml ampoule.

POM **Protamine** *(EDL 4.2)*
Injection, Protamine sulphate 10 mg per ml; in 5 ml amp.

PHYTOMENADIONE

Indications: Antagonist to warfarin; prophylaxis against haemorrhagic disease of the newborn.

Precautions: Reduce dose in elderly; hepatic impairment; not an antidote to heparin; pregnancy (Appendix 2); **interactions**: Appendix 1.

Adverse effects: Hypersensitivity reactions including flushing, dyspnoea, bronchospasm, dizziness, hypotension and respiratory or circulatory collapse which may be due to polyethoxylated castor oil surfactant in some injection formulations rather than due to phytomenadione.

Nursing considerations: •Check the brand name labels for administration route restrictions, e.g., ***Konakion® MM*** may be admnistered by slow I.V. injection or by I.V. infusion in D_5W but not for I.M. injection. While ***Konakion®*** may be administered by I.M. or slow I.V. injection but not for I.V. infusion. It contains polyethoxylated castor oil which should not be diluted.
•Assist with checking prothrombin time (PT) to determine dosage effectiveness.
•Observe patient closely for signs of adverse reactions viz weakness, dyspnoea, tachycardia and hypotension which may gradually progress to shock; report them to physician.

Dose: *Warfarin-induced hypoprothrombinaemia*; *no bleeding or minor bleeding*, by slow intravenous injection, ADULT 500 micrograms or by mouth, ADULT 5 mg; *less severe haemorrhage*, by mouth or by intramuscular injection, ADULT 10–20 mg; *severe haemorrhage*, ADULT, by slow intravenous injection, 2.5–5 mg; very rarely up to 50 mg (but risk of overcorrection with high dosage). *Haemorrhagic disease of the newborn, treatment*, by intravenous or intramuscular injection , NEONATE 1 mg with further doses if necessary at 8-hour intervals *Haemorrhagic disease of the*

newborn, prophylaxis, by intramuscular injection, NEONATE 0.5–1 mg as single dose or by mouth, 2 mg followed by a second dose after 4–7 days and for breastfed babies a third dose after 1 month.

POM **Phytomenadione** *(WMF 10.2)*
Tablets, Phytomenadione 10 mg.
Injection (Solution for injection), Phytomenadione 10 mg/ml, 5-ml ampoule.

POM **Phytomenadione** *(EDL 4.2)*
Injection, Phytomenadione 10 mg per ml; in 1 ml amp.

6.3 Antiplatelet drugs

Platelets play a central role in haemostasis and thrombosis. Aggregation of platelets with adherence to vascular endothelium is induced by many endogenous agents, including adenosine diphosphate, thrombin and adrenaline. By decreasing platelet aggregation, antiplatelet drugs may inhibit thrombus formation on the arterial side of the circulation, where thrombi are formed by platelet aggregation and anticoagulants have little effect. Antiplatelet drugs have little effect in venous thrombo-embolism.

Dipyridamole is used with anticoagulants to prevent thrombus formation on prosthetic valves. As a vasodilator, dipyridamole may cause headache, hypotension and flushing in addition to nausea and diarrhoea.

Aspirin inhibits the synthesis of thromboxane A_2 TXA_2 which is a potent platelet aggregating agent. It has shown encouraging results in the secondary prevention of thrombotic cerebrovascular or cardiovascular disease.

DIPYRIDAMOLE

Therapeutic category: Antiplatelet Agent; Vasodilator, Coronary.
Indications: Modification of platelet function.
Precautions: Angina, aortic stenosis, recent myocardial infarction, migraine, hypotension.
Interactions: Anticoagulants, antacids.
Adverse effects: GI upset, throbbing headache, hypotension.
Advice to patients: See label 22 in Appendix 6.
Nursing considerations: •Administer on an empty stomach, one hour before meals (or with meals, if patient develops GI distress).
•Teach patient to report signs of bleeding or prolonged bleeding.
•Tell patient to avoid hazardous activities until stabilised on drug because dizziness may occur.
•Advise patient to avoid sudden posture changes to minimize the risk of orthostasis.
Dose: By mouth, 300-600 mg daily in 3-4 divided doses.
By I.V. Injection, diagnostic only.
See lit.

POM **Dipyridamole** *(EDL 11.2)*
Tablets, Dipyridamole 25 mg, 100 mg.
Injection, Dipyridamole 25 mg per ml; in 2 ml amp.

6.4 Antifibrinolytic drugs and haemostatics

Epsilon Aminocaproic Acid (EACA) or Aminocaproic acid is a synthetic inhibitor of fibrinolysis used clinically as adjunctive therapy in haemophilia, as therapy for bleeding from fibrinolytic therapy, and as prophylaxis for rebleeding from intracranial aneurysms.

It is rapidly absorbed orally and is cleared from the body by the kidney. The usual oral dose of EACA is 6 g 4 times a day. When the drug is administered intravenously, a 5 g loading dose should be infused over 30 minutes to avoid hypotension.

Adverse effects of the drug include intravascular thrombosis from inhibition of plasminogen activator, hypotension, myopathy, abdominal discomfort, diarrhoea, and nasal stuffiness.

EPSILON AMINOCAPROIC ACID

Synonym: Aminocaproic Acid.
Therapeutic category: Haemostatic Agent.
Indications: Severe haemorrhage associated with excessive fibrinolysis.
Contra-indications: Severe renal impairment; intravascular coagulation.
Precautions: Renal impairment (reduce dose); haemophiliacs.
Interactions: •Oral contraceptives (increased toxicity).
Adverse effects: Diarrhoea, headache, hypotension, dizziness, erythema, skin rash, nausea, heartburn, conjunctival suffusion, nasal stuffiness, diuresis, muscle pain and weakness.
Nursing considerations: •Rapid I.V. administration of the undiluted drug is not recommended; give I.V. slowly over 1 hour to avoid hypotension (dilution is in NS or D_5W).
•Parenteral drug product should be inspected visually for particulate matter and discolouration prior to administration.
•Teach patient/family to report signs of bleeding in skin or stools (melaena).
•Advise patient to change position slowly to minimise

orthostatic hypotension.

Dose: *Acute bleeding syndrome due to elevated fibrinolytic activity,* Adult, by mouth, 5 g during first hour; followed continuously by 1 g per hour for approx. 8 hours or until bleeding stops. By I.V. infusion, 4-5 g in 250 ml of diluent during first hour; followed by continuous infusion at the rate of 1g per hour in 50 ml of diluent; continue for 8 hours or until bleeding stops.
Maximum daily dose (by mouth or I.V.): 30 g.

Note: In the management of acute bleeding syndromes, oral dosage regimens are the same as the I.V. dosage regimens. Diluents for I.V. infusion include dextrose 5% or 0.9% sodium chloride. Rapid I.V. injection (IVP) should be avoided since hypotension, bradycardia, and arrhythmia may result.

POM **Epsilon aminocaproic acid** *(EDL 11.3)*
Tablet, Aminocarproic acid (ACA) 500 mg.
Injection, Aminocaproic acid 100 mg, lipid thromboplastin (TPT) 2 mg per ml; in 5 ml, 10 ml amps.

6.5 Plasma substitutes

Dextran 70 and **polygeline** are macromolecular substances which are metabolized slowly; they may be used to expand and maintain blood volume in shock arising from conditions such as burns or septicaemia. They are rarely needed when shock is due to sodium and water depletion as, in these circumstances, the shock responds to water and electrolyte repletion.

Plasma substitutes should not be used to maintain plasma volume in conditions such as burns or peritonitis where there is loss of plasma protein, water and electrolytes over periods of several days. In these situations, plasma or plasma protein fractions containing large amounts of albumin should be given.

Plasma substitutes may be used as an immediate short-term measure to treat massive haemorrhage until blood is available, but large volumes of some plasma substitutes can increase the risk of bleeding by depleting coagulation factors. Dextran may interfere with blood group cross-matching or biochemical measurements and these should be carried out before the infusion is started.

DEXTRANS 70

Dextran is a representative plasma substitute. Various preparations can serve as alternatives.

Indications: Short-term blood volume expansion.

Contra-indications: Severe congestive heart failure, renal failure; bleeding disorders such as thrombocytopenia and hypofibrinogenaemia.

Precautions: Cardiac disease or renal impairment; monitor urine output; avoid haematocrit falling below 25–30%; where possible, monitor central venous pressure; can interfere with blood group cross-matching and biochemical tests—take samples before start of infusion; monitor for hypersensitivity reactions; pregnancy (Appendix 2).

Adverse effects: Hypersensitivity reactions including fever, nasal congestion, joint pains, urticaria, hypotension, bronchospasm—rarely severe anaphylactoid reactions; transient increase in bleeding time.

Nursing considerations: •Ensure patient is well hydrated at the start of therapy.
•Discontinue dextran if urine specific gravity is low, and/or if oliguria or anuria occurs, or if there is a precipitous rise in central venous pressure or sign of circulatory overloading.
•Note that Dextran may interfere with analysis of blood grouping, cross matching, bilirubin, blood glucose, and protein; therefore ensure that blood for investigation is obtained before drug therapy commences.
•Observe closely for signs of anaphylaxis especially during early phase of infusion.

Dose: *Short-term blood volume expansion*, by rapid intravenous infusion, adult 500–1000 ml initially, followed by 500 ml if necessary; total dosage should not exceed 20 ml/kg during the initial 24 hours; if required 10 ml/kg daily may be given for a further 2 days (treatment should not continue for longer than 3 days); child total dosage should not exceed 20 ml/kg.

POM **Dextran 70** *(WMF 11.1)*
Infusion (Solution for infusion), Dextran 70 6% in glucose intravenous infusion 5% or sodium chloride intravenous infusion 0.9%.

POM **Dextran 40** *(EDL 11.4)*
Injection, Dextran 10% in normal saline or 5% glucose; in 500 ml bottle.

POM **Dextran 70 & 110** *(EDL 11.4)*
Injection, Dextran 6% in normal saline or 5% glucose; in 500 ml bottle.

POLYGELINE

Polygeline is a representative partially degraded gelatin. Various preparations can serve as alternatives.

Indications: Correction of low blood volume.

Contra-indications: Severe congestive heart failure; renal failure.

Precautions: Blood samples for cross-matching should be taken before infusion; haemorrhagic diasthesis; congestive heart failure, renal impairment, hypertension, oesophageal varices; **interactions**: Appendix 1.

Adverse effects: Hypersensitivity reactions including urticaria—rarely severe anaphylactoid reactions; transient increase in bleeding time.

Dose: *Correction of low blood volume*, by intravenous infusion, initially 500–1000 ml of a 3.5% solution.

POM **Polygeline** *(WMF 11.1)*
Infusion (Solution for infusion), Polygeline 3.5% with electrolytes, 500-ml bottle.

POM **Polygeline** *(EDL 11.4)*
Injection, Polygeline 3.5% solution with suitable electrolyte; in a 500 ml bottle.

6.6 Plasma fraction for specific use

Factor VIII is essential for blood clotting and the maintenance of effective haemostasis; von Willebrand factor is a mediator in platelet aggregation and also acts as a carrier for factor VIII. Blood coagulation factors VII, IX, and X are essential for the conversion of factor II (prothrombin) to thrombin. Deficiency in any of these factors results in haemophilia. Bleeding episodes in haemophilia require prompt treatment with replacement therapy. **Factor VIII**, used for the treatment of haemophilia A, is a sterile freeze-dried powder containing the blood coagulation factor VIII fraction prepared from pooled human venous plasma. Standard factor VIII preparations also contain von Willebrand factor and may be used to treat von Willebrand disease. Highly purified preparations, including recombinant factor VIII, are available; they are indicated for the treatment of haemophilia A but do not contain sufficient von Willebrand factor for use in the management of von Willebrand disease.

Factor IX Complex is a sterile freeze-dried concentrate of blood coagulation factors II, VII, IX and X derived from fresh venous plasma. Factor IX complex which is used for the treatment of haemophilia B may also be used for the treatment of bleeding due to deficencies of factor II, VII, and X. High purity preparations of factor IX which do not contain clinically effective amounts of factor II, VII, and X are available. A recombinant factor IX preparation is also available.

Factor VIII concentrate

Plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). WHO Technical Report Series, No. 840, 1994, Annex 2.

Factor VIII concentrate is a complementary preparation and a representative coagulation factor preparation. Various preparations can serve as alternatives.

Indications: Control of haemorrhage in haemophilia A.

Precautions: Intravascular haemolysis after large or frequently repeated doses in patients with blood groups A, B, or AB (less likely with high potency, highly purified concentrates).

Adverse effects: Allergic reactions including chills, fever.

Dose: *Haemophilia A*, by slow intravenous infusion, ADULT and CHILD according to patient's needs.

POM **Factor VIII concentrate** *(WMF 11.2)*
Infusion (Powder for solution for infusion), factor VIII 250–1500 units.

Factor IX complex (coagulation factors II, VII, IX, X) concentrate

Plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). WHO Technical Report Series, No. 840, 1994, Annex 2.

Factor IX complex concentrate is a complementary preparation and a representative coagulation factor preparation. Various preparations can serve as alternatives.

Indications: Replacement therapy for

RETURN

factor IX deficiency in haemophilia; bleeding due to deficiencies of factors II, VII or X.

Contra-indications: Disseminated intravascular coagulation.

Precautions: Risk of thrombosis (probably less risk with highly purified preparations).

Adverse effects: Allergic reactions including chills, fever.

Dose: *Haemophilia B*, by slow intravenous infusion, ADULT and CHILD according to patient's needs and specific preparation used

Treatment of bleeding due to deficiencies in factor II, VII or X as well as IX, by slow intravenous infusion, ADULT and CHILD according to patient's needs.

POM **Factor IX complex** *(WMF 11.2)*
Infusion (Powder for solution for infusion), factor II, VII, IX, and X 500–1500 units.

HUMAN ALBUMIN

Synonym: Normal Human Serum Albumin; Salt Poor Albumin.

Therapeutic category: Plasma Volume Expander; Blood Product Derivative.

Indications: In emergency, to prevent or treat hypovolaemic syndromes and to avoid occurence of cardiovascular collapse; nuclear jaundice in the newborn; as replacement therapy, to increase the albumin fraction in serum or correct protein deficiency in conditions such as serious hepatic disorders, decompensated nephrotic syndrome, chronic condition in burn cases; cerebral oedema.

Contra-indications: Volaemic overload, asystolia, severe deterioration of general circulation.

Precautions: Dehydration (alternate with suitable rehydrating solution), circulatory overload (check central venous B.P. and pulmonary capillary pressure regularly); should be injected alone (normal diluents are saline and glucose solutions).

Interactions: •Not to be mixed with other medications.

Nursing considerations: •Administer I.V. slowly (rapid infusion may cause hypotension).

•Monitor vital signs carefully; observe for signs of vascular overload e.g. heart failure or pulmonary oedema.

•Discard unused or cloudy solutions.

•Watch out for allergic reactions such as urticaria, rash, pyrexia, rigor or chill and immediately inform physician.

•Watch for haemorrhage or shock if used after surgery or injury.

Dose: By intravenous infusion (20 drops per minute), *shock*, 125-150 ml.
Child: 1-2 ml/kg b.wt.
Serious burns, double the dosage on first day and the normal dosage on the subsequent days.
Nuclear jaundice in the newborn , 10-15 ml associated with exchange transfusion.
Replacement therapy, 125-250 ml daily.
Child: 2-5 ml/kg b. wt daily.
Newborn: 5-15 ml/kg b.wt daily.

POM **Human Albumin** *(EDL 11.5)*
Injection, Human albumin 20% solution.

POM **Human Albumin** *(May & Baker)*
A 20% solution of purified human serum albumin of placental origin with poor salt content.
Pack - 50 ml vial plus infusion set.

6.7 Vitamins

Vitamins are used for the prevention and treatment of specific deficiency states or when the diet is known to be inadequate. It has often been suggested but never convincingly proved, that subclinical vitamin deficiencies cause much chronic ill-health and liability to infections. This has led to enormous consumption of vitamin preparations, which have no more than placebo value. Most vitamins are comparatively non-toxic but prolonged administration of high doses of retinol (vitamin A), ergocalciferol (vitamin D2) and pyridoxine (vitamin B6) may have severe adverse effects.

Retinol (vitamin A) is a fat-soluble substance stored in body organs, principally the liver. Periodic high-dose supplementation is intended to protect against vitamin A deficiency which is associated with ocular defects particularly xerophthalmia (including night blindness which may progress to severe eye lesions and blindness), and an increased susceptibility to infections, particularly measles and diarrhoea. Universal vitamin A distribution involves the periodic administration of supplemental doses to all preschool-age children with priority given to age groups, 6 months to 3 years, or regions at greatest risk. All mothers in high-risk regions should also receive a high dose of vitamin A within 8 weeks of delivery. Since vitamin A is associated with a

teratogenic effect it should be given in smaller doses (no more than 10 000 units/ day) to women of child-bearing age. It is also used in the treatment of active xerophthalmia. Doses of vitamin A should be administered orally immediately upon diagnosis of xerophthalmia and thereafter patients with acute corneal lesions should be referred to a hospital on an emergency basis. In women of child-bearing age there is a need to balance the possible teratogenic effects of vitamin A should they be pregnant with the serious consequences of xerophthalmia. Where there are severe signs of xerophthalmia high dose treatment as for patients over 1 year should be given. When less severe symptoms are present (for example night blindness) a much lower dose is recommended. Vitamin A therapy should also be given during epidemics of measles to reduce complications.

Vitamin B is composed of widely differing substances which are, for convenience, classed as 'vitamin B complex'. **Thiamine** (vitamin B_1) is used orally for deficiency due to to inadequate dietary intake. Severe deficiency may result in 'beri-beri'. Chronic dry 'beri-beri' is characterized by peripheral neuropathy, muscle wasting and weakness, and paralysis; wet 'beri-beri' is characterized by cardiac failure and oedema. Wernicke-Korsakoff syndrome (demyelination of the CNS) may develop in severe deficiency. Thiamine is given by intravenous injection in doses of up to 300 mg daily (parenteral preparations may contain several B group vitamins) as initial treatment in severe deficiency states. Potentially severe allergic reactions may occur after parenteral administration. Facilities for resuscitation should be immediately available. **Riboflavin** (vitamin B_2) deficiency may result from reduced dietary intake or reduced absorption due to liver disease, alcoholism, chronic infection or probenecid therapy. It may also occur in association with other deficiency states such as pellagra. **Pyridoxine** (vitamin B_6) deficiency is rare as the vitamin is widely distributed in foods, but deficiency may occur during isoniazid therapy and is characterized by peripheral neuritis. High doses are given in some metabolic disorders, such as hyperoxaluria and it is also used in sideroblastic anaemia. **Nicotinic acid** inhibits the synthesis of cholesterol and triglyceride and is used in some hyperlipidaemias. Nicotinic acid and **nicotinamide** are used to prevent and treat nicotinic acid deficiency (pellagra). Nicotinamide is generally preferred as it does not cause vasodilation. **Hydroxocobalamin** is the form of vitamin B_{12} used to treat vitamin B_{12} deficiency due to dietary deficiency or malabsorption (see section 6.1).

Folic acid is essential for the synthesis of DNA and certain proteins. Deficiency of folic acid or vitamin B_{12} is associated with megaloblastic anaemia. Folic acid should not be used in undiagnosed megaloblastic anaemia unless vitamin B_{12} is administered concurrently, otherwise neuropathy may be precipitated (see section 6.1). Supplementation with folic acid 400 micrograms daily is recommended for women of child-bearing potential in order to reduce the risk of serious neural tube defects in their offspring (see section 6.1).

Ascorbic acid (vitamin C) is used for the prevention and treatment of scurvy. Claims that ascorbic acid is of value in the treatment of common colds are unsubstantiated.

The term **vitamin D** covers a range of compounds including **ergocalciferol** (vitamin D_2) and **colecalciferol** (vitamin D_3). These two compounds are equipotent and either can be used to prevent and treat rickets.

Simple deficiency of vitamin D occurs in those who have an inadequate dietary intake or who fail to produce enough colecalciferol (vitamin D_3) in their skin from the precursor 7-dehydrocholesterol in response to ultraviolet light.

Children with dark skin must continue vitamin D prophylaxis for up to 24 months because of their inability to produce enough vitamin D_3 in their skin. Dark skin with a high melanin content must be exposed to daylight longer than light skin in order to obtain the same synthesis of vitamin D_3. Vitamin D is also used in deficiency states caused by intestinal malabsorption or chronic liver disease and for the hypocalcaemia of hypoparathyroidism.

Vitamin K is necessary for the production of blood clotting factors (see section 6.2).

ASCORBIC ACID

Synonym: Vitamin C
Indications: Prevention and treatment of scurvy.
Adverse effects: Gastrointestinal disturbances reported with large doses.
Dose: *Prophylaxis of scurvy*, by mouth, ADULT and CHILD 25–75 mg daily.
Treatment of scurvy, by mouth, ADULT and CHILD not less than 250 mg daily in divided doses.
See also under the proprietary preparations below.

OTC **Ascorbic acid** *(WMF 27.1)*
Tablets, Ascorbic acid 50 mg.

OTC **Vitamin C** *(EDL 27.1)*
Tablet, Ascorbic acid 100 mg, 200 mg, 500 mg.
Effervescent Tablet, Ascorbic acid 1 g
Syrup, Ascorbic acid 100 mg, 300 mg, 500 mg per 5 ml.

OTC **ASCO-J**® *(Juhel)*
Tablets, Vitamin C 100 mg; 500 mg.
100 mg - 50; 500; 1000.
500 mg - 100.
Syrup, Ascorbic acid BP 100 mg per 5 ml.
Pack – 100 ml in amber bottle.

OTC **ASCORBION C**® *(Mopson)*
Tablet, Vitamin C 100 mg.
100 mg - 50, 100, 1000.
Syrup, Vitamin C 300 mg per 5 ml.
Pack - 100 ml.

OTC **ASCORVIT**® *(Sam)*
Tablet (Chewable), Vitamin C 100 mg.
100 mg - 1000's.

OTC **CHEWETTE C**® *(Hovid)*
Tablet (Orange flavour), Vitamin C 100 mg; orange coloured tab. marked 'CHEWETTE 100' on one side.
100 mg - 60 x 12.
Tablet (Black currant), Vitamin C 100 mg; purple coloured tab. marked 'CHEWETTE 100' on one side.
100 mg - 150.
Dose: *As dietary supplement*, 300-400 mg per day or as required.

OTC **EM-VIT-C**® *(Emzor)*
Tablet, Ascorbic acid 100 mg.
100 mg - 100; 1000
Tablet (Chewable), Ascorbic acid 100 mg.
100 mg - 10 x 30; 100; 1000.
Syrup, Ascorbic acid 100 mg per 5 ml.
Pack - 100 ml; 2 L.

OTC **ESOCEE**® *(Jawa)*
Syrup, Ascorbic acid 100 mg per 5 ml.
Pack - 100 ml x 20's
Drops, Ascorbic acid 100 mg per ml.
Pack - 15 ml

OTC **HEALTHILIFE STYLE VITAMIN C**® *(Biofem)*
Tablet (Chewable), Ascorbic acid 500 mg

OTC **LIMVIT**® *(Ranbaxy)*
Syrup, Ascorbic acid 100 mg per 5 ml
Pack - 100 ml.

OTC **NAVIC**® *(NASDMU)*
Tablet, Vitamin C 100 mg; white biconvex tab. marked 'NAVIC' on one side and 'NASDMU' on the reverse.
Pack - 100; 1000.

OTC **RAB-C-VITE**® *(Rajrab)*
Tablet, Ascorbic acid 100 mg; white scored tab.
100 mg - 1000.

OTC **REDOXON**® *(Swipha)*
Effervescent tablet, Ascorbic acid 1 g; orange coloured tab.
1 g - 10.

OTC **TACORANGE**® *(SKG)*
Syrup, Vitamin C 100 mg per 5 ml; orange flavoured syrup.
Pack - 100 ml.
Dose: *As dietary supplement*, child (below 12 years), 2.5-5 ml daily; above 12 years, 10 ml daily.
Treatment, child (below 12 years), 2.5-5 ml 3 times daily; above 12 years, 10 ml 3 times daily.

OTC **TAMIN-C**® *(Leady)*
Syrup, Vitamin C 100 mg per 5 ml; available in both lemon and orange flavours.
Pack - 100 ml.

OTC **VITACEE**® *(Pharma-Deko)*
Syrup, Vitamin C.
Pack - 100 ml.
Dose: Children and adult, 5-15 ml daily.
Drops, Vitamin C 100 mg per ml.
Pack - 15 ml.
Dose: Child (under 1 year), 0.3 ml daily; Over 1 year, 0.6 ml daily.
Doses should be dropped on the back of the tongue or mixed with milk, fruit juices and other liquids.

OTC **Vitamin C** *(Afrab-Chem)*
Tablet, Ascorbic acid 100 mg.

OTC **Vitamin C** *(Chemo-Pharma)*
Tablet, Ascorbic acid 100 mg
Tablet *(Chewable)*, Ascorbic acid 100 mg.
100 mg - 1000

OTC **Vitamin C** *(Emzor)*
Tablet, Ascorbic acid 100 mg; white to off-white biconvex tab.
100 mg - 100; 1000.
Syrup, Ascorbic acid 100 mg per 5 ml; clear yellow orange flavoured syrup.
Pack - 100 ml; 2 L.

OTC **Vitamin C** *(Juhel)*
Tablet, Ascorbic acid 100 mg; orange flavoured or plain tab.
100 mg - 100; 1000.

OTC **Vitamin C** *(Leady)*
Syrup, Ascorbic acid 100 mg per 5 ml; orange-yellow syrup.
Pack - 100 ml; 2 L.

OTC **Vitamin C** *(Novel)*
Tablet, Ascorbic acid 100 mg; white shallow concave tab. marked 'Vit C 100' on one side and 'NOVEL' on the reverse.
Pack - 1000.
Tablet (Chewable), Ascorbic acid 100 mg
100 mg - 1000.

OTC **Vitamin C** *(Ulticare-Lyka)*
Tablet, Ascorbic acid 100 mg.
100 mg - 100; 1000.

COD LIVER OIL

Indications: Treatment of vitamin A and vitamin D related deficiencies.
Dose: By mouth, Adult, 1 capsule 3 times daily.

OTC **Cod Liver Oil** *(EDL 27.1)*
Capsules or Syrup, Vitamin A 600-1000 i. u, vitamin D 75-100 i. u. per gram.

OTC **NUTRIHEALTH COD LIVER OIL®** *(Hovid)*
Capsule , Vitamin A 600 i. u, vitamin D 60 i. u.
Pack - 100.

OTC **SILVACOD®** *(Justeen)*
Capsules, Codliver oil BP 300 mg.
Pack - 10 x 10's

OTC **SUPA-NOVA COD LIVER OIL®** *(SKG)*
Liquid , Vitamin A 7000 i. u, vitamin D 800 i. u., vitamin E 1 i.u.
Pack - 150 ml.
Dose: By mouth, Adult, 10ml daily; child (1-6 months), 2.5 ml daily; 6-12 months, 5 ml daily; over 12 months, 5-10 ml daily.
Note: If infant is fed with dried milk, use half of the above prescribed doses.

OTC **TAVON®** *(Justeen)*
Capsules, Codliver oil BP 300 mg.
Pack - 10 x 10's
Capsules, Codliver oil BP 1000 mg.
Pack - 2 x 15's

OTC **TENDERWELL'S COD LIVER OIL®** *(Diamond Remedies)*
Capsules, Cod liver oil 300 mg, 1000 mg; green/yellow coloured caps.
Pack - 2 x 15.

OTC **VITAL'S COD LIVER OIL®** *(Strides Vital)*
Capsules, Cod liver oil 300 mg, 1000 mg; oval shaped natural coloured soft gelatin cap. containing clear yellow oily liquid.
300 mg -10 x 10's
1000 mg - 2 x 15's.

With Vitamin B Complex
OTC **CLO+BKO®** *(Strides Vital)*
Capsule, Cod liver oil, Vitamin B complex.
Pack - 3 x 10's

CYANOCOBALAMIN

See Cyanocobalamin in Section 6.1.

POM **Vitamin B_{12}** *(EDL 27.1)*
Tablet, Cyanocobalamin 0.05 mg
Injection, Hydroxocobalamin 0.25 mg, 1 mg per ml.

ERGOCALCIFEROL

Ergocalciferol is a representative vitamin D compound. Various vitamin D compounds can serve as alternatives.
Synonym: Vitamin D_2
Indications: Prevention of vitamin D deficiency; vitamin D deficiency cased by malabsorption or chronic liver disease; hypocalcaemia of hypoparathyroidism.
Contra-indications: Hypercalcaemia; metastatic calcification.
Precautions: Ensure correct dose in infants; monitor plasma calcium at weekly

intervals in patients receiving high doses or those with renal impairment; nausea and vomiting—may indicate overdose and hypercalcaemia; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Symptoms of overdosage include anorexia, lassitude, nausea and vomiting, diarrhoea, weight loss, polyuria, sweating, headache, thirst, vertigo, and raised concentrations of calcium and phosphate in plasma and urine; tissue calcification may occur if dose of 1.25 mg continued for several months.

Nursing considerations: •Teach patient early symptoms of hypercalcaemia and to report them namely weakness, fatigue, somnolence, headache, anorexia, dry mouth, metallic taste, nausea, vomiting, cramps, diarrhoea, muscle pain, bone pain, and irritability.

•Advise patient on the dietary sources of vitamin D viz egg yolk, diary products, cod, sardines and salmon.

•Instruct patient to avoid magnesium supplements or magnesium-containing antacids.

Dose: *Prevention of vitamin D deficiency*, by mouth, ADULT and CHILD 10 micrograms (400 units) daily.
Treatment of vitamin D deficiency, by mouth, ADULT 1.25 mg (50 000 units) daily for a limited period; CHILD 75–125 micrograms (3000–5000 units) daily.
Hypocalcaemia associated with hypoparathyroidism, by mouth, ADULT 2.5 mg (100 000 units) daily; CHILD up to 1.5 mg (60 000 units) daily.

POM **Ergocalciferol** *(WMF 27.1)*
Tablets, Ergocalciferol 1.25 mg (50 000 units).
Capsules, Ergocalciferol 1.25 mg (50 000 units).
Oral solution, Ergocalciferol 250 micrograms/ml (10 000 units/ml).

NOTE: IF THERE IS NO PLAIN VITAMIN D TABLET AVAILABLE FOR THE TREATMENT OF SIMPLE DEFICIENCY, CALCIUM AND ERGOCALCIFEROL TABLETS MAY BE USED BUT THE CALCIUM IS UNNECESSARY.

Tablets, Ergocalciferol 10 micrograms (400 units), calcium lactate 300 mg, calcium phosphate 150 mg.

POM **Vitamin D** *(EDL 27.1)*
Tablet or Capsules, Ergocalciferol 0.25 mg (10,000 units), 1.25 mg (50,000 units).
Oral Solution, Ergocalciferol 0.25 mg per ml.

NICOTINAMIDE

Nicotinamide is a representative vitamin B substance. Various compounds can serve as alternatives.

Indications: Treatment of pellagra.

Dose: *Treatment of pellagra*, by mouth, ADULT up to 500 mg daily in divided doses.

OTC **Nicotinamide** *(WMF 27.1)*
Tablets, Nicotinamide 50 mg.

PHYTOMENADIONE

Synonym: Vitamin K_1

Therapeutic category: Fat Soluble Vitamin.

Indications: Prevention and treatment of haemorrhage or threatened haemorrhage as a result of severe hypoprothrombinaemia due, for instance, to overdosage of anticoagulants; haemorrhage in the newborn.

Contra-indications: Avoid in patients with pronounced diathesis; hypersensitivity to the drug; neonates and infants, late pregnancy.

Precautions: Restrict I.V. administration for emergency use only, and it should be given very slowly; G6PD deficiency and vitamin E deficiency (risk of haemolysis).

Interactions:
•Decreased effect of warfarin sodium, dicumarol.

Adverse effects: Rarely severe shock-like reactions; sweating, dyspnoea, pain, tenderness at injection site.

Dose: *In severe, life-threatening haemorrhage during anticoagulant therapy*, by slow i.v. injection, 10 mg; increased up to 20 mg as required.
Haemorrhage or threatened haemorrhage in newborn or premature infants, Prevention, 1 mg i.m. immediately post-partum; Treatment, 1 mg/kg i.m. daily for 1-3 days.

Note: The dosage in neonates should not exceed 5 mg during the first few days of life because of the immaturity of the hepatic enzyme system.

POM **Phytomenadione** *(EDL 4.2)*
Injection, Phytomenadione 10 mg per ml; in 1 ml amp.

POM **KONAKION®** *(Swipha)*
Injection, Phytomenadione 10 mg per ml; in 1 ml amp.
Pack - 25.

PYRIDOXINE

Synonym: Vitamin B_6

Indications: Treatment of pyridoxine deficiency due to metabolic disorders; isoniazid neuropathy; sideroblastic anaemia

Precautions: **interactions**: Appendix 1.

Adverse effects: Generally well tolerated, but chronic administration of high doses may cause peripheral neuropathies.

Advice to patients: Dietary sources of pyridoxine include red meats, bananas, potatoes, yeast, lima beans, whole grain cereal; do not exceed recommended doses.

Nursing considerations: •Stress importance of compliance and good nutrition if prescribed for maintenance therapy to prevent reoccurence of deficiency.
•Explain that Pyridoxine when used in combination therapy with isoniazid has a specific therapeutic purpose and is not *"just a vitamin"*, and therefore the need for adhering to therapeutic regimen.
•Advise patient to avoid vitamin supplements, unless directed by the doctor.
•Teach patient dietary sources of vitamin B_6.

Dose: *Deficiency states*, by mouth, ADULT 25–50 mg up to 3 times daily.
Isoniazid neuropathy, prophylaxis, by mouth, ADULT 10 mg daily.
Isoniazid neuropathy, treatment, by mouth, ADULT 50 mg 3 times daily.
Sideroblastic anaemia, by mouth, ADULT 100–400 mg daily in divided doses.

POM **Pyridoxine** *(WMF 27.1)*
Tablets, Pyridoxine HCl 25 mg.

POM **Vitamin B_6** *(EDL 27.1)*
Tablets, Pyridoxine HCl 10 mg, 20 mg, 50 mg.

RETINOL

Synonym: Vitamin A

Indications: Prevention and treatment of vitamin A deficiency; prevention of complications of measles.

Precautions: Pregnancy (teratogenic; see notes above and Appendix 2); breastfeeding (Appendix 3).

Adverse effects: No serious or irreversible adverse effects in recommended doses; high intake may cause birth defects; transient increased intracranial pressure in adults or a tense and bulging fontanelle in infants (with high dosage); massive overdose can cause rough skin, dry hair, enlarged liver, raised erythrocyte sedimentation rate, raised serum calcium and raised serum alkaline phosphatase concentrations.

Advice to patients: Avoid use of mineral oil when taking drug; take with food for better absorption; notify physician of nausea, vomiting, anorexia, malaise, drying or cracking of skin or lips, irritability, headache, or loss of hair.

Nursing considerations: •Do not give by I.V. push; patients receiving more than 25,000 units per day should be closely monitored for toxicity.
•Teach patient nutritional sources of vitamin A viz yellow and deep green leafy vegetables, liver and egg yolk.

Dose: *Prevention of vitamin A deficiency* (universal or targeted distribution programmes), by mouth, INFANT under 6 months, 50 000 units, 6–12 months, 100 000 units every 4–6 months, preferably at measles vaccination; CHILD over 1 year (preschool), 200 000 units every 4–6 months; ADULT , 200 000 units every 6 months; ADULT pregnant woman, maximum of 10 000 units daily or maximum 25 000 units weekly; ADULT mothers, 200 000 units at delivery or within 6 weeks.
Treatment of xerophthalmia, by mouth, INFANT under 6 months, 50 000 units on diagnosis, repeated next day and then after 2 weeks; 6–12 months, 100 000 units immediately on diagnosis, repeated next day and then after 2 weeks; CHILD over 1 year and ADULT (except woman of child-bearing age) 200 000 units on diagnosis, repeated next day and then after 2 weeks; ADULT (woman of child-bearing age, see notes above), severe signs of xerophthalmia, as for other adults; less severe cases (for example, night blindness), 5000–10 000 units daily for at least 4 weeks or up to 25 000 units weekly.

NOTE: ORAL VITAMIN A PREPARATIONS ARE PREFERRED FOR THE PREVENTION AND TREATMENT OF VITAMIN A DEFICIENCY. HOWEVER, IN SITUATIONS WHERE PATIENTS HAVE SEVERE ANOREXIA OR VOMITING OR ARE SUFFERING FROM MALABSORPTION, A WATER-MISCIBLE INJECTION PREPARATION MAY BE ADMINISTERED INTRAMUSCULARLY.

POM **Retinol** *(WMF 27.1)*
Sugar-coated tablets (Coated tablets), Retinol (as palmitate) 10 000 units.
Capsules, Retinol (as palmitate) 200 000 units.

RETURN

Oral solution (oily), Retinol (as palmitate) 100 000 units/ml.
Water-miscible injection (Solution for injection), Retinol (as palmitate) 50 000 units/ml, 2-ml ampoule.

POM **Vitamin A** *(EDL 27.1)*
Tablets or Capsules, Vitamin A 1.5 mg, 7.5 mg, 15 mg (or 5000, 25,000, or 50,000 i.u. resp.)

POM **AROVIT®** *(Swipha)*
Tablet (Chewable), Synthetic Vitamin A 50,000 i.u.; orange coated tab.

RIBOFLAVIN

Synonym: Vitamin B_2
Indications: Vitamin B_2 deficiency.
Advice to patients: Take with food (absorption is enhanced by food); large doses may cause bright yellow or orange urine; dietary sources of riboflavine include liver, kidney, dairy products, green vegetables, eggs, whole grain cereals, yeast, mushroom.
Nursing considerations: •Give with food for better absorption.
•Advise patient to avoid alcohol.
•Inform patient about dietary sources of vitamin B_2; that urine may turn bright yellow.
Dose: *Treatment of vitamin B_2 deficiency*, by mouth, ADULT and child up to 30 mg daily in divided doses.
Prophylaxis of vitamin B_2 deficiency, by mouth, ADULT and child 1–2 mg daily.

POM **Riboflavin** *(WMF 27.1)*
Tablets, Riboflavin 5 mg.

POM **Vitamin B_2** *(EDL 27.1)*
Tablet, Riboflavine 5 mg

POM **Riboflavine** *(Adler)*
Tablet, Riboflavine 5 mg
5 mg - 50.

POM **RIBOSAM®** *(Sam)*
Tablet, Riboflavin 5 mg
5 mg - 1000.

POM **Vitamin B_2** *(Novel)*
Tablet, Riboflavin 3 mg.
3 mg - 1000.

THIAMINE

Synonym: Vitamin B_1
Indications: Prevention and treatment of vitamin B_1 deficiency.
Precautions: Parenteral administration (see notes above); breastfeeding (Appendix 3).
Advice to patients: Dietary sources include legumes, pork, beef, whole grains, yeast, fresh vegetables.
Nursing considerations: •Rotate sites of I.M. injection if pain occurs; application of cold may decrease pain.
•I.V. injection should be given slowly (over 10 minutes); have adrenaline ready for anaphylaxis.
•Parenteral route shoud be used only when patient can't take by mouth.
•Thiamine malabsorption may occur in alcoholism, cirrhosis, or GI disease.
Dose: *Mild chronic thiamine deficiency*, by mouth, ADULT 10–25 mg daily.

POM **Thiamine** *(WMF 27.1)*
Tablets, Thiamine HCl 50 mg.

POM **Vitamin B_1** *(EDL 27.1)*
Tablets, Thiamine HCl 25 mg, 50 mg.
Injection, Thiamine HCl 25 mg per ml; in 1-ml amp.

VITAMIN A plus VITAMIN E

Indications: Vitamin deficiency states (e.g. in malnutrition and malabsorption syndromes; more frequently in old age); lesions of the skin and mucous membranes susceptible to infection; night blindness, xerophthalmia; deafness due to disorders of the inner ear or due to old age, tinnitus; male sterility.
Precautions: Pregnancy; hypervitaminosis A; never exceed recommeded dosage; vitamin A deficiency due to impaired lipid absorption should be treated with parenteral vitamin A.
Adverse effects: Usually hypervitaminosis due to overdosage.
Nursing considerations: See under Vitamin A and Vitamin E.
Dose: Adult and child over 12 years, 1 chewable tab. daily; treatment should be evaluated after 4 weeks.

POM **ROVIGON®** *(Swipha)*
Tablet (chewable), vitamin A 9,000 mcg (30,000 i.u.), vitamin E 70 mg, carbohydrate 836 mg (14.3KJ).

Vitamin B_{12} plus Vitamin B_6 plus Vitamin B_1

Indications: Vitamin B_6 deficiency symptoms, adjuvant in neuralgias and neuritis, sciatica, lumbago. Chronic intoxications, especially alcoholism. As adjuvant in radiation injuries.
Interaction: Increased pyridoxine will

decrease levodopa effect.
Dose: By mouth, 1-2 tabs to be taken with liquid every day.
By I.M. injection, 1amp. daily.

POM **ANCOPIR®** *(Supreme)*
Tablet, Vitamin B_{12} 0.3 mg, vitamin B_6 100 mg, vitamin B_1 200 mg; s-c tab.
Pack - 20; 10 x 100.
Injection, Vitamin B_{12} 1.0 mg, vitamin B_6 50 mg, vitamin B_1 200 mg, lidocaine HCl 10 mg.
Pack - 5; 5 x 20.

POM **NEUROBION®** *(Biofem)*
Tablet, Thiamine disulfide 100 mg, Pyridoxine HCl 200 mg, Cyanocobalamin 200 ug; white, shiny, round coated tabs, steeply convexed on both sides.
Pack: 20's (in blister).
Injection, Thiamine HCl 100 mg, Pyridoxine HCl 100 mg, Cyanocobalamin 1000 µg; in ampoules.
Pack: 3's.

VITAMIN B COMPLEX

Indications: General deficiency states of the B-Vitamins; supplementation of diet; adjuct to treatment withbroad spectrum antibiotics.
Dose: 1-2 tabs daily or 5-10 ml syrup daily.
Infants and Young Children: 2.5 ml daily.
Older Children (School age): 2.5-5 ml daily

OTC **Vitamin B Complex** *(EDL 27.1)*
Tablet or Syrup, Nicotinamide 20 mg, thiamine HCl 5 mg, riboflavin 2 mg, pyridoxine HCl 2 mg per tab. or 5 ml syrup.

OTC **AFRABLEX®** *(Afrab-Chem)*
Tablet or Syrup, Vitamin B Complex (EDL).

OTC **B-PLAN®** *(Food & Pharma)*
Syrup, Vitamin B_1 5 mg, vitamin B_2 2 mg, nicotinamide 20 mg, vitamin B_6 2 mg per 5 ml.
Pack - 100 ml; 200 ml.
Dose: Adult, 5 ml twice daily
Child, 5 ml once daily.

OTC **BECOMBEE®** *(Ranbaxy)*
Syrup, Vitamin B Complex (EDL).
Pack - 180 ml.

OTC **BECOMBION®** *(Farmex-Meyer)*
Capsule, Vitamin B_1 3 mg, Vitamin B_2 1 mg, Vitamin B_6 1 mg, Vitamin B_{12} 2 mcg, calcium pantothenate 1 mg, folic acid 100 mg, nicotinamide 10 mg.
Pack - 30.
Dose: One capsule twice daily
Syrup, Vitamin B_1 5 mg, vitamin B_2 2 mg, vitamin B_6 2 mg, nicotinamide 30 mg per 5 ml.
Pack - 150 ml; 300 ml.

OTC **BECOTONE®** *(Rajrab)*
Tablet, Vitamin B Complex (EDL); yellow scored tab.
Pack - 100; 1000.
Syrup, Vitamin B Complex (EDL).
Pack - 2 L.

OTC **BECOZYM®** *(Swipha)*
Syrup, Vitamin B Complex (EDL); yellow syrup.

OTC **BEVITEX®** *(Dizpharm)*
Tablet, Vitamin B Complex (EDL)
Pack - 50; 1000.

OTC **BIOVIT®** *(Daily Need)*
Syrup, Vitamin B Complex.
Pack - 180 ml.

POM **COXON-B®** *(Beta Drugs)*
Injection, Vitamin B_1 (Thiamine HCl) 20 mg, vitamin B_2 (Riboflavin sodium phosphate) 2.74 mg, vitamin B_6 (Pyridoxin HCl) 2 mg, Nicotinamide 30 mg, Sodium pantothcyanate 1 mg per 2-ml ampoule.
Pack – 2-ml x 10's; 2-ml x 100's.

OTC **EM-B-PLEX®** *(Emzor)*
Tablet, Vitamin B Complex.
Pack - 1000
Syrup, Vitamin B Complex.
Pack - 100 ml; 2 L.

OTC **NABCO®** *(NASDMU)*
Tablet, Vitamin B_1 1.0 mg, vitamin B_2 1.0 mg, vitamin B_6 0.5 mg, nicotinamide 15.0 mg; yellow deep concave tab. marked 'NABCO' on one side and 'NASDMU' on the reverse.
Pack - 100; 1000.

OTC **THERAPLEX®** *(Therapeutic)*
Syrup, Vitamin B_1 3mg, vitamin B_2 1 mg, nicotinamide 10 mg, vitamin in B_6 1 mg, in flavoured base.

OTC **Vitamin B Complex** *(BCN)*
Syrup, Vitamin B_1 5 mg, Vitamin B_2 2 mg, Vitamin B_6 2 mg, nicotinamide 20 mg per 5 ml.
Pack - 4000 ml.

OTC **Vitamin B Complex** *(Emzor)*
Tablet, Vitamin B Complex (EDL); orange-

yellow tab marked 'EMZOR'.
Pack - 100; 1000
Syrup, Vitamin B Complex (EDL); yellow orange flavoured syrup.
Pack - 100 ml; 2 L.

OTC **Vitamin B Complex** *(Evans)*
Tablet, Vitamin B_1 5 mg, B_2 2 mg, B_6 2 mg, nicotinamide 20 mg; mottled yellow biconvex tab. with a triangular mark on one side.
Pack - 1000.
Dose: Adult, one tablet 3 times daily.
Child, one tablet 1-2 times daily.

OTC **Vitamin B Complex** *(Jawa)*
Syrup, Vitamin B_1 5 mg, Vitamin B_2 2 mg, Vitamin B_6 2 mg, Nicotinamide 20 mg per 5 ml.
Pack – 100 ml x 20's.

OTC **Vitamin B Complex** *(Juhel)*
Tablet, Vitamin B Complex.
Pack - 1000
Syrup, Vitamin B_1 5 mg, Vitamin B_2 2 mg, Nicotinamide 20 mg, Pyridoxine 2 mg per 5 ml.
Pack – 100 ml in amber bottle.

OTC **Vitamin B Complex** *(Leady)*
Syrup, Vitamin B Complex; clear orange-red syrup.
Pack - 100 ml; 2 L.

OTC **Vitamin B Complex** *(Mopson)*
Tablet, Vitamin B_1 1.0 mg, vitamin B_2 1.0 mg, nicotinamide 15 mg.
Pack - 1000.
Syrup, Vitamin B_1 5 mg, vitamin B_2 2.0 mg, vitamin B_6 2.0 mg, nicotinamide 20 mg.
Pack - 100 ml, 2 L.

OTC **Vitamin B Complex** *(Novel)*
Tablet, Vitamin B complex (EDL); orange yellow tab. marked 'NOVEL'.
Pack - 1000.

OTC **Vitamin B Complex** *(Ulticare-Lyka)*
Tablet, Vitamin B_1 1 mg, Vitamin B_2 1 mg, nicotinamide 15 mg; orange-yellow tab. marked 'B.Co.'
Pack - 100; 1000.

OTC **Vitamin B Complex** *(Vitabiotics)*
Tablet, Vitamin B_1 5 mg, vitamin B_2 2 mg, vitamin B_6 2 mg, nicotinamide 20 mg.
Pack - 100's.
Syrup, Vitamin B_1 5 mg, vitamin B_2 2 mg, vitamin B_6 2 mg, nicotinamide 20 mg.
100 ml.

VITAMIN E

Synonym: Tocopherols
Therapeutic category: Fat Soluble Vitamin; Topical Vitamin.
Indications: Vitamin E deficiency resulting from impaired absorption, increased requirements due to diet rich in polyunsaturated fats; supplement to parenteral feeding; haemolytic anaemia due to Vitamin E deficieny.
Interactions: •Decreased absorption with mineral oil.
•Delayed absorption of iron.
•Increased effect of oral anticoagulants.
Adverse effects: Rarely nausea, diarrhoea, intestinal cramps.
Nursing considerations: •Advise patient to swallow capsule whole, not crushed or chewed.
•Teach patient symptoms of Vitamin E toxicity which include blurred vision, diarrhoea, dizziness, flu-like symptoms, nausea, headache.
•Teach patient the dietary sources of Vitamin E viz dark green leafy vegetable, nuts, eggs, liver, palm oil, vegetable oils, diary products.
Dose: By mouth, Adult, *Prophylaxis*, 100-300 mg daily.
Treatment, 300-600 mg daily.

OTC **Vitamin E** *(EDL 27.1)*
Tablets or Capsules, Alpha-tocopheryl acetate 10, 30, 50, 100 units (or 10, 30, 50 or 100 mg).

OTC **EPHYNAL®** *(Swipha)*
Tablet (Chewable), DL alpha-tocopherol acetate 100 mg; cream coloured tab.
100 mg - 100.

OTC **EVITOL®** *(Dizpharm)*
Tablet, dl-alpha tocopherol acetate 25 mg (25 I.U.).
25 mg - 25

OTC **NEWVIT-E®** *(Pharmabox)*
Capsule, Vitamin E USP 1000 I.U. (as dl-a-tocopheryl acetate 1000 I.U.); pale yellow, transparent soft capsules.
Pack - 50's.
Dose: By mouth, 100-1000 I.U. per day.

OTC **NUTRIHEALTH VITAMIN E®** *(Hovid)*
Capsules, d-alpha tocopherol 200 i.u.
200 i.u. - 50.

YEAST BPC

Indications: Treatment and prevention of Vitamin B deficiency states.
Dose: Adults and Children over 12 years, 2-4

tabets daily.
Children (5-12 years), 1-2 tablets daily.
Children (under 5), up to 1 tablet daily.

OTC **Yeast BPC** *(EDL 27.1)*
Tablet, Yeast 300 mg.

Some proprietary multivitamin and mineral preparations

OTC **ABIDEC®** *(NGC)*
Drops, Vitamin A palmitate 4000 units (4 mg), ergocalciferol 400 units (0.01 mg), vitamin B_1 1.00 mg, vitamin B_2 0.5467 mg, vitamin B_6 0.50 mg, nicotinamide 5.00 mg, vitamin C 50 mg per 0.6 ml; clear yellow liquid.
Pack - 25 ml (with dropper).
Dose: Infants (under 1 year), 0.3 ml once daily; Older children, 0.6 ml once daily.

OTC **AFRABVITE®** *(Afrab-Chem)*
Capsule, Vitamin A 5000 i.u., Vitamin D_2 500 i.u., vitamin B_1 3000mcg, vitamin B_2 2000mcg, vitamin B_6 10mg, vitamin B_{12} 2mcg, nicotinamide 20mg, calcium pantothenate 1mg, folic acid 5mg, vitamin C 25mg.
Pack - 30; 500.
Dose: Adult, one capsule daily.
Child (above 6 years), one capsule every other day.
Syrup, Vitamin A 5000 i.u., vitamin B_1 2.5mg, vitamin B_2 1mg, vitamin B_6 1mg, vitamin C 50mg, vitamin D2 1000 i.u., nicotinamide 10mg per 5ml.
Pack - 100 ml.
Dose: Child (below 12 years), 5-10ml daily
Adult and child (above 12 years), 10-15 ml daily.
Drop, Vitamin A 4000 i.u., vitamin B_1 1mg, vitamin B_2 0.4mg, vitamin B_6 0.5mg, vitamin C 25mg, vitamin D_2 400i.u., nicotinamide 5mg per 0.6ml.
Pack - 15 ml.
Dose: Child (under 1 year), 0.3ml (5 drops) daily.
Child (over 1 year), 0.6ml (10 drops) daily.

OTC **APPETONE®** *(Justeen)*
Capsules, Multivitamin, iron & minerals
Pack - 2 x 15's; 21's

OTC **ARCOGIN®** *(Strides Vital)*
Capsule, Multivitamin, Mineral, Ginseng.
Pack - 3 x 10's

OTC **BEGROCIT®** *(Supreme)*
Tablet (effervescent), Vitamin B_1 15mg, vitamin B_2 15mg, vitamin B_6 10mg, nicotinamide 50mg, biotin 0.15mg, vitamin B_{12} 10mcg, vitamin C 1g, calcium pantothenate 25mg, calcium carbonate 156mg, calcium glycerophosphate 327mg.
Pack - 10.
Dose: One effervescent tab. up to3 times daily; to be dissolved in a glass of water.

POM **BETALIFE®** *(Diamond Remedies)*
Capsule, Ginseng extract powder 3000 mcg, Vitamin A (as Palmitate) 2000 I.U., Vitamin B_1 1 mg, Vitamin B_2 1 mg, Vitamin B_6 1.34 mg, Vitamin B_{12} 1 mcg, Vitamin D_3 200 I.U., Vitamin E 5 mg, Calcium Pantothenate 1 mg, Nicotinamide 15 mg, Folic acid 50 mcg, Calcium 75 mg, Phosphorus 58 mg, Iron 5 mg, Copper 0.01 mg, Iodine 0.0015 mg, Magnesium 1 mg, Potassium 1 mg, Zinc 0.15 mg, Molybdenum 0.1 mg.
Pack - 2 x 15.
Dose: One capsule daily.

OTC **CENTRUM®** *(Matbeny)*
Tablet, 30 Vitamins and minerals
Pack - 30; 100.
Dose: One tab. daily.

OTC **CHEMVIT®** *(Chemiron)*
Tablet and Syrup, Multivitamins.

OTC **DANZA®** *(Strides Vital)*
Caplet, Multivitamin and minerals; brown capsule shaped tab.
Pack - 3 x 10's.

POM **DAY-BY-DAY®** *(Greenlife)*
Tablet, Vitamin A (as Acetate) 2500 I.U., Vitamin D_3 200 I.U., Vitamin B_1 1 mg, Vitamin B_2 1 mg, Vitamin B_6 0.5 mg, Niacinamide 15 mg.
Pack - 2 x 15.
Capsule, Vitamin A (as Palmitate) 2500 I.U., Vitamin B_1 1.0 mg, Vitamin B_2 1.0 mg, Vitamin B_6 1.34 mg, Vitamin B_{12} 1 mcg, Vitamin D_3 200 I.U., Vitamin E 5 mg, Calcium Pantothenate 1.0 mg, Folic Acid 50 mcg, Nicotinamide 15 mg, Calcium 190 mg, Phosphorus 150 mg, Iron 5 mg, Copper 0.01 mg, Iodine 0.0015 mg, Magnesium 1 mg, Manganese 0.01 mg, Molybdenum 0.1 mg, Potassium 1 mg, Zinc 0.15 mg.
Pack - 2 x 15.
Dose: One capsule per day, to be taken at the main meal.

OTC **DECAVIT–Plus®** *(GSK)*
Capsule, Vitamin A (palmitate) 2000 I.U., vitamin D_3 200 I.U., DL-alpha tocopherol acetate

RETURN

10 mg, vitamin B_1 15 mg, vitamin B_2 3 mg, vitamin B_6 2 mg, vitamin B_{12} 5 mcg, biotin 3 mcg, calcium D-pantothenate 3 mg, ascorbic acid 50 mg, folic acid 25 mcg, nicotinamide 15 mg, para amino benzoic acid 50 mg, L-lycine HCl 20 mg, rutin 10 mg, Iron 10 mg, potassium 2 mg, copper 1 mg, zinc 1 mg, manganese 1 mg, calcium 50 mg, pollen extract 16.6 mg.
Pack - 28.
Dose: One capsule daily.

OTC **EMVITE®** *(Emzor)*
Tablet, Multivitamin, light brown s-c tab.
Pack - 100, 1000.
Syrup, Multivitamin.
Pack - 100 ml; 2 L
Drops, Multivitamin.
Pack - 15 ml.

OTC **EMZORON®** *(Emzor)*
Capsule, Iron + Multivitamin + Minerals.
Pack - 30; 120.

POM **ESSENTIAL FORTE®** *(May & Baker)*
Capsule, Essential phospholids (EPL) substance 300 mg, vitamin B_1 6 mg, vitamin B_2 6 mg, vitamin B_6 6 mg, vitamin B12, nicotinamide 30 mg, vitamin E-acetate 6 mg.
Pack - 30; 50; 850.
Dose: 2 capsules 3 times daily.

OTC **EVE 500®** *(Strides Vital)*
Capsule, Evening primrose oil 500 mg.
Pack – 3 x 10's.

OTC **FERRON-350®** *(Justeen)*
Capsules, Multivitamin and minerals
Pack - 2 x 15's

OTC **FIDVITE®** *(Fidson)*
Capsule, Vitamin A 2000 i.u., vitamin B_1 1 mg, vitamin B_2 1 mg, vitamin B_6 1.34 mg, nicotinamide 15 mg, calcium pantothenate 1 mg, vitamin B_{12} 1 mcg, vitamin C 33.3 mg, vitamin D_3 200 i.u., Calcium 190 mg, phosphorous 150 mg, iron 5 mg, copper 0.01 mg, iodine 0.0015 mg, magnesium 1 mg, manganese 0.01 mg, potassium 1 mg, zinc 0.15 mg.
Pack - 30.

OTC **GEVRAL®** *(Matbeny)*
Powder, Concentrated protein 50%, carbohydrate 6 g, calories 57%, sodium <1.2%, plus 23 vitamins and minerals per satchet; powder for oral mixture.
Pack - 14 satchets.
Dose: 1-2 satchets every 24 hours.
Note: Empty one satchet into a glass, add 115 ml of water, milk or other liquid, stir and drink.

OTC **HEALTHILIFE STYLE 4/40 Plus®** *(Biofem)*
Capsule, Essential vitamins and herbs for the over 40's.
Pack - 30's (in blister).

OTC **HEALTHILIFE STYLE SUPER DYNAVITES®** *(Biofem)*
Capsule, Vitamins and minerals.
Pack - 30's (in blister).

OTC **HEALTHILIFE STYLE MEGA DYNAVITES®** *(Biofem)*
Capsule, Vitamins, minerals and herbs.
Pack - 30's (in blister).

OTC **HEMDYN®** *(Justeen)*
Capsules, Multivitamin and minerals
Pack - 2 x 15's
Tablet, Multivitamin and minerals
Pack - 2 x 10's

OTC **HEMCAP®** *(Justeen)*
Capsules, Multivitamin and minerals
Pack - 2 x 15's

OTC **J-VITE®** *(Juhel)*
Syrup, Vitamin A (as Palmitate), Vitamin B_1 1000 IU, Vitamin B_2 1500 mcg, Vitamin B_{12} 2500 ng, Vitamin C 40000 mcg
Vitamin D_2 200 IU, Nicotinamide 10000 mcg per 5 ml.
Pack – 100 ml in amber bottle.

OTC **JEXTRA-C®** *(Juhel)*
Tablet, Ascorbic acid 200 mg, Riboflavine 1 mg, Thiamine HCl 1 mg, Folic acid 5 mg.
Pack - 500.
Dose: 1-2 tabs. daily.

OTC **JUNIVITE®** *(BCN)*
Syrup, Vitamin A 2500 units, vitamin B_1 0.5mg, vitamin B_2 0.6mg, vitamin C 15mg, vitamin D 250 units, nicotinamide 5mg per 5ml; orange flavoured syrup.
Pack - 100ml.
Dose: Child (6 months - 2 years), 2.5 ml; 2- 5 years, 5 ml; over 5 years, 10 ml.
To be taken twice daily with meals; may be diluted with water.

OTC **MARINA 1000®** *(Strides Vital)*
Capsule, Fish lipid oil 1000 mg.
Pack – 2 x 15's.

OTC **MATERNA®** *(Matbeny/Lederle)*
Tablet, 21 Vitamins and minerals.
Pack - 100
Dose: One tab. daily.

OTC **MEGAVIT®** *(Afrab-Chem)*
Tablet and Oral Drops,

OTC **MIM®** *(Adler)*
Capsule, Multivitamin and minerals.
Pack - 30:
Dose: One capsule daily
Syrup, Multivitamin and minerals
Pack - 300 ml.
Dose: Adult, 5-10 ml twice a day
Child (2-6 years) 2.5-5 ml twice a day
Pregnancy, 10-15 ml 2-3 times a day.

OTC **MULTIVITE®** *(Evans)*
Tablet, Vitamins A (2,500 i.u.), B1 (2,500 mcg), B_2 (2,500 mcg), B_6 (250 mcg), B_{12} (2,500 ng), C (30 mg), D (250 i.u.) and nicotinamide 10 mg; dark brown s-c tab. with pleasant flavour.
Pack - 50; 1000.
Dose: Adult, 2 tablets daily with meals;
Child (5-12 years), 1 tablet daily with meals; to be chewed or swallowed whole.
Syrup, Vitamins A (1,000 i.u.), B_1 (1,500 mcg), B_2 (1,500 mcg), B_{12} (2,500 ng), C (40,000 mcg), D (200 i.u.) and nicotinamide (10,000 mcg) per 5 ml; thick, golden yellow, pleasant tasting syrup.
Pack - 100 ml.
Dose: Child (2-12 years), 10ml daily.
Drop, Vitamins A (1,500 i.u.), B_1 (500 mcg), B_2 (500 mcg), B_6 (500 mcg), C (25,000 mcg), D_2 (100 i.u.), D-panthenol (1000 mcg) and nicotinamide 2500 mcg; clear, bright, pleasant tasting liquid in tamper-proof amber bottle with glass dropper.
Dose: Infant (0 -6 months), 0.3 ml daily; 6 months - 2 years, 0.6 ml daily; to be administered undiluted or with milk or water.

OTC **NOVAVITE®** *(SKG)*
Syrup, Vitamin A 1000i.u., vitamin B_1 1.5 mg, vitamin B_2 1.5 mg, vitamin B_{12} 2.5 mcg, vitamin C 40 mg, vitamin D 200 i.u., nicotinamide 10 mg per 5 ml.
Pack - 100 ml; 200 ml; 1 L.
Dose: Child (2 years and above), 10 ml daily.

OTC **NULIFE®** *(Diamond Remedies)*
Tablet, Vitamin A (as Acetate) 2500 I.U., Vitamin B_1 1 mg, Vitamin B_2 1 mg, Vitamin B_6 0.5 mg, Vitamin C 25 mg, Vitamin D_3 200 I.U., Niacinamide 15 mg; s-c tab.
Pack - 3 x 10 (in blister).
Capsule, Multivitamin and minerals; red/black cap.
Pack - 2 x 15.
Tonic, Iron, vitamin B_{12}, folic acid.
Pack - 200 ml.

OTC **NUTRAVIT®** *(Hovid)*
Syrup, Lysine HCl 100 mg, vitamin A 4000 mg, vitamin B_1 2 mg, vitamin B_2 1.46 mg, vitamin B_6 2 mg, vitamin B_{12} 1.5 mcg, vitamin C 17.5 mg, vitamin D 400 mg, calcium pantothenate 3.25 mg, nicotinamide 10 mg per 5 ml; in orange flavoured base.
Pack - 100 ml.

OTC **NUTRIHEALTH BETATON®** *(Hovid)*
Capsule, Beta-Carotene 3 mg, vitamin D3 400 i.u., gamma linoleic acid 10%, vitamin B_1 20 mg, vitamin B_2 5 mg, vitamin B3 50 mg, vitamin B6 10 mg, D-Panthenol 10 mg, D-Biotin 0.25 mg, vitamin B_{12} 50 mcg, folic acid 1 mg, vitamin C 150 mg, vitamin E 10 i.u., inositol 25 mg, choline bitartrate 25 mg, calcium pantothenate 5 mg, calcium 46.51 mg, phosphorus 42.37 mg, iron 3.29 mg, manganese 0.5 mg, copper 0.99 mg, zinc 0.53 mg, molybdenum 0.1 mg, potassium 5 mg, lecithin 28 mg, magnesium 7.54 mg.
Pack - 30.

OTC **NUTRIVIN®** *(Fidson)*
Capsule, Vitamin A (as Palmitate) BP 2000 I.U., Vitamin D_3 BP 200 I.U., Vitamin B_1 BP 1.0 mg, Vitamin B_2 BP 1.0 mg, Vitamin B_6 BP 0.5 mg, Vitamin B_{12} BP 0.5 mcg, Vitamin E BP 5 I.U., Vitamin C BP 50.0 mg, Iron (elemental) BP 15.0 mg, Calcium Pantothenate BP 1.0 mg, Nicotinamide BP 15.0 mg, Calcium (Dibasic as Phosphate) BP 76.0 mg, Phosphorus (Dibasic as Phosphate) BP 58.0 mg, Copper (as Sulphate) BP 0.45 mg, Iodine (Potassium iodide) BP 0.075 mg, Magnesium (as Sulphate) BP 0.5 mg, Manganese(as Sulphate) BP 0.5 mg, Molybdenum (Sodium molybdate) BP 0.1 mg, Potassium (as Iodide) BP 2.0 mg, Zinc (as Sulphate) BP 0.5 mg.
Pack - 2 x 15 (in blisters).
Dose: Adults and children over 12 years, one capsule with liquid each day.
Syrup, Vitamin A (as Palmitate) 1000 I.U., Vitamin B_1 BP 1.5 mg, Vitamin B_2 BP 1.5 mg, Vitamin B_6 BP 1.0 mg, Vitamin B_{12} BP 2.5 mcg, Vitamin C BP 50.0 mg, Vitamin D_3 BP 200 I.U., Nicotinamide BP 10.0 mg per 5 ml.
Pack - 100 ml.
Dose: Child (2-12 years): 5-10 ml daily.

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OTC **OBRON-6®** *(Neimeth)*
Capsule, Iron (as sulphate) 18 mg, vitamin A 500 units, vitamin D_2 400 units, vitamin B_1 2 mg, vitamin B_2 2 mg, vitamin C 60 mg, vitamin B_6 2.5 mg, calcium pantothenate 10 mg, folic acid 0.8 mg, niacinamide 20 mg, manganese 4 mg, zinc 15 mg, fluoride 15 mg, calcium carbonate 200 mg.
Dose: One capsule to be taken once daily.

OTC **ORHEPTAL®** *(Farmex-Meyer)*
Capsule, Iron (as fumarate) 30 mg, copper 1 mg, zinc 15 mg, manganese 3 mg, calcium 90 mg, magnesium 45 mg, vitamin B_1 5 mg, vitamin B_{12} 1 mcg, folic acid 0.1 mg.
Pack - 30.
Dose: One capsule twice daily.
Syrup, Liver extract 23.4 mg, vitamin B_1 0.98 mg, Vitamin B_2 0.89 mg, niconamide 3.92 mg, Vitamin B_6 0.39 mg, dexpanthenol 0.51 mg, Vitamin B_{12} 0.6 mcg, ferric ammonium citrate 32.18 mg, quinine HCl 0.15 mg, trace elements per 5 ml; ethanol content 13.5%.
Pack - 165 ml; 300 ml; 1 L.
Dose: Adult, 15 ml 3 times daily.
Children and adolescents, 5 ml 3 times daily.

OTC **PHARMADEC®** *(Pharma-Deko)*
Syrup, Vitamins A (1000 i.u.), D_2 (200 i.u.), B_1 (1.5 mg), B_2 (1.5 mg), B_6 (1.0 mg), B_{12} (2.5 mcg), C (40 mg) and nicotinamide 10 mg per 5 ml.
Pack - 100 ml.
Dose: Adult, 15-30 ml daily;
Child (over 2 years), 10 ml daily.
Drops, Vitamins A (300 i.u.), D (400 i.u.), B_1 (1.0 mg), B_2 (0.40 mg), B_6 (0.50 mg), C (50 mg) and nicotinamide 0.50 mg per 0.60 ml.
Pack - 15 ml.
Dose: By mouth, child (under 1 year), 0.3 ml daily; over 1 year, 0.6 ml daily.

OTC **RENOVITE®** *(Justeen)*
Capsules, Multivitamin and minerals
Pack - 30's

OTC **SALVITE®** *(Strides Vital)*
Capsule, Multivitamin and minerals; oblong brown cap. marked 'SALVITE'.
Pack - 2 x 15's; 60's.

OTC **SANATOGEN®** *(Swipha)*
Tablets, (Chewable) Multivitamin; red, biconvex s-c tab.
Pack - 10; 30.
Dose: One tab. daily.
Junior Tablets, (Chewable) Multivitamins; bright yellow biconvex s-c tab with orange flavour.
Pack - 30.

OTC **STRESSTABS 600®** *(Matbeny)*
Tablet, Vitamin E 45 i.u., Vitamin C 600 mg, folic acid 400 mcg, vitamin B_1 20 mg, vitamin B_2 10 mg, niacinamide 100 mg, vitamin B_6 10 mg, vitamin B_{12} 25 mcg, calcium pantothenate 25 mg, copper 3 mg, zinc sulphate 23.9 mg; f-c tab.
Pack - 30; 60.
Dose: One tab. daily. Not recommended for children under 12 years.

OTC **SUPER MULTIVITAMIN®** *(P.Z.)*
Capsule, Vitamin A, D, C, B_1, B_2 and nicotinamide.
Dose: One capsule daily up to 21 days with water or milk.

OTC **SUPRADYN®** *(Swipha)*
Capsule, 12 vitamins, 8 minerals plus trace elements.
Pack - 30.
Dose: One capsule daily.

POM **SUPRAFIT®** *(Swipha)*
Tablet, Vitamin A (as Acetate) 10000.00 I.U., Cholecalciferol 1000.00 I.U., Thiamine Nitrate 10.00 mg, Riboflavin 10.00 mg, Pyridoxine HCl 3.00 mg, Cyanocobalamin 15.00 mcg, Nicotinamide 100.00 mg, Calcium Pantothenate 16.30 mg, Ascorbic Acid 150.00 mg, alpha-Tocopheryl Acetate 25.00 mg, Biotin 0.25 mg, Calcium Phosphate 129.00 mg, Magnesium Oxide light 60.00 mg, Dried Ferrous Sulphate 32.04 mg, Manganese Sulphate 2.03 mg, Total Phosphorus in the preparation 25.80 mg, Copper Sulphate pentahydrate 3.39 mg, Zinc Sulphate 2.20 mg, Sodium Molybdate dihydrate 0.25 mg, Borax 0.88 mg.
Pack - 30.
Dose: 1 tablet daily.

POM **SUPRA-KIDS®** *(Swipha)*
Tablet, Vitamin A 1000 I.U., Vitamin B_1 1.4 mg, Vitamin B_2 1.6 mg, Vitamin B_6 2.0 mg, Vitamin B_{12} 3 mcg, Vitamin C 60 mg, Vitamin D 100 I.U. Vitamin E 5 mg, Nicotinamide 9 mg, Calcium Pantothenate 4.6 mg, Taurine 100 mg, Aspartane 5 mg.
Pack - 30.
Dose: Child (3-6 years), 1 tablet per day; 7-12 years, 2 tablets per day.

OTC **THIOCAL®** *(Therapeutic)*
Syrup, L-Lysine 25 mg, liquid glucose 750 mg, vitamins B_1 2 mg, vitamin B_2 1 mg, vitamin B_6

2 mg, vitamin B_{12} 5 mcg, nicotinamide 15 mg, folic acid 200 mcg, ferric ammonium citrate 25 mg per 5 ml; in a pleasantly flavoured syrup base.
Pack - 100 ml; 200 ml; 750 ml.

OTC **TROPITONE®** *(Strides Vital)*
Tablet, Multivitamin.
Pack - 3 x 12's; 2 x 15's

OTC **ULTRATONE®** *(Strides Vital)*
Capsule, Multivitamin and minerals; oblong chocolate brown cap. marked 'ULTRATONE'.
Pack - 2 x 15's; 21's.

OTC **VICAPS®** *(Supreme)*
Capsule, Vitamin A 6000 I.U., vitamin D_2 600 I.U., vitamin E 0.1 mg, vitamin B_1 3 mg, vitamin B_2 3 mg, vitamin B_6 1 mg, vitamin$_{12}$ 3 mcg, nicotinamide 20 mg, calcium pantothenate 5 mg, ascorbic acid 75 mg, dibasic calcium phosphate 170 mg, iron (as sulphate) 50 mg, copper (as sulphate) 1 mg, magnesium (as sulphate) 1 mg, manganese (as sulphate) 1 mg.
Pack - 30.
Dose: Adult and child above 12 years, by mouth, 1 capsule daily; to be taken with a meal preferably breakfast and swallowed whole with sufficient liquid.

OTC **VIGOR®** *(Diamond Remedies)*
Capsule, Multivitamin and minerals with ginseng extract; chocolate brown cap.
Pack - 2 x 15.

OTC **VITAGRO®** *(Interpharma)*
Capsule, Vitamin A 5000 I.U., Vitamin D_3 (Cholecalciferol, stabilised) 400 I.U., Vitamin E (Tocopheryl acetate B.P.) 15 mg, Vitamin B_1 5 mg, Vitamin B_2 5 mg, Vitamin B_6 2 mg, Vitamin B_{12} 5 mcg, Nicotinamide 45 mg, D-Panthenol 5 mg, Folic acid 1 mg, Vitamin C 75 mg, Ferrous fumarate 50 mg, Dibasic calcium phosphate 70 mg, Cupric Sulphate 0.1 mg, Manganese sulphate 0.01 mg, Zinc sulphate Heptahydrate 50 mg, Potassium iodide 0.025 mg, Magnesium Oxide (light) 0.15 mg.
Pack - 10; 30.
Dose: One capsule daily.

OTC **VITAHEXT-D®** *(NGC)*
Tablets, Multivitamins.

OTC **VITALITE®** *(Leady)*
Syrup, Multivitamin.

OTC **VITAPHOS-M®** *(Therapeutic)*
Syrup, Vitamin A 1000 i.u., vitamin B_1 1 mg, vitamin B_2 0.5 mg, vitamin D_3 200 i.u., nicotinamide 7.5 mg per 5 ml; in a banana flavoured base.

OTC **VITAVITE®** *(Strides Vital)*
Capsule, Multivitamin, minerals and iron; oblong black cap. marked ' VITAVITE'.
Pack - 2 x 15's.

POM **WINOFIT®** *(Zoomota)*
Capsule, Vitamin E 200 mg, Vitamin C 100 mg, Eicosapentaenoic acid 90 mg, Docosahexanoic acid 60 mg, Zinc sulfate 7.5 mg, Folic acid 2.5 mg, Manganese (as Sulfate) 2 mg, Vitamin B_6 1 mg, Copper (as Sulfate) 1 mg, Vitamin A 2500 IU (as betacarotene 30% dispersion), Chromium (as Picolinate) 100 mcg, Selenium (as Dioxide) 40 mcg; brown capsule.
Pack – 10's.
Indications: Fatigue, weakness, & ameliorating the effects of aging; Oxidative stress and tissue injury e.g. chronic diseases like arthritis, immunological disorders, nervous system disorders & cancer; Cardiovascular disease management as an adjuvant therapy; Supportive therapy in diabetes.
Dose: Adult, 1-2 capsules daily.

Multivitamin and amino acid preparations

POM **ASTYMIN®** *(Fidson)*
Capsule, L-leucine USP 18.3 mg, L-isoleucine USP 5.9 mg, L-lysine HCl 25.0 mg, L-phenylalanine USP 5.0 mg, L-threonine USP 4.2 mg, L-valine USP 6.7 mg, L-tryptophan USP 5.0 mg, DL-methionine USP 18.4 mg, 5-hydroxy Anthranilic Acid HCl 0.2 mg, Synthetic Retinol Concentrate (Powder Form) BP 2500 I.U., Colecalciferol BP 200 I.U., Thiamine Nitrate BP 5.0 mg, Riboflavin BP 3.0 mg, Nicotinamide BP 25.0 mg, Pyridoxine HCl BP 1.5 mg, Folic Acid BP 0.75 mg, Calcium Pantothenate BP 5.0 mg, Cyanocobalamin BP 2.5 mcg, Ascorbic Acid BP 40.0 mg, Alpha Tocopheryl Acetate BP 7.5 I.U.
Pack - Blister pack of 2 x 10 capsules with individual carton.
Indications: Deficiencies of or increased requirements of Amino Acids and vitamins in Malnutrition, Stress, Convalescence, Debility, Alcoholism, Following injury. As an adjunct to Antibiotics, Hypoglycemic drugs, Anti hypertensives, Anti TB drugs.
Dose: One capsule twice a day.

POM **ASTYMIN-SN®** *(Fidson)*
I.V. infusion, Each ml contains: L-Isoleucine

RETURN

USP 5.6 mg, L-Leucine USP 12.5 mg, L-Lysine HCl USP 11 mg, L-Methionine USP 3.5 mg, L-Phenylanine USP 9.35 mg, L-Threonine USP 6.5 mg, L-Tryptophan USP 1.3 mg, L-Valine USP 4.5 mg, L-Alanine USP 6.2 mg, L-Arginine HCl USP 9.55 mg, L-Aspartic acid BP 3.8 mg, L-Cysteine HCl USP 1.45 mg, L-Glutamic acid USP 6.5 mg, L-Histidine HCl H_2O AP 8.11 mg, L-Proline USP 3.3 mg, L-Serine USP 2.2 mg, L-Tyrosine USP 0.35 mg, Glycine USP 10.7 mg, Xylitol USP 50 mg, Water for injections BP q.s.

Pack – 200 ml (in USP type-1 bottle).

Indications: *Internal medicine* - Persistent pyrexial states, Severe malnutrition, Malignant diseases, Malabsorption in G.I. disorders. *Surgery* - Pre & Post operative conditions, Burns, Accidental trauma, Fracture of long bones.

Contraindications: Cardiac insufficiency, irreversible liver damage

Precautions: Signs of intolerance and increased renal losses resulting in amino acids disequilibrium are possible, if infusion rate is too high.

Dosage & Administration: *Adults*: 200-800 ml I.V./day

Children: 0.2-0.25 gm of Nitrogen/kg body weight

Drip Rate: 15-20 drops initially followed by 30-40 drops per minute.

6.8 Minerals

Calcium gluconate. Calcium supplements are usually only required where dietary calcium intake is deficient. This dietary requirement varies with age and is relatively greater in childhood, pregnancy and lactation due to an increased demand, and in old age, due to impaired absorption. In osteoporosis, a calcium intake which is double the recommended daily amount reduces the rate of bone loss. In hypocalcaemic tetany calcium gluconate must be given parenterally but plasma calcium must be monitored. Calcium gluconate is also used in cardiac resuscitation.

Iodine is among the body's essential trace elements. The recommended intake of iodine is 150 micrograms daily (200 micrograms daily in pregnant and breastfeeding women); in children the recommended intake of iodine is 50 micrograms daily for infants under 1 year, 90 micrograms daily for children aged 2–6 years, and 120 micrograms daily for children aged 7–12 years. Deficiency causes endemic goitre and results in endemic cretinism (characterized by deaf-mutism, intellectual deficit, spasticity and sometimes hypothyroidism), impaired mental function in children and adults and an increased incidence of still-births and perinatal and infant mortality. Iodine and iodides may suppress neonatal thyroid function and in general iodine compounds should be avoided in pregnancy. Where it is essential to prevent neonatal goitre and cretinism, iodine should not be witheld from pregnant women. Control of iodine deficiency largely depends upon salt iodization with potassium iodide or potassium iodate and through dietary diversification. In areas where iodine deficiency disorders are moderate to severe, **iodized oil** given either before or at any stage of pregnancy is found to be beneficial.

Sodium fluoride. Availability of adequate fluoride confers significant resistance to dental caries. It is now considered that the topical action of fluoride on enamel and plaque is more important than the systemic effect. Where the natural fluoride content of the drinking water is significantly less than 1 mg per litre, artificial fluoridation is the most economical method of supplementing fluoride intake. Daily administration of fluoride tablets or drops is a suitable alternative, but systemic fluoride supplements should not be prescribed without reference to the fluoride content of the local water supply; they are not advisable when the water contains more than 700 micrograms per litre. In addition, infants need not receive fluoride supplements until the age of 6 months. Dentifrices which incorporate sodium fluoride are a convenient source of fluoride. Individuals who are either particularly caries prone or medically compromized may be given additional protection by the use of fluoride rinses or by application of fluoride gels. Rinses may be used daily or weekly; daily use of a less concentrated rinse is more effective than weekly use of a more concentrated one. High-strength gels must be applied on a regular basis under professional supervision; extreme caution is necessary to prevent the child from swallowing any excess.

For the use of **iron** preparations in the treatment of anaemia see section 6.1.

ORAL CALCIUM

Indications: Osteoporosis of various origin; prevention of pre- and post-menopausal bone demineralisation; rickets and osteomalacia in addition to specific therapy; latent tetany, increased demand for calcium in pregnant and breast-feeding women, and in growing children; allergic conditions (supportive treatment).

Contra-indications: Hypercalcaemia e.g. in hyperparathyroidism, vitamin D overdosage, severe hypercalciuria, severe renal failure.

Precautions: Mild hypercalciuria, mild to moderate renal impairment, history of urinary calculi, high doses of vitamin D.

Interactions: Tetracycline, fluoride preparations, Vitamin D, milk and milk products, digitalis preparations.

Adverse effects: Mild GI disturbances such as bloating, contipation or diarrhoea.

Advice to patients: Do not take calcium supplements within 1-2 hours of taking other medicine by mouth or eating large amounts of fiber-rich foods; do not drink large amounts of alcohol or caffeine-containing beverages.

Nursing considerations: •Ensure that physician specifies the form of calcium to be administered.
•Administer oral calcium products 1-1½ hours after meals if GI upset occurs.
•I.V. infusion rates should not exceed 1.5-3.3 ml/minute, give dilute solution; observe patient closely for extravasation which is usually followed by severe necrosis and tissue sloughing.
•I.M. injection should be given in the gluteal muscle in the adult, only in emergency, usually in volumes less than 2 ml.
•Following injection, patient should be recumbent for 15 minutes.
•Phytic acid (in bran and whole cereals) and phosphorous (in milk and diary products) may interfere with absorption of calcium.
•Dietary sources include legumes, soya beans, spinach, deep green leafy vegetables.
•Calcium gluconate and calcium lactate contain 9% and 13% elemental calcium respectively.

Dose: Usually 500-1000 mg elemental calcium daily; up to 2000 mg daily in severe cases.
Child (3-7 years): ½ adult dose.

POM **Calcium** *(EDL 27.2)*
Tablet, Calcium gluconate 600 mg.
Tablet (effervescent), Calcium gluconate 1 g.

POM **Calcium Lactate** *(Emzor)*
Tablet, Calcium Lactate 300 mg; white biconvex tab.
300 mg - 500; 1000.

POM **Calcium Lactate** *(Juhel)*
Tablet, Calcium Lactate 300 mg.
300 mg - 100.

POM **Calcium Lactate** *(Rajrab)*
Tablet, Calcium Lactate 300mg; cream-coloured scored tab.
300 mg - 100, 1000.

POM **Calcium Lactate** *(Adler)*
Tablets, Calcium lactate 300mg.
300 mg - 100; 1000.

POM **CALCIUM-SANDOZ®** *(Novartis)*
Tablet, (effervescent), Calcium lactate-gluconate 2.94 g plus calcium carbonate 0.30 g (equiv. to 500 mg ionizable calcium).

POM **CALCIVIT®** (*Therapeutic)*
Tablet, Calcium lactate.

With Vitamin C
POM **CA-C 1000 SANDOZ®** *(Oculus)*
Tablets (effervescent), calcium lactate gluconate 1.0 g plus calcium carbonate 0.327 g (equiv. to 260 mg ionizable calcium), ascorbic acid (vitamin C) 1.0 g, sodium bicarbonate (274 mg sodium) 1.0 g, sugar 2.0 g.
Indications: For oral calcium and vitamin C therapy.
Advice to patients: See label 13 in Appendix 6.
Dose: Adult and children of school age: 1 effervescent tab. daily.
Child (3-7 years): ½ effervescent tab. daily.

With Vitamin D and other Minerals.
POM **CALTRATE PLUS®** *(Matbeny)*
Tablet, Calcium 600 mg, vitamin D 200 I.U., magnesium 40 mg, zinc 7.5 mg, copper 1 mg, manganese 1.8 mg, boron 250 mg.
Pack - 60.
Indications: Prevention of osteoporosis.
Dose: By mouth, Adult and child above 12 years, 1-2 tabs daily.

POM **CEECAL®** *(Afrab-Chem)*
Effervescent Tablet, Vitamin C 1000 mg, Calcium carbonate 625 mg, Vitamin D 300 I.U., Vitamin B_6 5 mg
Indications: The combination of vitamin C, Calcium and Vitamin D enhances the absorption and higher assimilation of calcium in the body. Recommended for: Bone disorders associated with calcium deficiency; Improves wounds healing; Protects & enhances cold recovery; Antioxidant; Calcium and vitamin sup-

RETURN

plement; Management of Hypocalcaemia; Connective tissue growth, healing and support; Bone growth & formation.

OTC **EFFCAL**® *(Ranbaxy)*
Effervescent tablet, Calcium (as Carbonate) BP 400 mg, Vitamin D_3 200 IU; available in orange and lemon flavours.
Pack – 10's (in tube); 25 x 2's (in strips).
Indications: As a supplemental source of calcium in the correction of dietary deficiencies or when normal requirements are high to arrest or slow bone demineralization in osteoporosis either as an adjunct to conventional therapy or when other effective treatments are contraindicated.
Dose: 1-2 tablets per day.
Put the tablet in half glass of water (approx. 130 ml) and drink the contents as soon as tablet dissolves.

PARENTERAL CALCIUM

Calcium gluconate is a complementary drug.
Indications: Hypocalcaemic tetany.
Contra-indications: Conditions associated with hypercalcaemia and hypercalciuria (for example some forms of malignant disease).
Precautions: Monitor plasma calcium concentration; **interactions**: Appendix 1.
Adverse effects: Mild GI disturbances; bradycardia, arrhythmia; irritation at injection site.
Dose: *Hypocalcaemic tetany*, by slow intravenous injection, ADULT 1 g (2.2 mmol) followed by continuous intravenous infusion of about 4 g (8.8 mmol) daily.
DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Calcium gluconate** *(WMF 27.2)*
Injection (Solution for injection), Calcium gluconate (monohydrate) 100 mg (Ca2+ 220 micromol)/ml; in 10-ml ampoule.

POM **Calcium** *(EDL 27.2)*
Injection, Calcium gluconate 10%, in 10 mg amp.

IODINE

Indications: Prevention and treatment of iodine deficiency.
Contra-indications: Breastfeeding (Appendix 3).
Precautions: Over 45 years old or with nodular goitre (especially susceptible to hyperthyroidism when given iodine supplements—iodized oil may not be appropriate); may interfere with thyroid-function tests; pregnancy (see notes above and Appendix 2).
Adverse effects: Hypersensitivity reactions; goitre and hypothyroidism; hyperthyroidism.
Dose: *Endemic moderate to severe iodine deficiency*, by intramuscular injection, ADULT women of child-bearing age, including any stage of pregnancy, 480 mg once each year; by mouth, ADULT during pregnancy and one year postpartum, 300–480 mg once a year or 100–300 mg every 6 months; women of child-bearing age, 400–960 mg once a year or 200–480 mg every 6 months
Iodine deficiency, by intramuscular injection, INFANT up to 1 year, 190 mg; CHILD and ADULT 380 mg (aged over 45 years or with nodular goitre, 76 mg but see also Precautions) (provides up to 3 years protection).
Iodine deficiency, by mouth, ADULT (except during pregnancy) and CHILD above 6 years, 400 mg once a year; ADULT during pregnancy, single dose of 200 mg; INFANT under 1 year, single dose of 100 mg; CHILD 1–5 years, 200 mg once a year.

POM **Iodine** *(WMF 27.2)*
Oily injection (Solution for injection), Iodine (as iodized oil) 480 mg/ml. 0.5-ml ampoule, 1-ml ampoule.
NOTE: IODIZED OIL MAY ALSO BE GIVEN BY MOUTH.

SODIUM FLUORIDE

Indications: Prophylaxis of dental caries
Adverse effects: Occasional white flecks on teeth, rarely yellow brown discoloration; GI discomfort, muscle weakness, clonic convulsion followed by respiratory and cardiac failure may occur at high doses.
Advice to patients: Take with food (but not milk) to eliminate GI upset.
Nursing considerations: •Tablets may be dissolved in the mouth or sucked and taken preferably in the evening.
•When using mouthwashes, rinse mouth for 1 minute and spit out (most effective when used immediately after brushing teeth). Avoid eating, drinking, or rinsing mouth for 15 minutes after use.
•Avoid giving with milk or dairy products.
Dose: See lit.

POM **Sodium fluoride** *(EDL 27.2)*
Tablets, Sodium fluoride 1.1 mg, 2.2 mg. equivalent to 0.5 mg, 1 mg fluoride respectively.
See section 18.6 for Sodium flouride mouthwash.

6.9 Appetite Stimulants

Cyproheptadine is a serotonin and histamine antagonist with anticholinergic and sedative properties. Also has calcium channel-blocking property.
Pizotifen has an appetite-stimulating action suitable for increasing body weight in underweight anorectic patients. In elderly people, pizotifen has been shown to improve disturbed mood by alleviating symptoms such as hopelessness, feeling of dejection or oppression, asthenia, anxiety, restlessness, sleep disturbances, and impairment of concentration or memory. Also used for the prophylaxis of migraine.

CYPROHEPTADINE

See under Section 8.1

CYPROHEPTADINE plus VITAMINS plus AMINOACIDS

Indications: Stimulation of appetite and as an anti-allergic.
Contra-indications: Urinary retention, glaucoma, acute asthma, elderly debiliated patients, stenosing peptic ulcer, prostatic hypertrophy, lactation and neonates; hypersensitivity to any of the ingredients.
Adverse effects: Most commonly drowsiness; others are dry mouth, dizziness, paradoxical excitement in children and nausea.
Advice to patients: May cause drowsiness; if affected do not drive or operate machinery or appliances, which require alertness.
Dose: *For appetite stimulation and as an anti-allergic*, Adult & children (7-14 years), 10 ml to be taken 3 times daily; Children (2-6 years), 5 ml to be taken 2 times daily.

OTC **CYPRIVIT®** *(Farmex)*
Syrup, Cyproheptadine HCl BP 2 mg, vitamin B_1 BP 1 mg, vitamin B_2 BP 0.5 mg, vitamin B_6 BP 0.5 mg, niacinamide BP 10 mg, vitamin B_{12} BP 1 mcg, L-Lysine BP 60 mg, glycine BP 40 mg per 5 ml.
Pack – 100 ml; 200 ml.

PIZOTIFEN

Therapeutic category: Orexigenic
Indications: Anorexia of somatic or psychogenic origin in underweight patients in addition to treatment of the underlying condition; mood elevation in the elderly.
Precautions, Interactions, etc: See under Pitzofen in section 1.9.
Dose: By mouth, Adult: initially 0.5 mg once daily; increased progressively up to 0.5 mg 3 times daily.
Child (2-6 years): 0.25-0.5 mg daily; 6-12 years: 0.5-1.0 mg daily in 2-3 divided doses or according to patients needs.
Mood elevation in elderly patients: initially 0.5 mg daily;increased prefer ably by 0.5 mg daily up to a daily optimum of 2-3 mg in divided doses, and following improvement doses should be gradually reduced.
Not recommended for children below 1 year of age.

POM **MOSEGOR®** *(Novartis)*
Tablets, Pizotifen (as the hydrogen malate) 0.5 mg (s-c tab), 1.0 mg (scored tab).
Syrup, Pizotifen (as the hydrogen malate) 0.5 mg per 10 ml.

6.10 Solutions correcting water, electrolyte and acid–base disturbances

6.10.1 Oral electrolyte solutions
6.10.2 Parenteral electrolyte solutions
6.10.3 Water

6.10.1 Oral electrolyte solutions

6.10.1.1 Oral rehydration
6.10.1.2 Oral potassium

6.10.1.1 Oral rehydration

Replacement of fluid and electrolytes orally can be achieved by giving oral rehydration salts—solutions containing sodium, potassium and glucose. Acute diarrhoea in children should always be treated with oral rehydration solution according to plans A, B, or C as shown.

Treatment of dehydration: WHO recommendations

According to the degree of dehydration, health professionals are advised to follow one of 3 management plans.

Plan A: no dehydration. Nutritional advice and increased fluid intake are sufficient

(soup, rice, water and yoghurt, or even water). For infants aged under 6 months who have not yet started taking solids, oral rehydration solution must be presented before offering milk. Mother's milk or dried cow's milk must be given without any particular restrictions. In the case of mixed breast-milk/formula feeding, the contribution of breastfeeding must be increased.

Plan B: moderate dehydration. Whatever the child's age, a 4-hour treatment plan is applied to avoid short-term problems. Feeding should not therefore be envisaged initially. It is recommended that parents are shown how to give approximately 75 ml/kg of oral rehydration solution with a spoon over a 4-hour period, and it is suggested that parents should be watched to see how they cope at the beginning of the treatment. A larger amount of solution can be given if the child continues to have frequent stools. In case of vomiting, rehydration must be discontinued for 10 minutes and then resumed at a slower rate (about one teaspoonful every 2 minutes). The child's status must be re-assessed after 4 hours to decide on the most appropriate subsequent treatment. Oral rehydration solution should continue to be offered once dehydration has been controlled, for as long as the child continues to have diarrhoea.

Plan C: severe dehydration. Hospitalization is necessary, but most urgent priority is to start rehydration. In hospital (or elsewhere), if the child can drink, oral rehydration solution must be given pending, and even during, intravenous infusion (20 ml/kg every hour by mouth before infusion, then 5 ml/kg every hour by mouth during intravenous rehydration. For intravenous supplementation, it is recommended that compound solution of sodium lactate (see section 26.2) is administered at a rate adapted to the child's age (infant under 12 months: 30 ml/kg over 1 hour then 70 ml/kg over 5 hours; child over 12 months: the same amounts over 30 minutes and 2.5 hours respectively). If the intravenous route is unavailable, a nasogastric tube is also suitable for administering oral rehydration solution, at a rate of 20 ml/kg every hour. If the child vomits, the rate of administration of the oral solution should be reduced.

ORAL REHYDRATION SALTS

Glucose salt solution

sodium chloride	2.6 g/litre of clean water
sodium citrate	2.9 g/litre of clean water
potassium chloride	1.5 g/litre of clean water
glucose (anhydrous)	13.5 g/litre of clean water

When glucose and sodium citrate are not available, they may be replaced by

sucrose (common sugar)	27 g/litre of clean water
sodium bicarbonate	2.5 g/litre of clean water

NOTE: THE SOLUTION MAY BE PREPARED EITHER FROM PREPACKAGED SUGAR/SALT MIXTURES OR FROM BULK SUBSTANCES AND WATER. SOLUTIONS MUST BE FRESHLY PREPARED, PREFERABLY WITH RECENTLY BOILED AND COOLED WATER. ACCURATE WEIGHING AND THOROUGH MIXING AND DISSOLUTION OF INGREDIENTS IN THE CORRECT VOLUME OF CLEAN WATER IS IMPORTANT. ADMINISTRATION OF MORE CONCENTRATED SOLUTIONS CAN RESULT IN HYPERNATRAEMIA.

CHOLERA: IN CASES OF CHOLERA, ORAL REHYDRATION SALTS CONTAINING A HIGHER CONCENTRATION OF SODIUM MAY BE REQUIRED TO PREVENT HYPONATRAEMIA.

Indications: Dehydration from acute diarrhoea.

Precautions: Renal impairment.

Adverse effects: Vomiting—may indicate too rapid administration; hypernatraemia and hyperkalaemia may result from overdose in renal impairment or administration of too concentrated a solution.

Dose: *Fluid and electrolyte loss in acute diarrhoea*, by mouth, ADULT 200–400 ml solution after every loose motion; INFANT and CHILD according to Plan A, B or C (see notes above).

OTC **Oral Rehydration Salt** *(EDL 18.6.2)*
Powder, Glucose 20g, Potassium chloride 1.5g, Sodium citrate dihydrate 2.9g (or Sodium bicarbonate 2.5g), Sodium chloride 3.5g.
See section 4.3.1 for the proprietary preparations.

6.10.1.2 Oral potassium

Compensation for potassium loss is necessary in patients taking digoxin or antiarrhythmic drugs where potassium depletion may induce arrhythmias. It is also necessary in patients with secondary hyperaldosteronism (renal artery stenosis, liver cirrhosis, the nephrotic syndrome, severe heart failure) and those with excessive loss of potassium in the faeces (chronic diarrhoea associated with intestinal malabsorption or laxative abuse).

Measures to compensate for potassium loss may also be required in the elderly since they often take inadequate amounts in the diet (but see warning on use in renal insufficiency, below). Measures may also be required during long-term administration of drugs known to induce potassium loss (for example, corticosteroids). Potassium supplements are seldom required with the small doses of diuretics given to treat hypertension. Potassium-sparing diuretics (rather than potassium supplements) are recommended for prevention of hypokalaemia due to diuretics such as furosemide or the thiazides when these are given to eliminate oedema (see section 5.2.3).

For the prevention of hypokalaemia doses of potassium chloride 2 to 4 g (approximately 25 to 50 mmol) daily by mouth are suitable in patients taking a normal diet. Smaller doses must be used if there is renal insufficiency (common in the elderly) otherwise there is a danger of hyperkalaemia.

Larger doses may be required in established potassium depletion, the quantity depending on the severity of any continuing potassium loss (monitoring of plasma potassium and specialist advice required).

Potassium depletion is frequently associated with metabolic alkalosis and chloride depletion and these disorders require correction.

POTASSIUM CHLORIDE

Indications: Prevention and treatment of hypokalaemia (see notes above).

Contra-indications: Severe renal impairment; plasma potassium concentration above 5 mmol/litre.

Precautions: Elderly, mild to moderate renal impairment (close monitoring required, Appendix 4), history of peptic ulcer; important: special hazard if given with drugs liable to raise plasma potassium concentrations such as potassium-sparing diuretics, ACE inhibitors or ciclosporin, for other **interactions**: Appendix 1.

Adverse effects: Nausea and vomiting, gastrointestinal irritation.

Advice to patients: See label 21, 25 and 27 in Appendix 6.

Nursing considerations: •Administer with plenty of water and with food to minimize GI distress; advise patient to completely dissolve powder or effervescent tablet in glass of water or juice.
•Sustained release and wax matrix tablets must be swallowed whole and not allowed to dissolve in the mouth, not to be crushed or chewed.
•Teach patient to report symptoms of hyperkalaemia viz lethargy, confusion, diarrhoea, vomiting, fainting, and decreased output.
•Include potassium rich food in the diet viz banana, orange juice, avocado pears, carrots.
•Advise patient to avoid OTC products viz antacids, analgesics, vitamin preparations and salt substitutes unless on prescription.

Dose: *Prevention of hypokalaemia* (see notes above), by mouth, ADULT 20–50 mmol daily after meals.
Potassium depletion (see notes above), by mouth, ADULT 40–100 mmol daily in divided doses after meals: adjust dose according to severity of deficiency and any continuing loss of potassium.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Potassium chloride** *(WMF 26.1.2)*
Powder for oral solution, Potassium chloride 1.5 g (potassium 20 mmol, chloride 20 mmol).

POM **Potassium chloride** *(EDL 24.1)*
Tablet, (s-r), Potassium chloride 600 mg.
Oral Solution, Potassium Chloride 5%, 10%, 20%.

6.10.2 Parenteral electrolyte solutions

Solutions of electrolytes are given intravenously, to meet normal fluid and electrolyte requirements or to replenish substantial deficits or continuing losses, when the patient is nauseated or vomiting and is unable to take adequate amounts by mouth.

The nature and severity of the electrolyte imbalance must be assessed from the history and clinical and biochemical examination of each individual. Sodium, potassium, chloride, magnesium, phosphate, and water depletion can occur singly and in combination with or without disturbances of acid-base balance.

Isotonic solutions may be infused safely into a peripheral vein. More concentrated solutions, for example 20% glucose, are best given through an indwelling catheter positioned in a large vein.

Sodium chloride in isotonic solution provides the most important extracellular

ions in near physiological concentrations and is indicated in *sodium depletion* which may arise from conditions such as gastroenteritis, diabetic ketoacidosis, ileus and ascites. In a severe deficit of from 4 to 8 litres, 2 to 3 litres of isotonic sodium chloride may be given over 2 to 3 hours; thereafter infusion can usually be at a slower rate.

Excessive administration should be avoided; the jugular venous pressure should be assessed; the bases of the lungs should be examined for cepitations, and in elderly or seriously ill patients it is often helpful to monitor the right atrial (central) venous pressure

Chronic hyponatraemia should ideally be managed by fluid restriction. However, if sodium chloride is required, the deficit should be corrected slowly to avoid risk of osmotic demyelination syndrome; the rise in plasma-sodium concentration should be limited to no more than 10 mmol/litre in 24 hours.

The more physiologically appropriate **compound solution of sodium lactate** can be used instead of isotonic sodium chloride solution during surgery or in the initial management of the injured or wounded.

Sodium chloride and glucose solutions are indicated when there is *combined water and sodium depletion*. A 1:1 mixture of isotonic sodium chloride and 5% glucose allows some of the water (free of sodium) to enter body cells which suffer most from dehydration while the sodium salt with a volume of water determined by the normal plasma Na+ remains extracellular. Combined sodium, potassium, chloride, and water depletion may occur, for example, with severe diarrhoea or persistent vomiting; replacement is carried out with sodium chloride intravenous infusion 0.9% and glucose intravenous infusion 5% with potassium as appropriate.

Glucose solutions (5%) are mainly used to replace *water deficits* and should be given alone when there is no significant loss of electrolytes. Average water requirement in a healthy adult are 1.5 to 2.5 litres daily and this is needed to balance unavoidable losses of water through the skin and lungs and to provide sufficient for urinary excretion. Water depletion (dehydration) tends to occur when these losses are not matched by a comparable intake, as for example may occur in coma or dysphagia or in the aged or apathetic who may not drink water in sufficient amount on their own initiative.

Excessive loss of water without loss of electrolytes is uncommon, occurring in fevers, hyperthyroidism, and in uncommon water-losing renal states such as diabetes insipidus or hypercalcaemia. The volume of glucose solution needed to replace deficits varies with the severity of the disorder, but usually lies within the range of 2 to 6 litres.

Glucose solutions are also given in regimens with calcium, bicarbonate, and insulin for the emergency treatment of *hyperkalaemia*. They are also given, after correction of hyperglycaemia, during treatment of diabetic ketoacidosis, when they must be accompanied by continuing insulin infusion.

If glucose or sugar cannot be given orally to treat *hypoglycaemia*, glucose 50% may be given intravenously into a large vein through a large-gauge needle; this concentration is very irritant on extravasation and it is also viscous and difficult to administer. Larger volumes of less concentrated glucose solutions (10% or 20%) can be used as alternatives and are less irritant.

Sodium hydrogen carbonate (sodium bicarbonate) is used to control severe *metabolic acidosis* (as in renal failure). Since this condition is usually attended by sodium depletion, it is reasonable to correct this first by the administration of isotonic sodium chloride intravenous infusion, provided the kidneys are not primarily affected and the degree of acidosis is not so severe as to impair renal function. In these circumstances, isotonic sodium chloride alone is usually effective as it restores the ability of the kidneys to generate bicarbonate. In renal acidosis or in severe metabolic acidosis of any origin, for example blood pH < 7.1, sodium hydrogen carbonate (1.4%) may be infused with isotonic sodium chloride when the acidosis remains unresponsive to correction of anoxia or fluid depletion; a total volume of up to 6 litres (4 litres of sodium chloride and 2 litres of sodium hydrogen carbonate) may be necessary in the adult. In severe shock due for example to cardiac arrest, metabolic acidosis may develop without sodium depletion; in these

circumstances sodium hydrogen carbonate is best given in a small volume of hypertonic solution (for example 50 ml of 8.4% solution intravenously); plasma pH should be monitored. Sodium hydrogen carbonate is also used in the emergency management of *hyperkalaemia*.

Intravenous **potassium chloride** in sodium chloride infusion is the initial treatment for the correction of *severe hypokalaemia* when sufficient potassium cannot be taken by mouth. Potassium chloride concentrate may be added to sodium chloride 0.9% infusion, **thoroughly mixed**, and given slowly over 2 to 3 hours with specialist advice and ECG monitoring in difficult cases. Repeated measurements of plasma potassium are necessary to determine whether further infusions are required and to avoid the development of hyperkalaemia which is especially likely to occur in renal impairment.

Initial potassium replacement therapy should **not** involve glucose infusions because glucose may cause a further decrease in the plasma-potassium concentration.

GLUCOSE

Synonym: Dextrose

Indications: Fluid replacement without significant electrolyte deficit (see notes above); treatment of hypoglycaemia.

Precautions: Diabetes mellitus (may require additional insulin).

Adverse effects: Glucose injections, especially if hypertonic, may have a low pH and cause venous irritation and thrombophlebitis; fluid and electrolyte disturbances; oedema or water intoxication (on prolonged administration or rapid infusion of large volumes of isotonic solutions); hyperglycaemia (on prolonged administration of hypertonic solutions).

Nursing considerations: •Control infusion carefully, note that maximal rate of infusion is 0.5g/kg b.wt hourly; do not infuse concentrated solutions rapidly, may cause hyperglycaemia and fluid shift.

•Do not give Dextrose without saline solutions in blood transfusions; may cause clumping of blood cells.

•Observe closely for signs of overloading where fluid intake is restricted.

•Check infusion site regularly to prevent irritation or extravasation and phlebitis; change site immediately if there is sign of extravasation.

•Monitor I&O, VS, temperature (increasing fever may be sign of infection).

Dose: *Fluid replacement*, by intravenous infusion, ADULT and CHILD determined on the basis of clinical and, whenever possible, electrolyte monitoring (see notes above).

Treatment of hypoglycaemia, by intravenous infusion of 50% glucose solution into a large vein, ADULT, 25 ml (see also notes above).

POM **Glucose** *(WMF 26.2)*
Infusion (Solution for infusion), Glucose 5% (iso-osmotic), 10% (hyperosmotic), 50% (hyperosmotic).

POM **Glucose** *(EDL 24.2)*
Infusion, Dextrose 5, 10, 50% in water for injection.

POM **Dextrose** *(Dana)*
Infusion, Dextrose 5, 10, 50% in water for injection.
5% - 500 ml x 20's; 1000 ml x 10's.
10% - 500 ml x 20's; 1000 ml x 10's.
50% - 100 ml x 75's.

POM **Dextrose** *(Dizpharm)*
Infusion, Dextrose anhydrous 5 g per 100 ml.
Pack - 500 ml.

POM **UNIDEX®** *(Unique)*
Infusion (5%), Dextrose 5% in water for Injection; clear and colourless solution in transparent plastic bottle.
Pack - 500 ml; 1000 ml.
Infusion (10%), Dextrose 10% in water for Injection; clear and colourless solution in transparent plastic bottle.
Pack - 500 ml; 1000 ml.
Infusion (50%), Dextrose 50% in water for Injection; clear and colourless solution in transparent plastic bottle.
Pack - 100 ml.

GLUCOSE plus SODIUM CHLORIDE

Indications: Fluid and electrolyte replacement.

Precautions: Restrict intake in impaired renal function, cardiac failure, hypertension, peripheral and pulmonary oedema, toxaemia of pregnancy.

Adverse effects: Administration of large doses may give rise to oedema.

Nursing considerations: •See under Dextrose and Sodium Chloride.

Dose: *Fluid replacement*, by intravenous infusion, ADULT and CHILD determined on the basis of clinical and, whenever possible, electrolyte

monitoring (see notes above).

POM **Glucose plus sodium chloride** *(WMF 26.2)*
Infusion (Solution for infusion), Glucose 4%, sodium chloride 0.18% (1.8 g, 30 mmol each of Na+ and Cl- /litre).

POM **Glucose plus Sodium Chlorid** *(EDL 24.2)*
Infusion, Glucose plus Sodium Chloride 4.3% + 0.18%; 5% + 0.9% respectively.

POM **5%Dextrose Saline** *(Dana)*
Infuson, Dextrose monohydrate 5 g, sodium chloride 0.9 g per 100 ml.
Pack - 500 ml x 20's; 1000 ml x 10's.

POM **4.3%Dextrose Saline** *(Dana)*
Infusion, Dextrose monohydrate 4.3 g, sodium chloride 0.18 g per 100 ml.
Pack - 500 ml x 20's.

POM **5%Dextrose Saline** *(Dizpharm)*
Infusion, Dextrose anhydrous 5 g, sodium chloride 0.9 g per 100 ml.
Pack - 500 ml.

POM **UNIDEXAL-9®** *(Unique)*
Infusion, Dextrose 5 g, sodium chloride 0.9 g per 100 ml of water of injection; clear and colourless solution in transparent plastic bottle.
Pack - 500 ml; 1000 ml.

POM **UNIDEXAL-18®** *(Unique)*
Infusion, Dextrose 4.3%, sodium chloride 0.18% in water for injection; clear and colourless solution in transparent plastic bottle.
Pack - 500 ml; 1000 ml.

SODIUM CHLORIDE

Synonym: Normal saline.
Indications: Electrolyte and fluid replacement.
Precautions: Restrict intake in impaired renal function (Appendix 4), cardiac failure, hypertension, peripheral and pulmonary oedema, toxaemia of pregnancy.
Adverse effects: Administration of large doses may give rise to sodium accumulation and oedema.
Nursing considerations: •Avoid excessive administration
Dose: *Fluid and electrolyte replacement*, by intravenous infusion, ADULT and CHILD determined on the basis of clinical and, whenever possible, electrolyte monitoring (see notes above).

POM **Sodium chloride** *(WMF 26.2)*
Infusion (Solution for infusion), Sodium chloride 0.9% (9 g, 154 mmol each of Na+ and Cl- /litre).

POM **Sodium chloride** *(EDL 24.2)*
Infusion, Sodium Chloride 0.9%, 0.45%.

POM **Normal Saline** *(Dana)*
Infusion, Sodium Chloride 0.9 g per 100ml.
Pack - 500 ml x 20's; 1000 ml x 10's.

POM **Normal Saline** *(Dizpharm)*
Infusion, Sodium Chloride 0.9 g per 100ml.
Pack - 500 ml.

POM **UNISAL®** *(Unique)*
Infusion, Sodium Chloride 0.9% in water for injection; clear and colourless liquid in transparent plastic bottle.
Pack - 500 ml; 1000 ml.

SODIUM LACTATE, COMPOUND SOLUTION OF

Compound solution of sodium lactate is a representative intravenous electrolyte solution. Various solutions can serve as alternatives.
Synonym: Hartmann's solution; Ringer's lactate injection.
Indications: Pre- and perioperative fluid and electrolyte replacement; hypovolaemic shock.
Contra-indications: Metabolic or respiratory alkalosis; hypocalcaemia or hypochlorhydria.
Precautions: Restrict intake in impaired renal function, cardiac failure, hypertension, peripheral and pulmonary oedema, toxaemia of pregnancy; **interactions**: Appendix 1.
Adverse effects: Excessive administration may cause metabolic alkalosis; administration of large doses may give rise to oedema.
Nursing considerations: •Administer I.V. slowly to prevent pain at infusion site; check for extravasation.
•Observe patient closely for symptoms of alkalosis viz irritability, confusion, twitching, hyper-reflexia, slow respiration, cyanosis, irregular pulse.
•Avoid in patient with severe acidosis because rapid replacement of serum bicarbonate is required and sodium lactate is slowly metabolised to bicarbonate by the liver.
Dose: *Fluid and electrolyte replacement or hypovolaemic shock*, by intravenous infusion, ADULT and CHILD determined on the basis of

clinical and, whenever possible, electrolyte monitoring (see notes above).

POM **Compound sodium lactate solution** *(WMF 26.2)*
Infusion (Solution for infusion), Sodium chloride 0.6%, sodium lactate 0.25%, potassium chloride 0.04%, calcium chloride 0.027% (containing Na+ 131 mmol, K+ 5 mmol, Ca 2+ 2 mmol, HCO3 - (as lactate) 29 mmol, Cl- 111 mmol/litre).

POM **Hartmann's Solution** *(EDL 24.2)*
Infusion, Sodium chloride, potassium chloride, calcium chloride, sodium lactate.

POM **Ringer Lactate Solution** *(Dana)*
Infusion, Sodium chloride 3 g, potassium chloride 0.2 g, calcium chloride 0.135 g, sodium lactate 1.5 g per 500 ml.
Pack - 500 ml x 20's.

POM **UNIHART®** *(Unique)*
Infusion, Lactic acid 0.24 mg, sodium chloride 0.6 g, calcium chloride 0.027 g, sodium hydroxide 0.115 g and potassium chloride 0.04 g per 100 ml of water for injection; clear and colourless solution in transparent plastic bottle.
Pack - 500 ml.

SODIUM LACTATE BP

Indications: Diabetic coma, severe acidosis; burns, hyperkalaemia, uraemia.
Contra-indications: Alkalosis, lactoacidosis, hypokalaemia, respiratory acidosis.
Dose: See lit.

POM **Sodium Lactate BP** *(EDL 24.2)*
Infusion, Sodium Lactate BP.

SODIUM BICARBONATE

Synonym: Sodium hydrogen carbonate
Indications: Metabolic acidosis.
Contra-indications: Metabolic or respiratory alkalosis, hypocalcaemia, hypochlorhydria.
Precautions: Restrict intake in impaired renal function (Appendix 4), cardiac failure, hypertension, peripheral and pulmonary oedema, toxaemia of pregnancy; monitor electrolytes and acid-base status; **interactions**: Appendix 1.
Adverse effects: Excessive administration may cause hypokalaemia and metabolic alkalosis, especially in renal impairment; large doses may give rise to sodium accumulation and oedema.
Nursing considerations: •Check I.V. site regularly to avoid extravasation which may cause tissue sloughing, ulceration and necrosis.
Dose: *Metabolic acidosis*, by slow intravenous injection, ADULT and CHILD a strong solution (up to 8.4%) or by continuous intravenous infusion, ADULT and CHILD a weaker solution (usually 1.4%), an amount appropriate to the body base deficit (see notes above).

POM **Sodium bicarbonate** *(WMF 26.2)*
Infusion (Solution for infusion), Sodium hydrogen carbonate 1.4% (14 g, 166.7 mmol each of Na+ and HCO3 - /litre).
Injection (Solution for injection), Sodium hydrogen carbonate 8.4% (840 mg, 10 mmol each of Na+ and HCO3 - /10 ml).

POM **Sodium bicarbonate** *(EDL 24.2)*
Infusion, Sodium bicarbonate 1.4%; Isotonic solution in 10 ml amp.

POTASSIUM CHLORIDE

Indications: Electrolyte imbalance; see also oral potassium (section 6.10.1.2).
Precautions: For intravenous infusion the concentration of solution should not usually exceed 3.2 g (43 mmol)/litre; specialist advice and ECG monitoring (see notes above); renal impairment (Appendix 4); **interactions**: Appendix 1.
Adverse effects: Cardiac toxicity on rapid infusion.
Dose: *Electrolyte imbalance*, by slow intravenous infusion, ADULT and CHILD depending on the deficit or the daily maintenance requirements (see also notes above).
DILUTION AND ADMINISTRATION: MUST BE DILUTED AND THOROUGHLY MIXED BEFORE USE AND ADMINISTERED ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Potassium chloride** *(WMF 26.2)*
Concentrate for infusion (Concentrate for solution for infusion), potassium chloride 11.2% (112 mg, approximately 1.5 mmol each of K+ and Cl- /ml), 20-ml ampoule.

DARROW'S SOLUTION

Indications: Dehydration by loss of intestinal fluid, Correction of metabolic acidosis, hypokalaemia in diabetic coma.
Contra-indications: Acute renal insufficiency, hyperkalaemia, alkalosis.

Precautions: Pregnancy, Normal Circulation and diuresis to be restored before infusion.
Dose: 1 Litre over a period of 5 hours; maximum of 40-80 ml per kg body weight daily by slow I.V. infusion or S.C. injection.

POM **Darrow's Solution** *(EDL 24.2)*
Injection, Sodium Chloride, Potassium Chloride, sodium lactate.

POM **Darrow's Solution (Full Strength)** *(Dana)*
Infusion, Sodium chloride 2 g, Potassium chloride 1.3 g, Sodium lactate 2.95 g per 100 ml.
Pack - 500 ml x 20's; 1000 ml x 10's.

POM **Darrow's Solution (Half Strength)** *(Dana)*
Infusion, Sodium chloride 1 g, Potassium chloride 0.65 g, Sodium lactate 1.475 g per 100 ml.
Pack - 500 ml x 20's; 1000 ml x 10's.

POM **Darrow's Solution** *(Dizpharm)*
Infusion, Potassium Chloride, Sodium Chloride and Sodium Lactate.
Full Strength: 500 ml
Half Strength: 500 ml

POM **UNIDAR-H®** *(Unique)*
(Darrow's Solution Half Strength).
Infusion, Potassium chloride 0.13 g, sodium chloride 0.2 g, lactic acid 0.263 g, sodium hydroxide 0.105 g per 100 ml of water for injection; clear and colourless solution in transparent plastic bottle.
Pack - 500 ml; 1000 ml.

POM **UNIDAR-F®** *(Unique)*
(Darrow's Solution Full Strength).
Infusion, Potassium chloride 0.26 g, sodium chloride 0.4 g, lactic acid 0.526 g, sodium hydroxide 0.21 g per 100 ml of water for injection; clear and colourless solution in transparent plastic bottle.
Pack - 500 ml; 1000 ml.

MANNITOL

Therapeutic category: Osmotic Diuretic.
Pharmacology: Mannitol is an osmotic diuretic that increases the osmotic pressure of glomerular filtrate, inhibiting tubular reabsorption of water and electrolytes. It also elevates blood plasma osmolality, resulting in enhanced flow of water intro extracellular fluid.
Indications: Prevention of acute renal necrosis; increase of osmotic diuresis; oedema of the brain; emergency treatment of barbiturate intoxication; reduction of increased intraocular pressure.
Contra-indications: Extracellular dehydration; acute renal insufficiency; pulmonary congestion, CHF, intracranial bleeding.
Precautions: Electrolyte imbalance, GIT effects.
Adverse effects: Headache, nausea, vomiting, increased urination, dizziness, rash, blurred vision.
Nursing considerations: •Administer only when adequacy of renal function and urine flow are established (a test dose may be prescribed).
•Check that solution has not crystallized; if it has, especially at low tempertures, warm the bottle in hot water bath, shake vigorosly and then cool to body temperature before administering. Do not give solution with undissolved crystals.
•Check I.V. line patency at infusion site before and during administration. Give I.V. either continously or intermittently as prescribed.
•Avoid infiltration into adjoining tissues to prevent inflammation, oedema and necrosis; observe infusion site closely.
•Do not administer electrolyte-free mannitol solutions with blood, may cause agglutination of red blood cells.
•Teach patient to rise slowly from sitting and lying positions.
Dose: *Diuresis*, initially 200 mg/kg as a test dose by slow I.V. injection; then, 50-200 g by I.V. infusion over 24 hours.
Cerebral oedema, by rapid I.V. infusion, 1 g/kg as a 20% solution.

POM **Mannitol** *(EDL 24.2)*
Infusions, Mannitol 10%, 20%.

POM **Mannitol** *(Dana)*
Infusions, Mannitol 10%, 20%.
Pack - 500 ml x 20's.

POM **UNIMAN-10®** *(Unique)*
Infusion, Mannitol 10% in water for injection; clear and colourless solution.
Pack - 500 ml.

POM **UNIMAN-20®** *(Unique)*
Infusion, Mannitol 20% in water for injection; clear and colourless solution.
Pack - 500 ml.

RINGER'S SOLUTION B.P.

Indications: Replacement solution for gastrointestinal and surgery losses; hyponatraemia; rehydration solution.

Contra-indications: Hypertonic dehydration; isotonic and hypertonic hyperhydration; acute renal insufficiency.
Dose: See lit.

POM **Ringer's Solution B.P.** *(EDL 24.2)*
I.v. Infusions, Sodium chloride, potassium chloride, calcium chloride.

6.10.3 Water

WATER FOR INJECTIONS

Indications: In preparations intended for parenteral administration and in other sterile preparations.

POM **Water for injection** *(WMF 6.10.3)*
Injection, Sterile distilled water free from pyrogens; in 2-ml, 5-ml, 10-ml ampoules.

6.11 Peritoneal dialysis solution

Solutions for peritoneal dialysis are preparations for intraperitoneal use which contain electrolytes in a similar concentration to that in plasma, and also contain glucose or another suitable osmotic agent. Peritoneal dialysis solutions always contain sodium, chloride, and hydrogen carbonate or a precursor; they may also contain calcium, magnesium, and potassium.

In renal failure haemodialysis is the preferred method to correct the accumulation of toxins, electrolytes and fluid. Peritoneal dialysis is less efficient than haemodialysis, but it is preferred in children, diabetic patients, and patients with unstable cardiovascular disease; it is also used in patients who can manage their condition, or those who live far from a dialysis centre. It is unsuitable for patients who have had significant abdominal surgery.

In peritoneal dialysis, the solution is infused into the peritoneal cavity, where exchange of electrolytes takes place by diffusion and convection, and excess fluid is removed by osmosis, using the peritoneal membrane as an osmotic membrane. There are two forms of peritoneal dialysis:

- continuous ambulatory peritoneal dialysis (CAPD), in which dialysis is performed manually by the patient several times each day.
- automated peritoneal dialysis (APD), in which dialysis is performed by machine overnight.

The main complication of peritoneal dialysis is peritonitis, which often results from poor exchange technique; infections of the catheter exit site may also occur, again because of poor technique. With long-term dialysis progressive structural changes to the peritoneal membrane occur, ultimately resulting in dialysis failure.

PERITONEAL DIALYSIS SOLUTION

Peritoneal dialysis solution is a complementary preparation.
Indications: To correct electrolyte imbalance and fluid overload, and to remove metabolites, in renal failure.
Contra-indications: Abdominal sepsis; previous abdominal surgery; severe inflammatory bowel disease.
Precautions: Care required with technique to reduce risk of infection; warm dialysis solution to body temperature before use; some drugs may be removed by dialysis.
Adverse effects: Infection, including peritonitis; hernia; haemoperitoneum; hyperglycaemia, protein malnutrition; blocked catheter.
Dose: Individualized according to clinical condition, and based on blood results.

POM **Peritoneal dialysis solution** *(WMF 23.1)*
Dialysis solution (Solution for peritoneal dialysis), Intraperitoneal dialysis solution of appropriate composition.

POM **Intraperitoneal Dialysis Fluid B.P.C** *(EDL 23)*
Parenteral solution, Calcium chloride 0.22 g, Dextrose (anhydrous) 17.00 g, magnesium chloride 0.152 g, sodium acetate 4.76 g, sodium chloride 5.56 g, sodium metabisulphite 0.15 g.

POM **Haemodialysis Solution** *(EDL 23)*
Parenteral Solution, Containing sodium chloride, sodium acetate, calcium chloride, potassium chloride, magnesium chloride and lactic acid.

6.12 Parenteral nutrition

Parenteral nutrition (PN) is indicated only when adequate nutritional intake cannot be provided by the oral route. Candidates for PN include patients suffering GI disease or injury or who are undernourished and are being prepared for

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surgery, chemotherapy or radiation therapy. PN is also indicated in major surgery, trauma or burns, prolonged coma or refusal to eat and in some patients with renal or hepatic failure.

To maintain energy balance and tissue synthesis, human beings require adequate sources of protein, carbohydrates, fats, electrolytes, vitamins, minerals and water. Thus, any total feeding concept must account for all seven basic categories. The components of PN solution include (see Table 6A below).

Table 6A - Nutrient Substrates in PN Solution

Source	
Energy	Dextrose, Intravenous fat emulsions
Nitrogen	Crystalline amino acids, protein hydrolysates
Electrolytes	Injectable salts of sodium, potassium, magnessium, calcium, Chloride, Phosphate, acetate.
Vitamins	Injectable fat-soluble vitamins (A, D, E, K) and water-soluble vitamins (B_1, B_2, B_6, B_{12}, C, nicotnic acid, pantothenic acid, biotin, folic acid).
Trace Minerals	Commercially available or extemporaneous preparations including iron, zinc, copper, manganese, chromium, iodide, selenium.
Water	Sterile water for injection.

Protein is given as mixtures of essential and non-essential synthetic L-amino acids. Energy is provided for the utilisation of amino acids for tissue maintenance. A mixture of fat (30 - 50%) and carbohydrate gives better utilisation of amino acid solutions than glucose alone. Glucose is the preferred source of carbohydrate but if more than 180g is given per day, frequent monitoring of blood glucose is required and insulin may be necessary. Fat emulsions have the advantages of a high energy to fluid volume ratio, neutral pH, and iso-osmolarity with plasma and provide essential fatty acids (e.g. intralipid).

PN therapy commences with a regimen that will supply per 24 hrs approx 25-33% of the patient's calculated energy and protein requirements. Following each 24-hour period, the therapy is advanced as tolerated. Thus, the average adult patient will receive 100% of the estimated goal for energy and nitrogen at the end of the third or forth day.

Commerably available PN solutions include **Aminoplasmal** (L5, 10 or Ped), **Aminoplex** (5, 12, 14, 24), **FreAmine**, **Intralipid** (10%, 20%).

Potential complications of PN include hydrothorax, pneumothorax, catherter embolism, arterial puncture, air embolism, myocardial perforation, sepsis, thrombosis, hyper-hypoglycaemia, hyperammonaemia, hypokalaemia, hypomagnesaemia, hypocalcaemia acidosis/alkalosis.

6.13 Oral glucose

ORAL GLUCOSE

OTC **ENERGIN®** *(Fidson)*

Tablet (Chewable), Dextrose Monohydrate, Starch, Citric acid, Pineapple, Flavour, Orange flavour, Magnesium stearate.

Pharmacology: After oral administration of glucose, dextrose (a monosaccharide) is absorbed rapidly by the small intestine, principally by an active mechanism. In patients with hypoglycemia, blood glucose concentration increases within 10 to 20 minutes after oral administration. Peak blood concentration may occur 40 minutes after oral administration.

Indications: In hypoglycemic state, for fast relief from low blood glucose level. Energin is an easily assimilable source of instant energy. Glucose, a monosaccharide, is administered by mouth or by intravenous infusion in the treatment of carbohydrate and fluid depletion.

It is administered orally in glucose tolerance test as a diagnostic aid for diabetes mellitus.

Contra-indications: Dextrose is contra-indicated in Glucose-Galactose malabsorption syndrome. Dextrose is contra-indicated in patients with diabetic coma while blood glucose levels are excessively high.

Adverse effects: A high dose of dextrose given by mouth may cause nausea and vomiting. Hyperphosphatemia may follow after prolonged use. Oral contraceptive may compound the effect of well-known risk factors, such as hypertension, diabetes, hyperlipidemias, age and obesity. In particular some progestogens are known to decrease HDL cholesterol and cause glucose intolerance, while estrogen may create a state of hyperinsulinism.

Dose: Suck or chew 1 - 2 tablets several times daily. To be administered orally.

6.14 Herbal preparations

BIO-STRATH® *(Swipha)*

Tablet, Combination of plasmolysed yeast and 16 medicine extracts namely angelica, balm, basil, chamomile, cinnamon, caraway, elder, fennel, horseradish, hyssop, lavender, liquorice, peppermint, parsley, sage and thyme.

Indications: For additional vitality, endurance, energy, increased memory function, concentration and healthy immune system function recommended for Professionals with hectic lifestyles, anyone recovering from illness, the elderly, people with a poor immune system, mothers juggling work and family, pregnant and lactating women, students suffering from mental fatigue, sports men and women.

Dose: Adults, 1-2 tablets3 times daily before meals with a little water or fruit juice. Child: ½ the adult dosage.

Elixir, Combination of plasmolysed yeast and 16 medicine extracts namely angelica, balm, basil, chamomile, cinnamon, caraway, elder, fennel, horseradish, hyssop, lavender, liquorice, peppermint, parsley, sage and thyme; naturally sweetened with honey, malt and orange juice which gives it a pleasant taste.

Pack - 100 ml.

Indications: see above.

Dose: Adults, 5-10 ml 3 times daily before meals undiluted or with a little fruit juice. Child: ½ the adult dosage.

GINKGOPAN® *(Pharmabox)*

Capsule, Ginseng 75.96 mg, Ginkgo Biloba leaf Ext. 60.72 mg, Fresh Garlic 799.32 mg; dark brown-colored soft gelatin capsules.

Pack - 30's.

Therapeutic category: Nutrition supplement, herbal.

Pharmacology: Ginkgopan is a nutrition supplement providing Ginseng, Ginkgo biloba and Fresh Garlic. Ginkgo Biloba has been used in cerebrovascular and peripherial vascular disorders and in multi infarct dementia. The fresh Garlic extract more recently has been investigated as lipid lowering and fibrinolytic agent.

Indications: For increasing cerebral and peripheral circulation and blood flow; For disturbed brain functions which result in dizziness, loss of memory and headache with anxiety; For reducing the risks of tinnitus, asthma, Alzheimer's disease, and heart and kidney disorders; For tonic, relief for fatigue, and convalescence; To improve skin texture, sexual performance and body resistance.

Contra-indications: Hypersensitivity to this medicine.

Precautions: Hypertension; children under 12 years ofage.

Adverse effects: Mild gastrointestinal discomfort, headache, allergic skin irrtation.

Dose: *Adults*, Usually one or two soft capsules twice daily.

GINMACTON® *(Pharmabox)*

Capsule, Ginkgo Biloba Ext. 80 mg; dark green coloured oblong soft capsule.

Pack - 30 capsules/box.

Generic name: Ginkgo Biloba Ext.

Indicatins: Treatment of blood circulation disorder in peripheral arteries (intermittent claudication); Treatment of dizziness, vascular or regressive tinnitus; Treatment of organic cerebral dysfunction that accompanies the athymia such as tinnitus, headache, hypomnessis, disorder in the concentration, depression, dizziness.

Contra-indication: Hypersensitivity to Ginkgo Biloba ext.

Adverse effects: Rarely, gastrointestinal discomfort, headache, allergic skin reaction.

Precautions: Hypertension; pregnancy; children under 12 years of age.

LIV. 52® *(Titan)*

Tablet, Pdrs. Capparis spinosa 65 mg, Cichorium intybus 65 mg, Mandur bhasma 33 mg, Solanum nigrum 32 mg, Terminalia arjuna 32 mg, Cassia occidentalis 16 mg, Achillea millefolium 16 mg, Tamarix gallica 16 mg. Processed in Eclipta alba, Phyllanthus amarus, Boerhaavia diffusa, Tinospora cordifolia, Raphanus sativus,Emblica officinalis, Plumbago zeylanica, Embelia ribes,Terminalia chebula, Fumaria officinalis.

Pack - 100.

Syrup, Exts. Capparis spinosa 34 mg, Cichorium intybus 34 mg, Solanum nigrum 16 mg, Terminalia arjuna 16 mg, Cassia occidentalis 8 mg, Achillea millefolium 8 mg, Tamarix gallica 8 mg per 5 ml. Processed in Eclipta alba, Phyllanthus amarus, Boerhaavia diffusa, Tinospora cordifolia, Raphanus sativus,Emblica officinalis, Plumbago zeylanica, Embelia ribes,Terminalia chebula, Fumaria officinalis.

Pack - 100 ml.

Therapeutic category: Hepatoprotective agent.

Pharmacology: Liv. 52 restores the functional efficiency of the liver by protecting the hepatic parenchyma and promoting hepatocellular regeneration. The antiperoxidative activity of Liv. 52 prevents the loss of functional integrity of the cell membrane, maintains cytochrome P-450, hastens the recovery period and ensures early restoration of hepatic functions in infective hepatitis. Liv. 52 facilitates rapid elimination of acetaldehyde, the toxic intermediate metabolite of alcohol metabolism, and ensures protection from alcohol-induced hepatic damage. Liv. 52 diminishes the

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lipotropic activity in chronic alcoholism, and prevents fatty infiltration of the liver. In pre-cirrhotic conditions, Liv. 52 arrests the progress of the disease and prevents further liver damage. As a daily health supplement, Liv. 52 improves appetite, the digestion and assimilation processes and promotes weight gain.

Indications: In the prevention and treatment of: Viral hepatitis; Alcoholic liver disease; Pre-cirrhotic conditions and early cirrhosis; Protein energy malnutrition; Loss of appetite; Radiation and chemotherapy-induced liver damage; As an adjuvant to hepatotoxic drugs; A valuable adjuvant during convalescence and prolonged illness.

Interactions: Liv. 52 reduces the blood level of ibuprofen, which may possibly suggest delayed absorption. It also reduces the bioavailability of tetracycline and doxycycline.

Dose: By mouth, *With Anti-TB Treatment,* 2 tabs b.i.d. along with anti-TB treatment.
In Acute Viral Hepatitis, Adult, 2 tabs t.i.d. or 15 ml 3-4 times daily.
Child (1-3 years), 2.5 ml b.i.d.; 3-8 years, 5 ml b.i.d.; 8-15 years, 7.5-10 ml 2-3 times daily or Child: 1 tab t.i.d.
In Cirrhosis, 2 tabs t.i.d. for 6-12 months.
In Chronic Active Hepatitis, 2 tabs t.i.d. for 6 months.
In Alcohol-Induced Liver Damage, 2 tablets t.i.d. for 1 month, then 1 tab t.i.d. for 6-12 months.
In Anorexia and Weight Loss, Adult, 2 tabs t.i.d. or 10 ml 2-3 times daily.
Child: 1 tab t.i.d. or 5 ml 2-3 times daily.
As a daily Health Supplement, 2 tabs b.i.d.

Ranbaxy's Garlic Pearls *(Ranbaxy)*
Pearl, Garlic oil 0.25% w/w, excipients q.s. to 250 mg; pure oil of raw garlic in soft gelatin pearl.
Pack - 30's; 100's (in bottles).

Indications: Ranbaxy's Garlic Pearls expel gas from the intestine. The tendency to gas formation is also reduced considerably due to the correction of the faulty digestion which is mainly responsible for excessive gas in the intestine. It relieves congestion in the chest and the nasal passage, thus minimizing the frequency of cold attacks. Garlic reduces high cholesterol levels. Garlic helps in easing disabling pains.

Dose: 1-2 pearls before or after meals.

RED GINSENG plus *(Pharmabox)*
Liquid, Purified water, Ground Fresh Ginseng, Korean Red Ginseng Extract, Citric Acid, Vitamin C, Fructose (100% Pure Korean Ginseng).
Pack - 20's; 100's.

Therapeutic category Ginseng extract.
Shake well before drinking. Best when chilled.

7. Drugs acting on the respiratory tract

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7.1 Antiasthmatic drugs
7.1.1 Bronchodilators
7.1.2 Corticosteroids
7.1.3 Prophylactic drugs
7.1.4 Inhaler devices
7.2 Expectorants and cough suppressants

7.1 Antiasthmatic drugs

7.1.1 Bronchodilators
7.1.2 Corticosteroids
7.1.3 Prophylactic drugs
7.1.4 Inhaler devices

Asthma

Asthma is a chronic inflammatory disease characterized by episodes of reversible airways obstruction due to bronchial hyperresponsiveness; inflammation may lead to irreversible obstruction in a few patients. A classification based on severity before the start of treatment and disease progression is of importance when decisions have to be made about management. It can be divided by severity into intermittent, mild persistent, moderate persistent and severe persistent. These are useful in the management of the disease since therapy has a stepwise approach which must be discussed with the patient before commencing therapy. The level of therapy is increased as the severity of the asthma increases with stepping-down if control is sustained (see tables on treatment below).

INHALATION

Medications for asthma can be administered in several different ways, including inhaled, oral and parenteral (subcutaneous, intramuscular, or intravenous). The main advantage of delivering drugs directly into the airways via inhalation is that high concentrations can be delivered more effectively and rapidly to the airways, and systemic adverse effects avoided or minimized.

It is important that patients receive careful instruction in the use of pressurized (aerosol) inhalation (using a metered-dose inhaler) to obtain optimum results. Before use, the inhaler should be shaken well. After exhaling as completely as possible, the mouthpiece of the inhaler should be placed well into the mouth and the lips firmly closed around it. The patient should

inhale deeply through the mouth while actuating the inhaler. After holding the breath for 10 seconds or as long as is comfortable, the mouthpiece should be removed and the patient should exhale slowly.

It is important to check that patients continue to use their inhalers correctly as inadequate technique may be mistaken for drug failure. Spacing devices provide a space between the inhaler and the mouth. They may be of benefit for patients such as the elderly, small children and the asthmatic who find inhalers difficult to use or for those who have difficulty synchronizing their breathing with administration of the aerosol. A large volume spacing device is also recommended for inhalation of high doses of corticosteroids to reduce oropharyngeal deposition which can cause candidosis. The use of metered-dose inhalers with spacers is less expensive and may be as effective as use of nebulizers, although drug delivery may be affected by choice of spacing device.

Breath-actuated devices including dry powder inhalers are also available.

Solutions for nebulization are available for use in acute severe asthma. They are administered over a period of 5–10 minutes from a nebulizer, usually driven by oxygen in hospital.

ORAL

The oral route is used when administration by inhalation is not possible. Systemic adverse effects occur more frequently when a drug is given orally rather than by inhalation. Drugs given by mouth for the treatment of asthma include beta$_2$ -agonists, corticosteroids, and theophylline.

PARENTERAL

Drugs such as beta$_2$-agonists, corticosteroids, and aminophylline may be given by injection in acute severe asthma when administration by nebulization is inadequate or inappropriate. If the patient is being treated in the community, urgent transfer to hospital should be arranged.

PREGNANCY

Poorly controlled asthma in pregnant women can have an adverse effect on the fetus, resulting in perinatal mortality, increased prematurity and low birth-weight. For this reason using medications to obtain optimal control of asthma is justified. Administration of drugs by inhalation during pregnancy has the advantage that plasma drug concentrations are not likely to be high enough to have an effect on the fetus. Acute exacerbations should be treated aggressively in order to avoid fetal hypoxia.

Acute exacerbation of asthma

Severe asthma can be fatal and **must** be treated promptly and energetically. Acute severe asthma attacks require hospital admission where resuscitation facilities are immediately available.

Severe asthma is characterized by persistent dyspnoea poorly relieved by bronchodilators, exhaustion, a high pulse rate (usually more than 110/minute) and a very low peak expiratory flow.

As asthma becomes more severe, wheezing may be absent. Patients should be given oxygen 40–60% (if available) (see also section 3.1.3). Patients should also be given **salbutamol** or terbutaline via a nebulizer. In emergencies where a nebulizer is not available, salbutamol 100 micrograms by aerosol inhalation can be repeated 10–20 times preferably using a large-volume spacing device. Patients should also be given a **corticosteroid**; for adults, prednisolone 30–60 mg by mouth or hydrocortisone 200 mg (preferably as sodium succinate) intravenously; for children, prednisolone 1–2 mg/kg by mouth (1–4 years, maximum 20 mg, 5–15 years, maximum 40 mg) or hydrocortisone 100 mg (preferably as sodium succinate) intravenously; if the patient experiences vomiting the parenteral route may be preferred for the first dose.

If response is inadequate, **ipratropium** by nebulizer should be considered. Most patients do not benefit from the addition of intravenous aminophylline or a parenteral beta$_2$-agonist; both cause more adverse effects than nebulized beta$_2$-agonists. Nevertheless, an occasional patient who has not been taking theophylline, may benefit from a slow intravenous infusion of aminophylline.

The use of **epinephrine** (**adrenaline**) (see section 8.2) in asthma has generally been superseded by beta$_2$-selective adrenoceptor agonists.

Treatment should **never** be delayed for investigations, patients should **never** be sedated and the possibility of

TREATMENT OF CHRONIC ASTHMA:
INFANTS AND YOUNG CHILDREN UNDER 5 YEARS OLD
Preferred treatments are in bold print

	Long-term Preventive	Quick Relief
STEP 4 Severe Persistent	Daily medications •**Inhaled corticosteroid**, beclometasone dipropionate MDI with spacer and face mask > 1 mg daily *or* nebulized beclometasone > 1 mg twice daily Consider short course of soluble prednisolone tablets, regular inhaled long-acting beta$_2$-agonist *or* modified-release theophylline *Also* , nebulized beta$_2$-agonist	• Inhaled short-acting bronchodilator: **inhaled beta$_2$-agonist** *or* ipratropium bromide as needed for symptoms, not to exceed 3–4 times daily
STEP 3 Moderate Persistent	Daily medications •**Inhaled corticosteroid** , beclometasone dipropionate MDI with spacer and face mask 400–800 micrograms daily *or* nebulized beclometasone $\leq$ 1 mg twice daily Consider short course of soluble prednisolone tablets, regular inhaled long-acting beta$_2$ -agonist *or* modified-release theophylline	• Inhaled short-acting bronchodilator: **inhaled beta2-agonist** *or* ipratropium bromide as needed for symptoms, not to exceed 3–4 times daily
STEP 2 Mild Persistent	Daily medications • Either **inhaled corticosteroid** , beclometasone dipropionate, 400–800 micrograms, *or* cromoglicate (use MDI with a spacer and face mask *or* use a nebulizer)	• Inhaled short-acting bronchodilator: **inhaled beta2-agonist** or ipratropium bromide as needed for symptoms, not to exceed 3–4 times daily
STEP 1 Intermittent	• None needed	• Inhaled short-acting

RETURN

TREATMENT OF CHRONIC ASTHMA:
ADULTS AND CHILDREN OVER 5 YEARS OLD
Preferred treatments are in bold print

	Long-term Preventive	Quick Relief
STEP 4 Severe Persistent	Daily medications • **Inhaled corticosteroid**, beclometasone dipropionate 0.8–2 mg + • Long-acting bronchodilator: *either* **long-acting inhaled beta$_2$-agonist**, *and/or* modified-release theophylline, *and/or* long-acting beta$_2$-agonist tablets or syrup + • corticosteroid tablets or syrup long term	• Short-acting bronchodilator: **inhaled beta$_2$-agonist** as needed for symptoms
STEP 3 Moderate Persistent	Daily medications • **Inhaled corticosteroid**, beclometasone diproprionate 0.8–2 mg daily in divided doses + if needed • Long-acting bronchodilator: *either* **long-acting inhaled beta$_2$-agonist**, modified-release theophylline, *or* long-acting beta$_2$-agonist tablets or syrup	• Short-acting bronchodilator: **inhaled beta$_2$-agonist** as needed for symptoms, not to exceed 3–4 times daily
STEP 2 Mild Persistent	Daily medications • Either **inhaled corticosteroid**, beclometasone dipropionate 100–400 micrograms twice daily, sodium cromoglicate *or* modified-release theophylline	• Short-acting bronchodilator: **inhaled beta$_2$-agonist** as needed for symptoms, not to exceed 3–4 times daily
STEP 1 Intermittent	• None needed	• Short-acting bronchodilator: **inhaled beta$_2$-agonist** as needed for symptoms (up to once daily) • Intensity of treatment will depend on severity of attack • Inhaled beta$_2$ -agonist or sodium cromoglicate before exercise or exposure to allergen
	Step down Review treatment every 3 to 6 months. If control is sustained for at least 3 months, a gradual stepwise	Step up If control is not achieved, consider step up. But first: review patient

pneumothorax should be considered. Patients who deteriorate further despite treatment may need intermittent positive pressure ventilation.

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (chronic bronchitis and emphysema) may be helped by an inhaled short-acting **beta$_2$-adrenoceptor agonist** used as required *or* when the airways obstruction is more severe, by an inhaled **anticholinergic (antimuscarinic) bronchodilator** or both if necessary. Although many patients are treated with an inhaled corticosteroid its role in chronic obstructive pulmonary disease is not clear at present. A limited trial of high-dose inhaled corticosteroid *or* an oral corticosteroid is recommended for patients with moderate airflow obstruction to determine the extent of the airway reversibility and to ensure that asthma has not been overlooked.

Long-term oxygen therapy prolongs survival in some patients with chronic obstructive pulmonary disease.

7.1.1. Bronchodilators

Beta$_2$-adrenoceptor agonists (beta$_2$-adrenoceptor stimulants)

The adrenoreceptors in bronchi are mainly beta$_2$ type and their stimulation causes bronchial muscles to relax. The beta$_2$-adrenoceptor agonists include **salbutamol**, terbutaline, and fenoterol.

When salbutamol is given by inhalation (100–200 micrograms) the effect can last as long as 4 hours thus making it suitable for both the treatment (see Tables) and prevention of asthma. Salbutamol can also be taken orally in a dose of 2–4 mg up to 4 times daily but is less effective and causes more adverse effects. It can also be given by injection for severe bronchospasm.

ADVERSE EFFECTS

Cardiovascular adverse effects (arrhythmias, palpitations and tachycardia) may occur with salbutamol, but are infrequent with inhaled preparations. Hypokalaemia may result from beta2 -adrenoceptor agonist therapy. Particular caution is required in severe asthma because this effect may be potentiated by concomitant treatment with xanthines (for example theophylline), corticosteroids, diuretics and hypoxia. Plasma potassium concentrations should be monitored in severe asthma.

Xanthines

Xanthines include **theophylline** and **aminophylline**. They relax bronchial smooth muscle relieving bronchospasm and also stimulate respiration. Absorption of theophylline from the gastrointestinal tract is usually rapid and complete. It is metabolized by the liver but its half-life can vary considerably in certain diseases including hepatic impairment and cardiac failure, with some coadministered drugs (see Appendix 1) as well as by factors such as age, smoking and alcohol intake. The half-life variation can be important because theophylline has a narrow margin between therapeutic and toxic effects. At therapeutic doses some patients experience nausea and diarrhoea and when plasma concentrations exceed the recommended range of 10–20 mg/litre (55–110 micromol/litre) arrhythmias and convulsions which may be fatal can occur. Monitoring of plasma concentrations is therefore recommended. Theophylline is used to treat chronic asthma, usually in the form of modified-release preparations which produce adequate plasma concentrations for up to 12 hours. It is used as an adjunct to beta2 -agonist or corticosteroid therapy when additional bronchodilation is required but there is an increased risk of adverse effects with beta2 -agonists (see above). When given as a single dose at night, modified-release preparations may be useful in controlling nocturnal asthma and early morning wheezing.

The absorption characteristics of modified-release theophylline peparations vary considerably and therefore it is important to keep the patient on the same brand-name formulation.

Theophylline is given by injection as aminophylline (a mixture of theophylline with ethylenediamine) which is 20 times more soluble in water than theophylline alone. It is administered by slow intravenous injection in severe asthma attacks.

Anticholinergic (antimuscarinic) bronchodilators

Ipratropium can provide short-term relief in chronic asthma, but short-acting beta$_2$-agonists work more quickly. Ipratropium is also used as a bronchodilator in chronic obstructive pulmonary disease.

Salmeterol is a new class of selective beta$_2$-adrenoceptor agonist and, at therapeutic dosage, it has little or no measurable cardiovascular effect. It produces long-lasting bronchodilatation of up to at least 12 hours in subjects with reversible airways obstructions. Salmeterol acts by inhibiting the release, from human lung, of mast cell derived mediators, such as histamine, leukotrienes and prostaglandins D_2. It inhibits bronchial hyper-responsiveness to inhaled allergen producing anti-inflammatory as well as bronchodilator activity. Salmeterol is not suitable for the relief of an acute attack (a short-acting beta$_2$-stimulant such as salbutamol should be used). It can be used together with the corticosteroid and not used to replace it.

AEROSOL INSTRUCTIONS

Beta-adrenergic drugs when administered by inhalation have a more rapid onset of action

and a longer duration of action than when administered orally. Inhalation of these sympathomimetic drugs also induces significant bronchodilation with only minimal adverse effects. Factors such as the rate and depth of inhalation, length of time that the breath is held after inhalation and placement of the inhaler mouthpiece into the mouth can affect the bronchial concentration of inhaled medications.

For the proper use of the pressurised metered-dose aerosol inhalers:

1. Shake the aerosol canister before each use and remove the cap.
2. Hold the inhaler about 2 inches from an open mouth or inhale the medication through a four-inch paper tube spacer placed on the end of the actuator in order to enhance the amount of medication reaching the bronchial receptors.
3. Tilt your head back slightly to form as straight a channel as possible to maximise the dept of airway penetration by the drug.
4. Breathe out fully but normally. The dose of the drug will be more uniformly distributed in the lungs when inhaled after a normal exhalation.
5. Breathe in deeply and slowly over 4-5 seconds while simultaneously depressing fully the top of the metal canister. A fourteen-fold higher concentration of the drug will be deposited in the lung after a slow 4-5 second inhalation (0.5 L/sec) as compared to a fast 1-2 second inhalation (2.0 L/sec) because more drug reaches the airways instead of impacting on the large airways. The dept of inhalation also enhances the amount of drug retained by the lung.
6. Hold your breathe for about 5-10 seconds after inhalation to prevent exhaling particles of drug which would normally deposit in the lung due to gravitational effects.
7. Allow 5-10 minutes for the first inhaled dose to take effect and repeat the above procedure if a second inhalation is prescribed.
8. Clean the inhaler thoroughly; remove the metal canister and rinse the plastic case and cap thoroughly under running water at least once a day.
9. Dry the plastic case and cap; and put the metal canister back into the case with a twisting motion, and then put the cap back on.
10. Do not store the inhaler near heat or an open flame because its contents are under pressure.

SALBUTAMOL

Salbutamol is a representative beta$_2$-adrenoceptor agonist. Various drugs can serve as alternatives.

Synonym: Albuterol.

Therapeutic category: Selective beta$_2$-agonist; Bronchodilator, Sympathomimetic.

Indications: Prophylaxis and treatment of asthma; premature labour (section 11.1)

Precautions: Hyperthyroidism, myocardial insufficiency, arrhythmias, susceptibility to QT-interval prolongation, hypertension, pregnancy (but appropriate to use; see also notes above); breastfeeding (Appendix 3); diabetes mellitus—especially intravenous administration (monitor blood glucose; ketoacidosis reported); **interactions**: Appendix 1.

Adverse effects: Hypokalaemia after high doses (see notes above); arrhythmias, tachycardia, palpitations, peripheral vasodilation, fine tremor (usually hands), muscle cramps, headache, insomnia, behavioural disturbances in children; hypersensitivity reactions including paradoxical bronchospasm, urticaria and angioedema; slight pain on intramuscular injection.

Advice to patients: Do not exceed recommended dosage; rinse mouth with water following each inhalation to help with dry throat and mouth; follow specific instructions accompanying inhaler; if more than one inhalation is necessary, wait at least 1 full minute between inhalations. May cause nervousness, restlessness, insomnia; if these effects continue after dosage reduction, notify physician; also notify physician if palpitations, tachycardia, chest pain, muscle tremors, dizziness, headache, flushing or if breathing difficulty persists.

Nursing considerations: •Before using, the inhaler must be shaken well.

•Relieve dry mouth with sips of water or gum.

•Assess lung sounds, pulse, and B.P. before administration and during peak of medication.

•Observe patient for wheezing after administration; if this occurs, call physician.

•Teach patient how to use metered dose inhaler.

Dose: *Chronic asthma* (when inhalation is ineffective), by mouth , ADULT 2–4 mg 3 or 4 times daily; in some patients up to maximum of 8 mg 3 or 4 times daily; CHILD under 2 years, 100 micrograms/kg 4 times daily, 2–6 years, 1–2 mg 3–4 times daily, 6–12 years, 2 mg 3–4 times daily.

Severe acute bronchospasm, by slow intravenous injection , ADULT 250 micrograms, repeated if necessary.

Relief of acute bronchospasm, by aerosol inhalation, ADULT 100–200 micrograms (1–2 puffs); CHILD 100 micrograms (1 puff) increased to 200 micrograms (2 puffs) if necessary; by intramuscular or subcutaneous injection, ADULT 500 micrograms repeated every 4 hours if necessary.

Prophylaxis of exercise-induced bronchospasm, by aerosol inhalation, ADULT 200 micrograms (2 puffs); CHILD 100 micrograms (1 puff) increased to 200 micrograms (2 puffs) if required.
Chronic asthma (as adjunct in stepped treatment), by aerosol inhalation, ADULT 100–200 micrograms (1–2 puffs) up to 3–4 times daily; CHILD 100 micrograms (1 puff) 3–4 times daily, increased to 200 micrograms (2 puffs) 3–4 times daily if necessary.
Severe acute asthma or chronic bronchospasm unresponsive to conventional treatment, by inhalation of nebulized solution, ADULT and CHILD over 18 months, 2.5 mg repeated up to 4 times daily; may be increased to 5 mg if necessary—medical assessment should be considered since alternative therapy may be indicated; CHILD under 18 months, clinical efficacy uncertain (transient hypoxaemia may occur—consider oxygen supplementation).

POM **Salbutamol** *(WMF 25.1)*
Tablets, Salbutamol (as sulfate) 2 mg, 4 mg
Syrup, Salbutamol (as sulfate) 2 mg/5 ml
Injection (Solution for injection), Salbutamol (as sulfate) 50 micrograms/ml, 5-ml ampoule.
Aerosol inhalation (Pressurized inhalation), Salbutamol (as sulfate) 100 micrograms/metered inhalation.
Nebulizer solution, Salbutamol (as sulfate) 5 mg/ml; in 20-ml ampoules.

POM **Salbutamol** *(EDL 26.1)*
Tablet, Salbutamol (as sulfate) 2 mg, 4 mg
Syrup, Salbutamol (as sulfate) 2 mg per 5 ml.
Aerosol Inhalation, Salbutamol 0.1 mg per metered dose.

POM **AEROBUTAMOL**® *(Korlyns)*
Inhaler, Salbutamol BP 100 mcg; white or slightly yellow suspension mixed with just right quantity of propellant and kept in a pressurized canister with a metered valve system.
Pack - 200 doses.

POM **ASMACARE**® *(Dana)*
Syrup, Salbutamol (as sulfate) BP 2 mg per 5 ml.
Pack - 100 ml.

POM **ASMALYN**® *(Mopson)*
Syrup, Salbutamol 2 mg per 5 ml.
Pack - 100 ml, 2 L.

POM **ASTHIN**® (*Titan*)
Tablet, Salbutamol 2 mg.
2 mg - 10 x 50.

POM **Salbutamol** *(Emzor)*
Tablet, Salbutamol 4 mg; white scored tab. marked 'EMZOR 4'.
4 mg - 500.

POM **Salbutamol** *(Vitabiotics)*
Tablets, Salbutamol (as sulfate) 4 mg.
4 mg - 500's.

POM **SALBUTOL**® *(Dizpharm)*
Inhaler, Salbutamol 0.1 mg per metered dose.

POM **VENTAMOL**® *(Hovid)*
Tablets, Salbutamol 2 mg, 4 mg.
2mg - 10 x 10 (blister).
4 mg - 1000
Syrup, Salbutamol 2 mg per 5 ml
Pack - 100 ml.

POM **VENTOLIN**® *(GSK)*
Tablets, Salbutamol (as Sulfate) 2 mg, pink tab. marked 'AH 1K' and '2'; 4 mg, pink tab. marked 'AH 2k' and '4'.
2 mg - 20; 100; 500.
4 mg - 20; 100, 500.
Syrup, Salbutamol (as Sulfate) 2 mg per 5 ml; fruit-flavoured, sugar- and colouring-free syrup.
Pack - 150 ml.
Inhaler, Salbutamol 100 mcg per dose; metered-dose aerosol.
Pack - 200 - dose unit.

POM **ZOTREX**® *(Fill Pharma)*
Tablets, Salbutamol (as sulfate) 2 mg, 4 mg.
2 mg - 500.

Other Preparations of Salbutamol
For Oral use:
POM **VOLMAX**® *(GSK)*
Tablets, Salbutamol sulfate 4 mg, white hexagonal controlled release tabs marked '4' on one side; 8 mg, white hexagonal controlled release tabs marked '8' on one side. Both have a hole in the outer coat which allows osmotically controlled release of the drug.
Advice to patients: See Label 25 in Appendix 6.
Dose: Adult, 8 mg twice daily.

Child (3-12 years), 4 mg twice daily.

For Parenteral Use:

POM **VENTOLIN**® *(GSK)*

Injection, Salbutamol sulfate 500 mg per ml; colourless or faintly straw-coloured solution in a 1ml clear, neutral glass amp.

Solution for intravenous infusion, Salbutamol sulfate 1000 mcg/ml (5 mg per 5 ml); colourless or faintly straw-coloured solution in a 5 ml clear neutral glass amp.

Note: To be diluted to 50% of the original strength before administration.

Parenteral preparations of Ventolin® should not be administered in the same syringe or infusion as any other medication.

Dose: *In severe bronchospasm and status asthmaticus*, By s.c. or i.m. injection, Adult, 500 mcg (8 mcg/kg b.w.), repeated every four hours as required.

By slow i.v. injection, adult, 250 mcg (4 mcg/kg b.w.), repeated if necessary.

By i.v. inusion, Adult, initially 5 mcg per minute, adjusted according to patient response and heart-rate usually in the range of 3-20 mcg per minute. Higher dosages may be used especially in patients with respiratory failure.

Child: Not recommended.

Preparation of Ventolin Solution for infusion: A suitable solution for infusion may be prepared by diluting 5 ml of Ventolin solution for intravenous infusion in 500 ml of an infusion solution such as Sodium Chloride and Dextrose Injection B.P to provide a salbutamol dose of 10 mcg per ml of solution.

SALMETEROL

Therapeutic category: Long acting selective B_2-agonist; Bronchodilator.

Indications: Long-term regular treatment of reversible airways obstruction in asthma (including patients with nocturnal asthma and exercise-induced asthma) and chronic bronchitis.

Precautions: Thyrotoxicosis, pregnancy, lactation.

Interactions: Non-selective beta-blockers such as propranolol; cardioselective beta-blockers.

Adverse effects: Tremor, paradoxical bronchospasm (discontinue treatment immediately), headache, subjective palpitations, hypokalaemia.

Advice to patients: Do not use to treat acute symptoms; do not exceed the prescribed dose of salmetrol; do not stop using inhaled or oral cortcosteroids without medical advise even if you "feel better"; shake well before using. Avoid spraying in eyes; remove the canister and rinse the plastic case and cap under warm water and dry daily. Store the canister with nozzle end down.

Nursing considerations: •Before using, the inhaler must be shaken well.
•Relieve dry mouth with sips of water or gum.
•Not to be used for the relief of acute attacks.
•Monitor lung sounds, pulse, B.P.
•Observe for wheezing after administration and notify physician if it occurs.
•Teach patient how to use metered dose inhaler.

Dose: By inhalation, 50 mcg (2 inhalations) twice daily; increased to 100 mcg (4 inhalations) twice daily in more severe airways obstruction.

Child: (over 4 years) 2 inhalations twice daily.

Not recommended for children under 4 years.

POM **SEREVENT**® *(GSK)*

Aerosol inhalation, Salmeterol (as the hydroxynaphthoic acid salt) 25 mcg per dose (actuation); in pressurised metered-dose inhaler. Each canister provides 120 actuations.

SALMETEROL plus FLUTICASONE

Indications: Treatment of Reversible Obstructive Airways Disease (ROAD) including asthma in children and adults, where use of a combination (bronchodilator and inhaled corticosteriod) is appropriate namely Patients on effective maintenance doses of long acting beta agonists and inhaled corticosteroids; Patients who are symptomatic on current inhaled corticosteriod therapy; Patients on regular bronchodilator therapy who require inhaled corticosteriods.

Treatment of Chronic Obstructive Pulmonary Disease (COPD) including chronic bronchitis and emphysema.

Contra-indications: History of hypersensitivity to any of the ingredients.

Precautions: Avoid use in acute attacks (fast and short acting bronchodilator e.g. salbutamol is required); avoid abrupt discontinuation of therapy in patients with asthma due to risk of excerbation; active or quiescent pulmonary tuberculosis; high doses and prolonged use may cause systemic effects namely Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. Monitor height of children on prolonged therapy regularly. Patients transferring from oral steroid therapy to inhaled fluticasone therapy should be monitored for possibility of impaired adrenal response (withdrawal of systemic therapy should be gradual). History of diabetes mellitus (may increase blood sugar levels). Pregnancy and lactation

Interactions: Avoid co-administration with ritonavir (may greatly increase fluticasone plasma concentrations), and beta blockers.
Adverse effects: Paradoxical bronchospasm may occur with an immediate increase in wheezing after dosing; discontinue medication and treat immediately with a fast and short acting inhaled bronchodilator).
Salmeterol, a beta-agonist, may cause tremor, subjective palpitations and headache; Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles); Arthralgia and hypersensitivity reactions including rash, oedema, angioedema, oropharyngeal irritations; Rarely, muscle cramps, hyperglycaemia.
Fluticasone propionate, a corticosteroid, may cause hoarsness and candidiasis (thrush) of the mouth and throat; Rarely, hypersensitivity reactions, respiratory symptoms (dyspnoea and/or bronchospasm) and very rarely, anaphylactic reactions.
Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma; Rarely, hyperglycaemia, anxiety, sleep disorders and behavioural changes, including hyperactivity and irritability (predominantly in children).
Dose: See under the preparations below.

POM **SERETIDE EVOHALER®** *(GSK)*
Aerosol Inhalation, (25/50 mcg), Salmeterol 25 mcg, fluticasone 50 mcg.
Aerosol Inhalation, (25/125 mcg), Salmeterol 25 mcg, fluticasone 125 mcg.
Aerosol Inhalation, (25/250 mcg), Salmeterol 25 mcg, fluticasone 250 mcg.
Dose: By inhalation, *Reversible Obstructive Airways Disease (ROAD)*, Adults and adolescents 12 years and older, 2 inhalations of 25/50 mcg or 25/125 mcg or 25/250 mcg twice daily.
Adults 18 years and older: may double dose for up to 14 days.
Children 4 years and older: 2 inhalations of 25/50 mcg twice daily.
Children under 4 years: not recommended.
Chronic Obstructive Pulmonary Disease (COPD), Adult, 2 inhalations of 25/125 mcg to 25/250 mcg twice daily.
No dosage adjustement is required in elderly, renal or hepatic impairment.

POM **SERETIDE ACCUHALER®** *(GSK)*
Aerosol Inhalation, (50/100 mcg), Salmeterol 50 mcg, fluticasone 100 mcg.
Aerosol Inhalation, (50/250 mcg), Salmeterol 50 mcg, fluticasone 250 mcg.
Aerosol Inhalation, (50/500 mcg), Salmeterol 50 mcg, fluticasone 250 mcg.
Dose: By inhalation, *Reversible Obstructive Airways Disease (ROAD)*, Adults and adolescents 12 years and older, 1 inhalation of 50/100 mcg or 50/250 mcg or 50/500 mcg twice daily.
Adults 18 years and older: may double dose for up to 14 days.
Children 4 years and older: 1 inhalation of 50/100 mcg twice daily.
Children under 4 years: not recommended.
Chronic Obstructive Pulmonary Disease (COPD), Adult, 1 inhalation of 50/250 mcg to 50/500 mcg twice daily.
No dosage adjustement is required in elderly, renal or hepatic impairment.

ADRENALINE

Synonym: Epinephrine.
Therapeutic category: Adrenergic Agonist; Bronchodilator; Sympathomimetic.
Indications: Severe acute attacks of bronchial asthma.
Contra-indications, Precautions, e.t.c: See Adrenaline in section 8.2.
Nursing considerations: •Read the labels to make sure you are using correct concentration, route and dosage.
•Shake before using; rotate IM/SC inj sites; massage after injection.
•Monitor injection site for tissue damage.
•Warn patient to avoid the use of OTC Adrenaline inhalation products; beta$_2$-adrenergic agents for inhalation are preferred.
Dose: By S. C. Injection, Adult, 0.2-0.5 ml (200-500 mcg) of a 1 in 1000 aqueous solution, repeated at intervals of 15-30 minutes if necessary.
Child: 0.01 ml (10 mcg) per kg body-wt.; up to a max. 0.5 ml (500 mcg) as a single dose.
See lit. for details.

POM **Adrenaline** *(EDL 26.1)*
Injection, Adrenaline (as bitartrate or HCl) 1 mg per ml (1 in 1000); in 1 ml amp.

AMINOPHYLLINE

Synonym: Theophylline ethylenediamine.
Therapeutic category: Bronchodilator.
Pharmacology: Aminophylline relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels by inhibitng phosphodiesterase, the enzyme that degrades cyclic AMP. It contains theophylline and ethylenediamine (2:1). See notes above.
Indications: Severe airways obstruction, status asthmaticus.
Contra-indications: Uncontrolled arrhythmias, hyperthyroidism, peptic ulcers, uncontrolled seizure disorders, hypersensitivity to xanthines or any component.

Precautions: Children, elderly, cardiac and liver diseases, history of peptic ulceration, breast-feeding, fever, epilepsy. Drug clearance is accelerated in smokers (may need to adjust dose).

Interactions: •Drugs which increase the half-life of aminophylline include propranolol, erythromycin, ciprofloxacin and contraceptive steroids.

•Drugs which shorten the half-life of aminophylline are phenytoin, carbamazepine, barbiturates, rifampicin.

•Hence, adjustment of dose is necessary when any of these drugs is co-administered with aminophylline to guide against toxicity.

Adverse effects: GI irritation, stimulation of the CNS, visual disorders, hypotension, hyperthermia, convulsions, headache, palpitation, tachycardia; collapse and sudden death if injected rapidly; pain at i.m. injection site.

Advice to patients: See Label 21 in Appendix 6. Take oral dose with a full glass of water; capsule forms may be opened and sprinkled on soft foods; notify physician if nausea, vomiting, severe GI pain, restlessness or irregular heartbeat occurs; do not drink or eat large quantities of caffeine-containing beverages or food (colas, coffee, chocolate); do not chew or crush enteric coated or sustained release products; take at regular intervals; notify physician if insomnia, nervousness, irritability, palpitations, seizures occur; do not change brands or doses without consulting physician. Check with doctor or pharmacist before taking other drugs including OTC medications.

Nursing considerations: •Administer orally with a full glass of water after meals to decrease GI upset, although food may delay absorption; do not crush sustained release or enteric coated drug products.

•I.V. dose should be diluted in D_5W to prevent the burning effect; use only clear solution; avoid IM inj, may cause pain and tissue damage.

•Monitor vital signs; record I&O.

•Encourage patient to drink adequate fluids to decrease mucous viscosity.

•Advise patient to avoid hazardous activities because dizziness may occur.

Dose: By mouth, 100-300 mg 3 -4 times daily after food.

By slow I.V. injection (over 20 mins), 200-500 mg (5 mg/kg) in 10-20 ml of water.

Child: 5 mg/kg.

See lit. for details.

POM **Aminophylline** *(EDL 26.1)*

Tablets, Aminophylline 100 mg, 200 mg.

Injection, Aminophylline 25 mg per ml; in 10 ml amp.

POM **ASTHAMED®** *(Fill Pharma)*

Tablet, Aminophylline BP 100 mg; f-c tab. 100 mg - 500's.

THEOPHYLLINE and AMINOPHYLLINE

Aminophylline is a representative xanthine bronchodilator. Various drugs including theophylline can serve as alternatives.

Indications: Chronic asthma including nocturnal asthma; acute severe asthma.

Contra-indications: Porphyria; known hypersensitivity to ethylenediamine (for aminophylline).

Precautions: Cardiac disease, hypertension, hyperthyroidism, peptic ulcer, epilepsy, hepatic impairment (Appendix 5), pregnancy (Appendix 2), breastfeeding (Appendix 3), elderly, fever; smokers may require larger or more frequent doses; **interactions**: Appendix 1.

Adverse effects: Nausea and other gastrointestinal disturbances, restlessness, anxiety, tremor, palpitations, headache, insomnia, dizziness; convulsions, arrhythmias and hypotension—especially if given by rapid injection; urticaria, erythema and exfoliative dermatitis—resulting from hypersensitivity to ethylenediamine component of aminophylline.

Dose: *Chronic asthma*, by mouth (as tablets), ADULT and CHILD over 12 years, 100–200 mg 3–4 times daily after food; by mouth (as modified-release tablets) ADULT 300–450 mg every 12 hours

Nocturnal asthma, by mouth (as modified-release tablets), ADULT total daily requirement as single evening dose.

NOTE: PLASMA THEOPHYLLINE CONCENTRATION FOR OPTIMUM RESPONSE 10–20 MG/LITRE (55–110 MICROMOL/LITRE); NARROW MARGIN BETWEEN THERAPEUTIC AND TOXIC DOSE; SEE NOTES ABOVE; A RANGE OF 5–15 MG/LITRE (27.5–82.5 MICROMOL/LITRE) MAY BE EFFECTIVE AND ASSOCIATED WITH FEWER ADVERSE EFFECTS.

Acute severe asthma (**not** previously treated with theophylline), by slow intravenous injection (over at least 20 minutes), ADULT and CHILD 5 mg/kg; maintenance, by intravenous infusion , ADULT 500 micrograms/kg/hour; CHILD 6 months–9 years, 1 mg/kg/hour, 10–16 years, 800 micrograms/kg/hour, adjusted according to plasma-theophylline

concentration.

NOTE: PATIENTS TAKING ORAL THEOPHYLLINE (OR AMINOPHYLLINE) SHOULD NOT NORMALLY RECEIVE INTRAVENOUS AMINOPHYLLINE UNLESS PLASMA-THEOPHYLLINE CONCENTRATION IS AVAILABLE TO GUIDE DOSAGE.

POM **Theophylline and Aminophylline** *(WMF 25.1)*
Tablets, Theophylline 100 mg.
Modified-release tablets, Theophylline 200 mg, 300 mg.
Injection (Solution for injection), aminophylline 25 mg/ml; in 10-ml ampoule

EPHEDRINE plus HYDROXYZINE plus THEOPHYLLINE

Therapeutic category: Antiasthmatic
Pharmacology: As a vasoconstrictor, ephedrine relieves congestion occuring in bronchial asthma. It is a bronchodilator. Theophylline is a bronchospasmolytic. Hydroxyzine modifies the central stimulatory action of ephedrine preventing excessive excitation.
Indications: Prophylactic and symptomatic treatment of bronchial asthma and of bronchospasm associated with respiratory disorders.
Contra-indications: CVS disease, hyperthyroidism, hypertension; hypersensitivity to the drug, early pregnancy.
Precautions: Elderly males; prostatic hypertrophy; road users.
Interactions: CNS depressants, alcohol.
Adverse effects: Palpitation; gastric irritation due to theophylline esp. when given on an empty stomach; insomnia, dryness of throat and nose; headache, sweating.
Advice to patients: See Label 2 in Appendix 6. May cause wakefulness or nervousness; do not take within 2 hours of bedtime to avoid insomnia.
Dose: Adult usually 1 tab. 2-4 times daily; or ½-1 tab. at bedtime in some patients.
Child (over 5 years) and sensitive adults, one-half the usual adult dose; 2-5 years, 2-5 ml 3-4 times daily.
Not recommended for children under 2 years.

POM **Ephedrine plus Hydroxyzine plus Theophylline** *(EDL 26.1)*
Tablet or Syrup, Ephedrine sulfate 25 mg, hydroxyzine HCl 10 mg, theophylline 130 mg per tab or 5 ml syrup.

POM **MARAX®** *(Neimeth)*
Tablet, Hydroxyzine HCl 10 mg, ephedrine sulfate 25 mg, theophylline 130 mg,
Pack - 20, 100.
Syrup, Hydroxyzine HCl 2.5 mg, ephedrine sulfate 6.25 mg, theophylline 32.5 mg per 5 ml.
Pack - 100 ml.

EPHEDRINE plus THEOPHYLLINE

Therapeutic category: Antiasthmatic, bronchodilator.
Indications: Suppression and symptomatic treatment of bronchial asthma. Also in chronic bronchitis and emphysema.
Contra-indications: Hypersensitivity to any of the components; porphyria, unstable angina, arrhythmias, severe hypertension, coronary disease, pregnancy.
Precautions: Renal disease, chest infection, smoking, phaeochromocytoma, prostate disease, diabetes, cardiac or liver disease, peptic ulcer, agitation, hyperthyroidism, glaucoma, elderly or lactation.
Interactions: Cimetidine, erythromycin, ciprofloxacin, oral contraceptives, tricyclics, sympathomimetics; anticonvulsants; diltiazem, verapamil, digoxin; rifampicin; sulphinpyrazone; diuretics; corticosteroids; guanethidine or methyldopa; interferons; MAOIs.
Adverse effects: Palpitations and changes in the heart beat, flushing, giddiness, headache, tremor, anxiety, restlessness, muscle weakness, nausea, vomiting, indigestion, increased thirst, sweating and problem passing water.
Advice to patients: To be taken with a full glass of water; notify physician if nausea, vomiting, seizures, insomnia, irritability, severe GI pain, restlessness, or irregular heart beat occurs; do not drink or eat large quantities of caffeine-containing beverages or food (colas, coffee, chocolate); take at regular intervals. Do not take within 2 hours of bedtime to avoid insomnia.
Nursing considerations: •Encourage patient to drink adequate fluids (2 litres per day) to decrease mucous viscosity.
•Advise patient to avoid hazardous activities if dizziness occurs.
Dose: 1 tab three times daily plus 1 tab at bedtime for patients who get attacks during the night. Not recommended for children under 12 years of age.

POM **Ephedrine plus Theophylline plus Phenobarbitone** *(EDL 26.1)*
Tablet, Ephedrine HCl 11 mg, theophylline 130 mg, phenobarbitone 8 mg.

POM **FRANOL®** *(Sanofi)*
Tablet, Ephedrine HCl 11 mg, theophylline 120 mg.

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Pack - 1000.

POM **ASMANOL-F**® *(Vitabiotics)*
Tablets, Ephedrine HCl 16 mg, theophylline 60 mg, chlorphenamine maleate 2 mg
Pack - 50's.
Dose: See lit.

IPRATROPIUM BROMIDE

Indications: Chronic asthma; chronic obstructive pulmonary disease.
Precautions: Prostatic hypertrophy; pregnancy; glaucoma (standard doses unlikely to be harmful; reported with nebulized drug, particularly in association with nebulized salbutamol).
Adverse effects: Occasionally, dry mouth; rarely, urinary retention, constipation.
Dose: *Chronic asthma or chronic obstructive pulmonary disease*, by aerosol inhalation, ADULT 20–40 micrograms, in early treatment up to 80 micrograms at a time, 3–4 times daily; CHILD up to 6 years, 20 micrograms 3 times daily, 6–12 years, 20–40 micrograms 3 times daily.

POM **Ipratropium bromide** *(WMF 25.1)*
Aerosol inhalation (Pressurized inhalation), Ipratropium bromide 20 micrograms/ metered dose.

7.1.2 Corticosteroids

INHALED CORTICOSTEROIDS
Inhaled corticosteroids, such as **beclometasone**, are the most effective anti-inflammatory medications for the treatment of asthma. They are recommended for the long-term control of asthma in patients using a beta$_2$-adrenoceptor agonist more than once a day. *Regular use* of inhaled corticosteroids reduces the risk of exacerbations of asthma.

Corticosteroids must be used regularly to obtain maximum benefit. Symptom control is usually effective after 3 to 7 days treatment. Long-term high-dose regimens of inhaled corticosteroids are useful for the treatment of severe persistent asthma because they both reduce the need for the long-term use of oral corticosteroids and have fewer systemic adverse effects.

Local adverse effects from inhaled corticosteroids include oropharyngeal candidosis, dysphonia and occasional coughing from upper airway irritation. The use of spacing devices reduces oropharyngeal deposition and thus reduces the incidence of candidosis. The risk for systemic effects of inhaled corticosteroids is small and is dependent upon the dose and potency of the corticosteroid as well as its bioavailability and the plasma half-life of its systemically absorbed fraction. Systemic effects are rare and include skin thinning and easy bruising, a small increased risk of glaucoma and cataracts, adrenal suppression, decrease of bone metabolism and growth retardation in children.

SYSTEMIC CORTICOSTEROIDS
Oral **corticosteroids** (sections 8.3 and 10.3) may be used as 'maximum therapy' to achieve control of a patient's asthma. This may be useful either when initiating long-term therapy for a patient with uncontrolled asthma or as a short 'rescue' course at any stage for acute exacerbation.

Long-term oral corticosteroid therapy may be required to control severe persistent asthma, but its use is limited by the risk of significant adverse effects. In these cases high-dose inhaled corticosteroids should be continued so that oral requirements are reduced to a minimum. Oral doses should be given as a single dose in the morning to reduce the disturbance to the circadian cortisol secretion. Dosage should always be adjusted to the lowest dose which controls symptoms.

Patient Advice: Patients on beclomethasone aerosol should be instructed:

1. To follow the techniques as salbutamol inhaler (see section 7.1.1).
2. Gargle or drink fluids immediately after using his beclomethasone to remove residual corticosteroids from the oral cavity.
3. Unlike with salbutamol, beclomethasone must be used continously on a daily basis even when he is asymptomatic.

BECLOMETHASONE

Beclometasone dipropionate is a representative corticosteroid. Various drugs can serve as alternatives.
Therapeutic category: Corticosteroid; Anti-inflammatory Agent.
Indications: Chronic asthma not controlled by short-acting beta$_2$-adrenoceptor agonists.
Precautions: See notes above; active or

quiescent tuberculosis; systemic therapy may be required during periods of stress or when airway obstruction or mucus prevent drug access to smaller airways; not for relief of acute symptoms; monitor height of children receiving prolonged treatment—if growth slowed, review therapy.

Adverse effects: Oropharyngeal candidosis, cough and dysphonia (usually only with high doses); adrenal suppression, growth retardation in children and adolescents, impaired bone metabolism, glaucoma and cataract (with high doses, but less frequent than with systemic corticosteroids); paradoxical bronchospasm—requires discontinuation and alternative therapy (if mild, may be prevented by inhalation of beta2 -adrenoceptor agonist or by transfer from aerosol to powder inhalation); rarely, urticaria, rash, angioedema.

CANDIDOSIS: CANDIDOSIS CAN BE REDUCED BY USE OF A SPACING DEVICE (SEE NOTES ABOVE); RINSING THE MOUTH WITH WATER AFTER INHALATION MAY HELP TO PREVENT CANDIDOSIS.

Advice to patients: See Label 8 in Appendix 6. Shake thoroughly before using; inhaled beclomethasone makes many asthmatics cough, to reduce chance, inhale drug slowly or use prescribed inhaled bronchodilator 5 minutes before beclomethasone is used; keep inhaler clean and unobstructed, wash in warm water and dry thoroughly; rinse mouth and throat after use to prevent Candida infection; report sore throat or mouth lesions to physician.

Nursing considerations: •Administer by inhalation; instruct patient to wait for one minute before taking subsequent puffs where necessary and to hold his breath after inhalation to enhance action of drug.

•Check mucous membranes for signs of fungal infection; advise patient to gargle/rinse mouth after use to prevent oral fungal infection..

•Relieve dry mouth with sips of water or gum.

•Teach patient proper inhalation techniques.

Dose: *Chronic asthma*, by aerosol inhalation (standard dose inhaler), ADULT 200 micrograms twice daily or 100 micrograms 3–4 times daily (in more severe cases, initially 600–800 micrograms daily); CHILD 50–100 micrograms 2–4 times daily or 100–200 micrograms twice daily.

Chronic asthma, by aerosol inhalation (high dose inhaler), ADULT 500 micrograms twice daily or 250 micrograms 4 times daily; if necessary may be increased to 500 micrograms 4 times daily; CHILD not recommended.

See also under the proprietary preparations below.

POM **Beclomethasone** *(WMF 25.1)*
Aerosol inhalation (Pressurized inhalation), Beclometasone dipropionate 50 micrograms/metered inhalation (standard dose inhaler), 250 micrograms/metered inhalation (high dose inhaler).

POM **Beclomethasone** *(EDL 26.1)*
Aerosol Inhalation, Beclomethasone dipropionate 0.05 mg per metered dose.

POM **BECOTIDE 50®** *(GSK)*
Aerosol Inhalation, Beclomethasone dipropionate 50 mcg per dose; metered-dose aerosol.

Dose: Adult, 4 inhalations (200 mcg) twice a day or 2 inhalations (100 mcg) 3-4 times daily; in more severe cases, initially 600-800 mcg per day reducing according to response.

Child, 1-2 inhalations (50-100 mcg) 2-4 times daily, according to the response.

POM **VIAREX®** *(Supreme)*
Aerosol Inhalation, Beclomethasone dipropionate 50 mcg (0.05 mg) per metered-dose; 200 nasal inhalations (10 ml) in pressurized container.

Other Preparations of Beclomethasone
POM **BECLOFORTE®** *(GSK)*
Aerosol Inhalation, Beclomethasone dipropionate 250 mcg per dose; high metered-dose inhaler.

Dose: Adult, maintenance dosage, 2 inhalations (500 mcg) twice a day, or 1 inhalation (250 mcg) 4 times daily; increased to 2 inhalations (500 mcg) 3-4 times daily if necessary, according to response.

Child, not recommended.

BUDESONIDE

Indications: Bronchial asthma requiring maintenance treatment with glucocorticoids for control of the underlying airways inflammation.

Contra-indications: Hypersensitivity to budesonide.

Adverse effects: Mild irritation in the throat, coughing, and hoarseness, candida infection in the oropharynx, contact dermatitis, urticaria.

Nursing considerations: •Teach patient how to use *Turbohaler*.

•Monitor patient for bronchospasm; stop medication and give a bronchodilator.

•Corticosteroids may mask symptoms of viral infection; monitor patient closely.
•Discontinue medication if IOP increases.

Dose: The dose is individual and should be adjusted to the smallest dose maintaining symptom control.
Adult: The usual dosage range is 200-800 mcg daily divided into 2-4 administrations. In severe cases, doses up to 1600 mcg may be required. At daily doses up to 400mcg the whole dose may be given at one occasion.
Child (3-7 years): 100-400 mcg either once daily or divided in 2-4 administrations; 7 years and above: 100-800 mcg daily divided into 2-4 administrations. Daily dose of up to 400 mcg may be given at one occasion.

POM **PULMICORT®** *(Reals)*
Turbohaler, Budesonide 100 mcg, 200 mcg, 400 mcg per dose; dry powder inhaler.

HYDROCORTISONE

See section 10.3

7.1.3 Prophylactic drugs

Sodium cromoglicate

Sodium cromoglicate prevents the asthmatic response to certain allergic and nonallergic stimuli. It may be used as long-term therapy early in the course of asthma. It reduces symptoms and the frequency of exacerbations and allows dosage reduction of bronchodilators and oral corticosteroids. Prophylaxis with sodium cromoglicate is generally less effective in adults than prophylaxis with inhaled corticosteroids, but long-tem use of inhaled corticosteroids may be associated with more adverse effects. Sodium cromoglicate is of value in the prevention of exercise-induced asthma, a single dose being inhaled 30 minutes beforehand. Sodium cromoglicate is of **no** value for the treatment of acute attacks of asthma. In general, sodium cromoglicate produces only minimal adverse effects such as occasional coughing upon inhalation of the powder formulation.

MAST CELL STABILISERS
Sodium cromoglycate and **Ketotifen** are not bronchodilators but prevent bronchoconstriction in patients with extrinsic or allergic asthma. They stabilise sensitised mast cells and inhibit the release of bronchoconstrictor agents including histamine, serotonin and slow-reacting substance.
Mast cell stabilisers are useful in extrinsic (allergic) asthma, particularly in children and young adults and can prevent exercise-induced asthma.Intrinsic asthma and chronic obstructive airways disease are not indications for these drugs.

LEUKOTRIENE RECEPTOR ANTAGONISTS (LTRA)
Zafirlukast is a competitive and highly selective leukotriene receptor antagonist indicated in asthma prophylaxis. The cysteinyl leukotrienes are pro-asthmatic mediators released from mast cells and eosinophils. They bind to cysteinyl leukotriene receptors causing smooth muscle contraction, airway oedema and altered cell activity associated with the inflammatory process, including eosinophil influx to the lung. Peak plasma concentrations of zafirlukast are achieved approximately 3 hours after oral administration. Food increases the variability in the bioavailability of zafirlukast and reduces bioavailability. It is extensively metabolised; urinary excretion accounts for about 10% dose and faecal excretion for 89%. It is not detected in the urine.

KETOTIFEN

Therapeutic category: Anti-asthmatic/ Antihistamine.
Indications: Long-term prevention of bronchial asthma, allergic bronchitis, asthmatic symptoms associated with hay fever.
Precautions: Withdraw anti-asthmatic drugs already in use gradually; co-administration with oral anti-diabetic agents; pregnancy, breast-feeding.
Interactions: Sedatives, hypnotics, antihistamines, alcohol.
Adverse effects: Sedation, dry mouth, slight dizziness, weight gain.
Advice to patients: See labels 2, 8, and 21 in Appendix 6.
Nursing considerations: •May cause drowsiness; warn patient to avoid hazardous tasks requiring mental alertness or physical coordination.
Dose: By mouth, Adult, 2 mg 1-2 times daily; increased up to 4 mg daily in 2 divided doses if necessary.
Child (6 months - 3 years), 0.5 mg twice daily; 3 years and over, 2 mg 1-2 times daily.

POM **Ketotifen** *(EDL 26.1)*
Tablet or Capsule, Ketotifen (as hydrogen fu-

marate) 1 mg.
Syrup, Ketotifen (as hydrogen fumarate) 1 mg per 5 ml.

POM **ZADITEN®** *(Novartis)*
Capsule, Ketotifen (as hydrogen fumarate) 1mg; white cap. marked 'CS'.
Tablet, Ketotifen (as hydrogen fumarate) 1 mg; white scored tab. Coded 'ZADITEN 1'.
Elixir, Ketotifen (as hydrogen fumarate) 1 mg per 5 ml.

SODIUM CROMOGLICATE

Sodium cromoglycate is a representative antiasthma drug. Various drugs can serve as alternatives.
Sodium cromoglycate is a complementary drug.
Synonym: Sodium cromoglycate
Therapeutic category: Anti-allergic/anti-asthmatic.
Indications: Prophylaxis of asthma; prevention of exercise-induced asthma.
Precautions: Pregnancy (appropriate to use; see notes above and Appendix 2); breastfeeding (Appendix 3).
Adverse effects: Coughing, transient bronchospasm.
Advice to patients: See Label 8 in Appendix 6. Do not discontinue abruptly; not effective for acute relief of symptoms; must be taken on regularly scheduled basis.
Nursing considerations: •Advise patient to clear as much mucous as possible before inhalation treatments.
•Teach patient proper inhalation technique (see Aerosol Instructions in section 7.1.1).
•Relieve irritating throat with sips of water or gargle.
Dose: *Prophylaxis of asthma and exercise-induced asthma*, by aerosol inhalation, ADULT and CHILD 10 mg 4 times daily, increased in severe cases or during periods of risk to 6–8 times daily; additional doses may be taken before exercise; when stabilized, may be possible to reduce to maintenance of 5 mg 4 times daily.

POM **Sodium cromoglycate** *(WMF 25.1)*
Aerosol inhalation (Pressurized inhalation), Sodium cromoglicate 5 mg/metered inhalation.

POM **Sodium Cromoglycate** *(EDL 26.1)*
Aerosol Inhalations, Sodium cromoglycate 1 mg, 5 mg per metered dose.

ZAFIRLUKAST

Therapeutic category: Leukotriene receptor antagonist (LTRA).
Indications: Prophylaxis of asthma.
Contra-indications: Hypersensitivity to the drug; history of moderate or severe renal impairment; hepatic impairment or cirrhosis; children under 12 years of age; breast-feeding.
Precautions: Elderly, pregnancy, renal impairment, labile or unstable asthma.
Interactions: •Warfarin (monitor prothrombin time closely).
•Theophylline, erythromycin and terfenadine may cause decreased plasma levels of zafirlukast.
•Aspirin may cause increased plasma level of zafirlukast.
Adverse effects: Headache; GI disturbances including nausea, vomiting, diarrhoea, abdominal pain; hypersensitivity reactions including urticaria and angioedema; rashes including blistering.
Advice to patients: See label 23 in Appendix 6.
Nursing considerations: •Give before meals for best absorption. •Advise patient to take with a full glass of water to reduce GI upset; food reduces bioavailability and should be avoided if possible.
•Advise patient to avoid hazardous activities if dizziness occurs.
•Zafirlukast is not recommended during lactation and in acute asthma.
Dose: By mouth, Adult and Child above 12 years, 20 mg twice daily.
Child under 12 years: **not** recommended.
Note: Higher doses are not recommended. As food may reduce the bioavailability, administer without meals.

POM **ACCOLATE®** *(Reals)*
Tablet, Zafirlukast 20 mg.

7.1.4 Inhaler Devices

VOLUMATIC® *(GSK)*
For use with Ventolin®, Becotide®, Ventide® and Becloforte® inhalers.
Aerosol inhaler should be released while the patient is breathing in. An inhaler device is used to coordinate these two actions and is particularly useful for patients with poor inhalation technique, for children, for patients requiring higher doses, for nocturnal asthma, and for patients prone to develop candidiasis with inhaled corticosteroids.
How To use:
1. Separate the two parts and assemble by lining up the notch of one half with the stot of the other, then press together.
2. Remove the cover from the mouth piece of the inhaler and shake the inhaler vigorously.

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3. Insert your inhaler into the Volumatic in the end opposite the mouth piece.
4. Place the mouthpiece of the Volumatic in your mouth and close your lips around it. Hold the Volumatic level.
5. Breath out gently (but not fully) and then …
6. Press the canister once to release a dose of the drug and then breathe in slowly and deeply through your mouth.
7. Hold your breath for 10 seconds or as long as is comfortable before breathing out slowly.
8. If you take a second dose, you should wait at least one minute before repeating steps 4 to 7.
9. After use, remove the inhaler and replace the cover on its mouthpiece.
10. To clean, separate the two halves of the Volumatic by pulling them apart and rinse both halves in warm water, dry carefully and store as normal.

7.2 Expectorants and cough suppressants

BROMHEXINE

Therapeutic category: Bronchial mucolytic.
Pharmacology: Bromhexine is a systemically active mucolytic agent. Increased sputum production becomes evident after 2-3 days following initiation of oral therapy. The break-down of acid mucopolysaccharide fibres makes the sputum thinner and less viscid and therefore more easily removed by coughing.
Indications: Conditions associated with congestion of the bronchi such as bronchitis.
Precautions: Gastric and duodenal ulceration, pregnancy.
Adverse effects: Occasional GI disturbances.
Dose: By mouth, Adult and Children (over 10 years), 8 mg 3 times daily; up to a max. 48 mg daily in adults.
Child (5-10 years), 4 mg 3 times daily.
Child (2-5 years), 4 mg 2 times daily.
Child (under 2 years), 1 mg 3 times daily.

POM **Bromhexine** *(EDL 26.2)*
Tablet, Bromhexine HCl 8 mg
Elixir, Bromhexine HCl 4 mg per 5 ml.

POM **BRONCHOLYTE**® *(NGC)*
Elixir, Bromhexine HCl 4 mg per 5 ml.
Pack - 100 ml.

POM **HOSOLVON**® *(Hovid)*
Tablet, Bromhexine HCl 8 mg
8 mg - 1000.
Elixir, Bromhexine HCl 4 mg per 5 ml.
Pack - 60 ml.

CODEINE

Therapeutic category: Narcotic antitussive
Indication: Cough
Contra-indications, Precautions, etc: See Morphine in Section 1.8.2.
Dose: Adult, 5 ml when required.
Child (up to 1 year), 5 ml of paediatric linctus; 1-5 years, 10 ml.

POM **Codeine** *(EDL 26.2)*
Linctus, Codeine phosphate 15 mg per 5 ml.
Paediatric Linctus, Codeine phosphate 3 mg per 5 ml.

GUAIFENESIN

Pharmacology: Guaiphenesin has an expectorant action which increases the output of respiratory tract fluid by reducing adhesiveness and surface tension. It reduces the viscosity of tenacious sputum. The increased flow of less viscid secretions promotes ciliary action and facilitates the removal of mucus. Guaiphenesin is readily absorbed from the gastro-intestinal tract. It is metabolised and excreted in the urine.
Indications: As an expectorant for the symptomatic relief of cough due to colds and minor upper respiratory infections.
Contra-indications: Hypersensitivity to guaiphenesin and bisulphites.
Precautions: Acute porphyria. Dosage for children under 2 years must be individualized.
Adverse effects: GI discomfort, nausea, vomitting. Rarely, diarrhoea, drowsiness, stomach pain.
Dose: By mouth, Adult, 10-20 ml every 4 hours; not to exceed 120 ml a day.
CHILD (2-6 years), 2.5-5 ml every 4 hours; not to exceed 30 ml a day.
6-12 years, 5-10 ml every 4 hours; not to exceed 60 ml a day.
Note: To help loosen mucus in the lungs, patients should drink a glass of water after each dose.

OTC **FENACOL** ®*(Hovid)*
Syrup, Guaiphenesin 100 mg per 5 ml; dark brown liquid with peppermint flavour.
Pack -120 ml; 240 ml.

METHADONE

Therapeutic category: Narcotic antitussive
Pharmacology: Methadone has a depressant action on the cough centre and is used to control non-productive cough of intractable disorders such as lung cancer.
Indications: Cough, see under the Pharmacology.

Contra-indications, Precautions, etc: See Morphine in section 1.8.2
Advice to patients: May cause drowsiness; avoid alcohol and other CNS depressants.
Dose: Adult, 2 mg 4 hourly.
Not recommended for children.

POM **Methadone** *(EDL 26.2)*
Linctus, Methadone HCl 2 mg per 5 ml.

COMPOUND COUGH PREPARATIONS *(EDL 26.2)*

OTC **AFIDIL®** *(Ranbaxy)*
Syrup, Triprolidine HCl 1.25 mg, pseudoephedrine HCl 30 mg per 5 ml.
Advice to patients: See label 2 in Appendix 6.
Pack - 100 ml.
Dose: 12 years and above, 10 ml 3 times daily;
6-12 years, 7.5 ml 3 times daily.

OTC **BELL'S BABY COUGH SYRUP®** *(De-Sears)*
Syrup, Squill oxymel 0.25 ml, ipecacuanha tincture 0.05 ml per 5 ml; pink syrupy liquid.
Pack - 100 ml.
Indications: For the relief of irritating coughs and symptoms of the upper respiratory tract infection.
Dose: By mouth, 5 ml every 4 hours.

OTC **BELL'S CHILDREN'S COUGH SYRUP®** *(De-Sears)*
Syrup, Guaiphenesin BP 50 mg per 5 ml; orange viscous liquid.
Pack - 100 ml.
Indications: For use as expectorant and upper respiratory tract decongestant.
Dose: By mouth, Child (2-6 years), 5 ml 3-4 times daily; 6-12 years, 10 ml 3-4 times daily.
Children under 2 years should use Bell's Baby Cough Syrup.

OTC **BELL'S GEE'S LINCTUS®** *(De-Sears)*
Linctus, Opium tincture 33% (equiv. to Morphine 800 mcg per 5 ml).
Pack - 100 ml.
Indications: For the suppression of coughs.
Dose: By mouth, Adult, 5 ml up to 4 times daily.

OTC **BENYLIN®** *(NGC)*
Syrup (Expectorant), Diphenhydramine HCl 14 mg, ammonium chloride 135 mg, menthol 1.1 mg per 5 ml.
Dose: Adult, 10 ml 4 times daily;
6-12 years, 5 ml 4 times daily.
Advice to patients: See Label 2 in Appendix 6.
Pack: 100 ml.
Syrup (for children), Diphenhydramine HCl 7 mg, sodium citrate 28.5 mg per 5 ml.
Pack: 100 ml.
Dose: Child (1-5 years), 5 ml three hourly;
6 years and above, 10 ml three hourly.
Syrup (with codeine), Diphenhydramine HCl 13.5 mg, codeine phosphate 10.95 mg, sodium citrate 54.4 mg, menthol 1.1 mg per 5 ml.
Dose: Adult, 10 ml 3-4 hourly;
Child (1-5 years), 2.5 ml 3-4 hourly;
6-12 years, 5 ml 3-4 hourly.

POM **BRONCHICUM®** *(May & Baker)*
Elixir, Tinct. black snakeroot 0.2 ml, tinct. grindel. 1 ml, tinct. pimpinell 0.2 ml, tinct. primrose 0.5 ml, tinct. quebracho 0.7 ml, tinct. thymi 1 ml, ephedrine HCl 0.15 g. menthol 0.02 g, sodium bromide 1 g, eucalyptus oil 0.01 ml, saponin 40 mg per 100 ml. Preparations without sodium bromide also available.
Pack - 100 ml.
Indications: Spasmodic cough, inflammation and mucous obstruction of the bronchi.
Dose: Adult, 5 ml every 2-3 hours.
Child: 2.5-5 ml 2-3 times daily depending on age.

OTC **CADIPHEN®** *(Interpharma)*
Syrup, Chlorpheniramine maleate U.S.P. 2 mg, Guaifenesin (Glyceryl guaiacolate) U.S.P. 80 mg, Ammonium chloride B.P. 100 mg, Sodium citrate B.P. 44 mg, Levo-menthol B.P. 0.8 mg, Terpin hydrate U.S.P. 4 mg, Tolu balsam U.S.P. 6 mg, Vasaka syrup 0.133 ml per 5 ml.
Pack - 100 ml.
Dose: *Adults*: 10 ml 3-4 times a day.
Children: 2.5-5 ml 3-4 times a day according to age.

OTC **CHEMEX®** *(Chemiron)*
Syrup, Diphenhydramine HCl, ammonium chloride, sodium citrate, menthol.
Advice to patients: See label 2 in Appendix 6.

OTC **CHERICOF®** *(Ranbaxy)*
Syrup, Chlorphenamine maleate 2 mg, dextromethorphan HBr 10 mg, phenylpropanolamine HCl 12.5 mg per 5 ml.
Advice to patients: See label 2 in Appendix 6.
Pack - 100 ml
Dose: Adult, 10 ml 3-4 times daily.
Child (2-6 years), 2.5 ml 3-4 times daily;
6-12 years, 5 ml 3-4 times daily.

OTC **COFLIN®** *(Vitabiotics)*

Syrup, Chlorphenamine maleate 2 mg, ammonium chloride 80 mg, sodium citrate 40 mg, menthol 2 mg, ephedrine HCl 6 mg per 5 ml.
Pack - 100 ml.
Dose: Adult, 5-10 ml 3-4 times daily
Child (1-5 years): 2.5-5 ml 3-4 times daily; 6-12 years, 5 ml 3-4 times daily.

OTC **COFMIX®** *(Farmex–Meyer)*
Syrup, Diphenhydramine HCl 15 mg, ammonium chloride 130 mg, sodium citrate 57 mg, menthol 1.1 mg per 5 ml.
Pack - 100 ml.
Dose: Adult, 5-10 ml 3-4 hourly.
Child, 2.5-5 ml 4 hourly.
Infant, 1.25-2.5 ml 3-4 hourly.

OTC **COFTA®** *(Evans)*
Syrup, Ipecacuanha tincture 100l, liquorice extract 250l, ammonia q.s, peppermint oil 6.9l, aniseed oil 2.6l per 5 ml; dark brown thick and good tasting liquid.
Pack - 60 ml.
Dose: Adult, 10-15 ml 3-4 times daily.
Child (6 months-2 years), 2.5 ml 3-4 times daily; 2-10 years, 5 ml 3-4 times daily; 10-15 years, 10 ml 3-4 times daily.
Tablets, Extract glycrrh. 49.95 mcg,menthol 5.99 mcg, tincture of capsicum 0.011 ml, oil pini pumil 0.001 ml, eucalyptus oil 0.02 ml, creosote 0.002 ml, anise oil 0.001 ml, mentholated peppermint oil 0.001 ml per tablet; mottled brown flat/plain tab. with menthol taste.
Pack - 20.
Dose: *Adult and chlidren over 10 years*, 1-2 tabs to be sucked 4 or more times a day or as required.

OTC **COPHEN®** *(Gateway)*
Syrup, Diphenhydramine HCl
Pack - 100 ml.

POM **COSCOPIN®** *(Fill Pharma)*
Linctus, Noscapine BP 7.0 mg, Ammonium chloride BP 28.0 mg, Sodium Citrate BP 3.25 mg, Chlorphenamine maleate BP 2.0 mg per 5 ml.
Pack - 100 ml.
Pharmacology: Coscopin contains Nosacapine, an alkaloid, which acts centrally to suppress continous and irritating cough. Nosacapin is potent and long lasting (up to 4 hours) antitussive agent which is non-constipating, non-habit forming and non-sedative. It has a weak bronchodilator property and stimulates the respiratory centre. Suppresses all kinds of cough without interfering with patient's ability to cough and bring up sputum voluntarily. Ammonium chloride and sodium citrate help in liquefying and expectoration of mucous with normal cough reflex, which is not blocked by Noscapine. Chlorphenamine maleate is a potent antihistamine which is used for the symptomatic treatment of cough and common cold.
Indications: For suppression of continous and irritating cough and for facilitation of expectoration; whooping cough.
Dose: Adults: 10-20 ml 3-4 times daily.
Child: 5-10 ml 2-3 times daily.
Paediatric suspension, Noscapine BP 1.83 mg, Ammonium chloride BP 7 mg, Sodium citrate BP 0.67 mg per ml.
Pack - 50 ml.
Dose: Child (1-3 years): 1.25-2.5 ml 2-3 times daily; 3-12 years, 3.75-5 ml 2-3 times daily.

OTC **D-KOFF®** *(Jawa)*
Syrup, Diphenhydramine HCl, bromhexine HCl, ammonium chloride, sodium citrate, menthol.
Pack - 100 ml x 20's

OTC **DIPHENKOF®** *(Leady)*
Syrup (Expectorant for Adult), Diphenhydramine HCl 12.5 mg, ammonium chloride 130 mg, sodium citrate 57 mg, menthol 1.1 mg per 5 ml.
Advice to patients: See label 2 in Appendix 6.
Syrup (for children), Diphenhydramine HCl 7 mg, sodium citrate 28.5 mg per 5 ml.

OTC **DOLYN®** *(Doyin)*
Syrup, Diphenhydramine HCl 12.5 mg, menthol 1.0 mg, ammonium chloride 100 mg, sodium citrate 50 mg per 5 ml; pleasantly flavoured syrup in tamper-proof bottle with company logo.
Pack - 100 ml.
Advice to patients: See label 2 in Appendix 6.
Dose: Adult, 10-15 ml every 3-4 hours.
Child (1-5 years), 2.5 ml every 3-4 hours; 6-12 years, 5 ml every 3-4 hours.

OTC **EMZOLYN®** *(Emzor)*
Syrup, Diphenhydramine HCl 14 mg, menthol 1.1 mg, ammonium chloride 135 mg, sodium citrate 57 mg per 5 ml; pleasantly flavoured syrup in tamper-proof bottle with company logo.
Pack - 100 ml; 2 L.
Advice to patients: See label 2 in Appendix 6.
Paediatric Syrup, Diphenhydramine HCl 7 mg, menthol 0.55 mg per 5 ml; pleasantly flavoured syrup in tamper-proof bottle with company logo.
Pack - 100 ml.

OTC **JULYN®** *(Juhel)*
Syrup, Diphenhydramine HCl 14 mg, ammonium chloride 135 mg, sodium citrate 57 mg, menthol 1.1 mg per 5 ml.
Pack – 100 ml in amber bottle.
Paediatric syrup, Diphenhydramine HCl 7 mg, sodium citrate 28.5 mg per 5 ml.
Pack – 100 ml in amber bottle.

OTC **KOFGO®** *(Farmex-Meyer)*
Syrup, Ephedrine HCl 5 mg, sodium citrate 40 mg, ammonium chloride 80 mg, chlorphenamine maleate 1 mg, menthol 1 mg per 5 ml.
Pack -100 ml.
Advice to patients: See label 2 in Appendix 6.
Dose: Adult, 5-10 ml every 3-4 hours;
Child, 2.5 ml every 3-4 hours.

OTC **KOFLIX®** *(Food & Pharma)*
Syrup (Expectorant), Diphenhydramine HCl 12 mg, ammonium chloride 130 mg, sodium citrate 57 mg, menthol 1.1 mg per 5 ml.
Advice to patients: See label 2 in Appendic A.
Pack -100 ml
Dose: Adult, 10 ml every 4 hours.
Child, 5 ml every 4 hours.

OTC **KUFDRYL®** *(Therapeutic)*
Syrup, Diphenhydramine HCl 15mg ammonium chloride 130 mg, menthol 1.10 mg per 5 ml.
Advice to patients: See label 2 in Appendix 6.

OTC **KIDI KUFDRYL®** *(Therapeutic)*
Syrup, Diphenhydramine HCl 7.5 mg, menthol 0.55 mg, sodium citrate 28.5 mg.
Advice to patients: See label 2 in Appendix 6.

OTC **LINCTIFED F®** *(SKG)*
Syrup, Codeine Phosphate 7.5 mg, guaiphenesin 100 mg, pseudoephedrine HCl 20 mg, triprolidine HCl 1.25 mg per 5 ml.
Pack - 60 ml.
Advice to patients: See label 2 in Appendix 6.
Dose: Adult and children over 12 years, 10 ml 3 times daily.

OTC **LINCTIFED P®** *(SKG)*
Paediatric Syrup, Codeine phosphate 3 mg, guaiphenesin 50 mg, pseudoephedrine HCl 12 mg, triprolidine HCl 0.6 mg.
Pack - 60 ml.
Advice to patients: See label 2 in Appendix 6.
Dose: Child (6-12 years), 10 ml 3 times daily;
2-5 years, 5 ml 3 times daily.

OTC **MEDIX COUGH®** *(Morison)*
Mixture, Ammonia plus ipecacuanha; dark brown liquid.
Pack - 100 ml.

OTC **MELROSUM®** *(May & Baker)*
Syrup, Mel (honey) 45 g, tinct, grindelia 0.2 ml, tinct. pimpinella 0.2 ml, tinct. primrose 1 ml, tinct. rose 1 ml, tinct. thyme 1.2 ml per 100 ml.
Pack - 100 ml.
Indications: Catarrhal disease of the respiratory organs especially in delicate patients, children and pregnant women.
Dose: Adult, 15 ml 3 times daily.
Adolescents and children over 12 years: 10 ml 3 times daily.
Child (over 3 years): 5 ml 3 times daily.
1-3 years: 2.5 ml 3 times daily.

POM **MELROSUM with Codeine®** *(May & Baker)*
Syrup, Codeine phosphate 0.1 g, mel (honey) 45 g, tinct. grindelia 0.2 ml, tinct. pimpinella 0.2 ml, tinct. primrose 1 ml. tinct. rose 1 ml, tinct. thyme 1.2 ml per 100 ml.
Pack - 100 ml.
Indications: Catarrhs of the respiratory tract with irritative and spasmodic cough.
Dose: Adult, 15 ml 3 times daily; Older children and juveniles: 10 ml 3 times daily; Infants: 5 ml 3 times daily
Babies over 6 months: 2.5 ml 2-3 times daily.

OTC **MENTHODEX®** *(De-Sears)*
Mixture, Ammonium chloride 200 mg, sodium citrate 100 mg, liquid extract of Tussilago 0.0008 ml, tolu tincture 0.002 ml, squill tincture 0.002 ml, liquid extract of Horehound 0.003 ml, menthol 15.5 mg per 10 ml; dark brown syrup with a characteristic odour and flavour.
Pack - 100 ml; 200 ml.
Indications: Contains expectorant and demulcent agents for the treatment of coughs and colds. It makes the cough more productive by loosening tenacious bronchial mucous. It combats the congestive symptoms that frequently accompany coughs and colds, and reduces bronchial and nasal congestion.
Dose: By mouth, Adult, 10 ml 3 times a day and at bedtime.
Child (7-14 years), 5 ml 3 times a day and at bedtime.
Do not exceed 4 doses in any 24 hours.

OTC **NEOFYLIN®** *(Mopson)*

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Syrup, Chlorphenamine maleate 2 mg, ammonium chloride 50 mg, sodium citrate 50 mg, citric acid 10 mg, ipecacuanha tincture 0.1 ml per 5 ml.
Pack - 100 ml, 2 L.

OTC **OSINEX®** *(Nemeith)*
Syrup, Chlorphenamine maleate 1 mg, phenylephrine HCl 5 mg, dextromethorphan hydrobromide 7.5 mg, glyceryl guaiacol ether 50 mg per 5 ml.
Pack - 100 ml; 1 L.
Dose: Adult, 15 ml 3-4 times daily.
Child (1-6 years): 5 ml 3 times daily; 6-12 years: 5-10 ml 3-4 times daily.

OTC **PARKALIN®** *(Pharma-Deko)*
Expectorant, Diphenhydramine HCl 14 mg, ammoniun chloride 135 mg, menthol 1.1 mg.
Syrup (with Codeine), Diphenhydramine HCl 14 mg, codeine phosphate 5.7 mg, menthol 1.1 mg.
Paediatric Syrup, Diphenhydramine HCl 7 mg.

OTC **PENTALYN®** *(Morison)*
Syrup, Diphenhydramine HCl, ammonium chloride, sodium citrate, menthol.
Pack - 100 ml
Advice to patients: See label 2 in Appendix 6.

POM **PHENSEDYL®** *(May & Baker)*
Linctus, Promethazine HCl 3.6 mg, ephedrine HCl 7.2 mg, codeine phosphate 9.0 mg per 5 ml.
Pack - 100 ml.
Indications: Dry irritating unproductive coughs, nasal decongestion, cold and allergy
Dose: Adult, 10 ml 2-3 times daily.
Child (over 10 years): 5 ml 2-3 times daily; 5-10 years, 2.5-5ml 2-3 times daily; 2-5 years, 2.5 ml 2-3 times daily.

OTC **PIRITON® Expectorant** *(Evans)*
Linctus, Chlorphenamine maleate 4 mg, ammonium chloride 200 mg, sodium citrate 88 mg per 10 ml
Indications: Expectorant for use in allergic symptoms that may be associated with upper respiratory tract infections including common colds and bronchitis; also loosens bronchial secretions thereby facilitating breathing.
Advice to patients: See Label 2 in Appendix 6.
Dose: Adult, 10 ml 3-4 times a day
Child (up to 1 year), ½ spoonful (2.5 ml) twice daily; 1-5 years, ½-1 spoonful (2.5-5.0 ml) 3 times daily; 6-12 years, 5-10 ml 3-4 times a day.

OTC **POLARAMINE® Expectorant** *(Supreme)*
Syrup, Dexchlorphenamine maleate 2 mg, pseudoephedrine sulfate 20 mg, guaifenesin 100 mg per 5 ml.
Pack - 100 ml; 120 ml.
Indications: Coughs; allergic disorders such as seasonal rhinitis and vasomotor rhinitis.
Advice to patients: See Label 2 in Appendix 6.
Dose: Adult and child above 12 years, 5-10 ml 3-4 times a day.
Child (2-6 years), 1.25-2.5 ml 3-4 times daily; 6-12 years, 2.5-5 ml 3-4 times a day.

OTC **ROMILAR®** *(Swipha)*
Syrup, Dexromethorphan hydrobromide 15 mg, ammonium chloride 90 mg, dexpanthenol 50 mg per 5 ml.
Dose: Adult, 2.5-5 ml 2-4 times daily.

OTC **SUDACOL®** *(SKG)*
Syrup, Guaiphenesin 100 mg, pseudoephedrine HCl 30 mg.
Pack - 100 ml.
Advice to patients: See label 2 in Appendix 6.
Dose: Adult and children over 12 years, 10 ml 3 times daily; 6-12 years, 5 ml 3 times daily; 1-6 years, 2.5 ml 3 times daily.

POM **TIXYLIX®** *(May & Baker)*
Linctus, Promethazine HCl 1.5 mg, pholcodeine 1.5 mg, ethanol 3.8% per 5 ml.
Pack - 100 ml.
Indications: Cough and colds especially irritating night coughs and spasms of whooping cough in children.
Dose: Child (3-5 years): 5 ml 2-3 times daily; 6-10 years, 5-10 ml 2-3 times daily.

OTC **TUSSIREX-F®** *(SKG)*
Syrup, Codeine Phosphate 7.5 mg, potassium guaiacolsulphonate 120 mg, pseudoephedrine HCl 20 mg, triprolidine HCl 1.25 mg per 5 ml.
Pack - 60 ml; 100 ml.
Advice to patients: See label 2 in Appendix 6.
Dose: Adult and children over 12 years, 10 ml 3 times daily.

OTC **TUSSIREX-P®** *(SKG)*
Paediatric Syrup, Codeine phosphate 5 mg, potassium guaiacolsulphonate 50 mg, pseudoephedrine HCl 12 mg, triprolidine HCl 0.6 mg.
Pack - 60 ml; 100 ml.
Advice to patients: See label 2 in Appendix 6.
Dose: Child (6-12 year s), 10 ml 3 times daily; 2-5 years, 5 ml 3 times daily.

OTC **TUSSYLIN®** *(Afrab-Chem)*
Syrup, Ammonium chloride 135 mg, diphenhydramine HCl 14 mg, sodium citrate 57 mg, mentol 1.1 mg per 5 ml.
Advice to patients: See Label 2 in Appendix 6
Pack - 100 ml.
Dose: Adult, 15-30 ml 2-3 times daily.
Child (above 12 years), 5 ml 2-3 times daily
Paediatric Syrup, Diphenhydramine HCl 7 mg, sodium citrate 28.5 mg, methol 0.55 mg per 5 ml.
Advice to patients: See label 2 in Appendix 6.
Pack - 100 ml.
Dose: Child (1-5 years), 5 ml 3 times daily;
Over 6 years, 10 ml 3 times daily.
Not recommended for children under one year.

OTC **UNIPLEX®** *(Daily Need)*
Syrup, Diphenhydramine HCl, ammonium citrate.

OTC **ZUBES COUGH SYRUP®** *(P.Z.)*
Paediatric Syrup, Ipecacuanha liquid extract B.P. 0.0119 ml, Squill Vinegar B.P.C. 0.1124 ml.
Dose: Child (over 6 months), 2.5 ml in water every 4 hours; 2-6 years, 5 ml every 4 hours.

OTC **ZUBES SOOTHING COUGH MIXTURE®** *(P.Z)*
Syrup, Mentol 16 mg, aniseed oil 11 mg, peppermint oil 8 mg.
Dose: Child (6-12 years), 5 ml every 6 hours.
Adult and child (over 12 years), 5-20 ml every 6 hours.

8. Antiallergics and drugs used in anaphylaxis

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8.1 Antihistamines
8.2 Sympathomimetic
8.3 Corticosteroids

Antiallergics and drugs used in anaphylaxis

The H_1-receptor antagonists are generally referred to as antihistamines. They inhibit the wheal, pruritus, sneezing and nasal secretion responses that characterize allergy. Antihistamines thus relieve the symptoms of allergic reactions, such as urticaria, allergic rhinitis, and allergic conjunctivitis; they also control pruritus in skin disorders, such as eczema. Antihistamines are used to treat drug allergies, food allergies, insect stings and some of the symptoms of anaphylaxis and angioedema. Drug treatment and other supportive care should not be delayed in critically ill patients (see Allergic Emergencies below). Specific precipitants should be sought and if identified, further exposure avoided and desensitization considered.

Drowsiness and sedation are particular disadvantages of the older antihistamines and the patient should be warned against driving or operating machinery. Other central nervous depressants, including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytics and neuroleptics, may enhance the sedative effects of antihistamines. Since antihistamines interfere with skin tests for allergy, they should be stopped at least one week before conducting a skin test.

Chlorphenamine is a typical, older sedative antihistamine. Newer antihistamines do not cause significant sedation. In practice, all antihistamines are equally effective in relieving the symptoms of allergic reactions and differ mainly in the intensity of sedative and anticholinergic (more correctly antimuscarinic) effects. Selection of an antihistamine should thus be based on the intended therapeutic use, the adverse reaction profile, and the cost.

Corticosteroids, such as **dexamethasone**, **hydrocortisone**, or **prednisolone**, suppress or prevent almost all symptoms of inflammation associated with allergy. The route of administration depends on the particular type of allergic condition. For example, for a mild allergic skin reaction, the best therapy may be the use of a corticosteroid ointment or cream. If the skin reaction does not respond to topical corticosteroid therapy, it may be necessary to give a corticosteroid orally.

Allergic reactions of limited duration and with mild symptoms, such as urticaria or allergic rhinitis, usually require no treatment. If on the other hand, symptoms become persistent, antihistamines constitute the mainstay of treatment. However, oral corticosteroids may be required for a few days in an acute attack of urticaria or for severe skin reactions. Oral corticosteroids are also used to relieve severe exacerbations in chronic urticaria, but long-term use should be avoided.

Corticosteroids may be used topically to reduce inflammation in allergic rhinitis but should only be used systemically for this condition when symptoms are disabling.

Adverse effects associated with long-term use of corticosteroids include inhibition of growth in children, disturbances of electrolyte balance leading to oedema, hypertension and hypokalaemia, with osteoporosis, spontaneous fractures, skin thinning, increased susceptibility to infection, mental disturbances and diabetes mellitus. For further information on the disadvantages of corticosteroids, see section 10.3.

Allergic emergencies

Anaphylactic shock and conditions such as angioedema are medical emergencies that can result in cardiovascular collapse and/or death. They require prompt treatment of possible laryngeal oedema, bronchospasm or hypotension. Atopic individuals are particularly susceptible. Insect stings and certain foods including eggs, fish, cow's milk protein, peanuts and

nuts are a risk for sensitized persons. Therapeutic substances particularly associated with anaphylaxis include blood products, vaccines, hyposensitizing (allergen) preparations, antibiotics (especially penicillins), iron injections, heparin, and neuromuscular blocking drugs. Acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs (NSAIDs) may cause bronchoconstriction in leukotriene-sensitive patients. In the case of drug allergy, anaphylaxis is more likely to occur after parenteral administration. Resuscitation facilities should always be available when injecting a drug associated with a risk of anaphylactic reactions.

First-line treatment of a severe allergic reaction includes administering epinephrine (adrenaline), keeping the airway open (with assisted respiration if necessary), and restoring blood pressure (laying the patient flat, raising the feet). Epinephrine (adrenaline) should immediately be given by intramuscular injection to produce vasoconstriction and bronchodilation and injection should be repeated if necessary at 5-minute intervals until blood pressure, pulse and respiratory function have stabilized. If there is cardiovascular shock with inadequate circulation, epinephrine (adrenaline) must be given cautiously by slow intravenous injection of a *dilute solution*. Oxygen administration is also of primary importance.

An antihistamine such as chlorphenamine is a useful adjunctive treatment given after epinephrine (adrenaline) injection and continued for 24 to 48 hours to reduce the severity and duration of symptoms and to prevent relapse. An intravenous corticosteroid such as hydrocortisone has an onset of action that is delayed by several hours but should be given to help prevent later deterioration in severely affected patients.

Further treatment of anaphylaxis may include intravenous fluids, an intravenous vasopressor such as dopamine, intravenous aminophylline or injected or nebulized bronchodilator, such as salbutamol.

Steps in the management of anaphylaxis:

1. Sympathomimetic

Epinephrine (adrenaline) by intramuscular injection using epinephrine injection 1 in 1000, ADULT and ADOLESCENT , 500 micrograms (0.5 ml); INFANT under 6 months 50 micrograms (0.05 ml); CHILD 6 months–6 years 120 micrograms (0.12 ml), 6–12 years 250 micrograms (0.25 ml)

NOTE: The above doses may be repeated several times if necessary at 5-minute intervals, according to blood pressure, pulse, and respiratory function.

If circulation inadequate, by slow intravenous injection using epinephrine injection 1 in 10 000 (given at a rate of 1 ml/minute), ADULT 500 micrograms (5 ml); CHILD 10 micrograms/kg (0.1 ml/kg), given over several minutes

2. **Vital functions**
Maintain an open airway; give oxygen by mask, restore blood pressure (lay patient flat, raise feet)
3. **Antihistamine** such as chlorphenamine by intravenous injection over 1 minute, ADULT 10–20 mg, repeated if required (maximum total dose 40 mg in 24 hours)
4. **Corticosteroids** such as hydrocortisone by slow intravenous injection, ADULT 100–300 mg; CHILD up to 1 year, 25 mg; 1–5 years, 50 mg; 6–12 years, 100 mg.
5. **Intravenous fluids:** start infusion with sodium chloride (0.5–1 litre during the first hour)
6. If the patient has asthma-like symptoms, give salbutamol 2.5–5 mg by nebulization or aminophylline 5 mg/kg by intravenous injection over at least 20 minutes.

8.1 Antihistamines

ASTEMIZOLE

Therapeutic category: Antihistamine, H_1 Blocker, Non-sedating.

Pharmacology: Astemizole is a non-sedative antihistaminic devoid of CNS and anticholinergic effects. It is a long-acting H_1-receptor antagonist.

Indications: Treatment of perenial and seasonal allergic rhinitis, hay fever, allergic conjuctivitis, urticaria and other allergic skin conditions.

Precautions: Pregnancy, hepatic or renal disease, lower respiratory disease.

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Interactions: Avoid co-administration with erythromycin and Ketoconazole. These combinations have been associated with QTc interval prolongation which can result in severe and potentially fatal ventricular cardiac arrhythmias.
(*Source: Antihistamine Update. Hosp. Med., 1995; 31:2-38*).

Adverse effects: Devoid of sedative or anti-cholinergic side-effects; occasional weight gain.

Advice to patients: See label 23 in Appendix 6. Take on an empty stomach at least 2 hours after a meal or 1 hour before a meal; may cause drowsiness; do not exceed recommended dose; notify physician or pharmacist if taking any heart medications. Because of its delayed onset, astemizole is useful for prophylaxis of allergic symptoms, rather than for acute relief.

Nursing considerations: •Give on an empty stomach at least 2 hours after a meal and inform patient to avoid eating for at least an hour after taking drug.
•Raise bed rails at night; may need assistance with ambulation.
•Advise patient to avoid alcohol and activities that require mental alertness.

Dose: By mouth, Adult and Children (over 12 years) 10 mg once daily.
Child (6-12 years), 5 mg once daily.

POM **Astemizole** *(EDL 3.1)*
Tablet, Astemizole 10 mg
Syrup, Astemizole 5 mg per 5 ml.

POM **ASTIZOL®** *(Supreme)*
Tablets, Astemizole 120 mg
10 mg - 10.

POM **HISMANAL®** *(CHI)*
Tablet, Astemizole 10 mg; white scored tab.
10 mg - 10; 30.
Suspension, Astemizole 2 mg per ml.
Pack - 30 ml.

CHLORPHENAMINE

Chlorphenamine is a representative sedative antihistamine. Various drugs can serve as alternatives.

Synonym: Chlorpheniramine.

Therapeutic category: Antihistamine, H_1 Blocker.

Indications: Symptomatic relief of allergy, allergic rhinitis (hay fever) and conjunctivitis, urticaria, insect stings and pruritus of allergic origin; adjunct in the emergency treatment of anaphylactic shock and severe angioedema.

Contra-indications: Prostatic enlargement, urinary retention; ileus or pyloroduodenal obstruction; glaucoma; child under 1 year.

Precautions: Pregnancy and breastfeeding (Appendices 2 and 3); renal and hepatic impairment (Appendices 4 and 5); epilepsy; **interactions**: Appendix 1.
SKILLED TASKS: May impair ability to perform skilled tasks, for example operating machinery, driving.

Adverse effects: Drowsiness (rarely paradoxical stimulation with high doses, or in children or elderly), hypotension, headache, palpitations, psychomotor impairment, urinary retention, dry mouth, blurred vision, gastrointestinal disturbances; liver dysfunction; blood disorders; also rash and photosensitivity reactions, sweating and tremor, hypersensitivity reactions (including bronchospasm, angiodema, anaphylaxis); injections may be irritant.

Advice to patients: See Label 2 in Appendix 6. May cause drowsiness, swallow whole, do not crush or chew sustained release product; avoid alcohol, may impair judgement and coordination.

Nursing considerations: •Give with meals if GI symptoms occur; may slightly reduce absorption. Do not crush or chew sustained release drug product.
•Give I.V. slowly; if adverse reactions occur, discontinue drug and notify physician.
•Relieve dry mouth with chewing gum or frequent sips of water.
•Raise bed rails, institute safety measures; may assist with ambulation.
Advise patient to avoid alcohol and driving.

Dose: *Allergy*, by mouth, ADULT 4 mg every 4–6 hours (maximum 24 mg daily); CHILD under 1 year not recommended, 1–2 years 1 mg twice daily, 2–5 years 1 mg every 4–6 hours (maximum 6 mg daily), 6–12 years 2 mg every 4–6 hours (maximum 12 mg daily).
Allergic reactions, by subcutaneous or intramuscular injection , ADULT 10–20 mg, repeated if required (maximum 40 mg in 24 hours); by subcutaneous injection CHILD 87.5 micrograms/kg, repeated if necessary up to 4 times daily.
Anaphylaxis (adjunct), by intravenous injection over 1 minute, ADULT 10–20 mg; child under 1 year 250 micrograms/kg, 1–5 years 2.5–5 mg, 6–12 years 5–10mg.

POM **Chlorphenamine** *(WMF 3.1)*

Tablets, Chlorphenamine maleate 4 mg.
Elixir (Oral solution), Chlorphenamine maleate 2 mg/5 ml [not included on WHO Model List].
Injection (Solution for injection), Chlorphenamine maleate 10 mg/ml; in1-ml ampoule.

OTC **Chlorphenamine** *(EDL 3.1)*
Tablet, Chlorphenamine maleate 4 mg.
Syrup, Chlorphenamine maleate 2 mg per 5 ml.
Injection, Chlorphenamine maleate 10 mg per ml; in 1 ml amp.

OTC **AHISTON®** *(Dizpharm)*
Tablet, Chlorphenamine maleate 2 mg.
2 mg - 1000.

OTC **ALLERGIN®** *(Afrab-Chem)*
Tablet, Chlorphenamine maleate 4 mg; light pink scored tab marked with the maker's symbol.
Pack - 1000.
Syrup, Chlorphenamine maleate 2 mg per 5 ml.
Pack - 60 ml; 2 L.

OTC **ANTIHIST®** *(Therapeutic)*
Tablet, Chlorphenamine maleate 4 mg; yellow scored tab.
4 mg - 100; 1000.

OTC **Chlorphenamine** *(Emzor)*
Tablet, Chlorphenamine maleate 4 mg.
4 mg - 1000.
Syrup, Chlorphenamine maleate 2 mg per 5 ml.
Pack - 2 L.

OTC **Chlorphenamine** *(Juhel)*
Tablet, Chlorphenamine maleate 4 mg.
4 mg - 1000.

OTC **Chlorphenamine** *(Novel)*
Tablet, Chlorphenamine maleate 4 mg
4 mg - 1000.

OTC **Chlorpheniraminme** *(Vitabiotics)*
Tablet, Chlorphenamine maleate 4 mg.
4 mg - 1000's

OTC **CPM** *(Sam)*
Tablet, Chlorphenamine maleate 4 mg.
4 mg - 1000.

OTC **DANA CPM®** *(Dana)*
Tablet, Chlorphenamine maleate 4 mg; yellow uncoated tab.
4 mg - 1000's.

OTC **HISTINE®** *(Fidson)*
Tablet, Chlorphenamine maleate 4 mg.
4 mg - 100

OTC **NISE®** *(Jawa)*
Syrup, Chlorphenamine maleate 2 mg per 5 ml.

OTC **PIRITON®** *(Evans)*
Tablet, Chlorphenamine maleate 4 mg; light yellow biconvex tab. marked 'PIRITON'.
4 mg - 50; 500.
Syrup, Chlorphenamine maleate 2 mg per 5 ml.
Pack - 150 ml.

CLEMASTINE

Therapeutic category: Antihistamine, H_1 Blocker.
Pharmacology: Clemastine is an H_1- receptor antagonist. It belongs to the benzhydryl ether group of antihistamines. It exerts a potent antihistaminic and antipruritic effect with a fast onset and long duration of action up to 12 hrs.
Indications: Hay fever, urticaria, pruritis; as an adjuvant in acute and chronic eczema, contact dermatitis and drug eruptions; insect stings and bites; as an adjuvant in anaphylactic or anaphylactoid shock and angioneurotic oedema; allergic reactions e.g. due to blood transfusion.
Contra-indications: Hypersensitivity to anti-histamines; children below 1 year of age.
Precautions: Road users; narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, prostatic hypertrophy with urinary retention and bladder- neck obstruction; pregnancy, breast-feeding.
Interactions: Sedatives, hypnotics, MAOI's, alcohol.
Adverse effects: Fatigue, sedation, occasionally CNS stimulation, particularly in children; rarely dry mouth, headache, dizziness, skin rash, nausea, gastralgia, constipation.
Advice to patients: See Label 2 in Appendix 6. Avoid alcohol; may cause drowsiness, may impair coordination or judgement.
Nursing considerations: •Raise bed rails, institute safety measures, assist ambulation.
•Encourage patient to rinse mouth frequently or chew gum for dry mouth.
•Instruct patient to change position slowly to avoid fainting.
Dose: By mouth, Adult and Children over 12 years, 1 mg twice daily; up to 6 mg daily in refractory cases.
Child (1-3 years), 0.25-0.5 mg; 3 - 6 years, 0.5 mg; 6-12 years, 0.5-1 mg; to be taken before breakfast and at bedtime.
By i.v. or i.m. injection, Adult, 2 mg

twice daily.
Child: 0.025 mg/kg daily by i.m.injection in 2 divided doses.

POM **Clemastine** *(EDL 3.1)*
Tablet, Clemastine (as hydrogen fumarate) 1 mg.
Elixir, Clemastine (as hydrogen fumarate) 0.5 mg per 5 ml.
Injection, Clemastine (as hydrogen fumarate). 1 mg per ml; in 2 ml amp.

POM **TAVEGYL®** *(Novartis)*
Tablet, Clemastine (as hydrogen fumarate) 1.0 mg
Syrup, Clemastine (as hydrogen fumarate)0.1 mg per ml.
Injection, Clemastine (as hydrogen fumarate) 1.0 mg per ml; in 2 ml amp.

CYPROHEPTADINE

Therapeutic category: Antihistamine, H_1 Blocker.
Pharmacology: Cyproheptadine is a serotonin and histamine antagonist with anticholinergic and sedative properties.
Indications: Allergy and pruritus; migraine headache; appetite stimulant.
Contra-indications: Therapy of an acute asthmatic attack; newborn or premature infants; nursing mothers; known sensitivity to cyproheptadine or drugs with similar chemical structure; concurrent use with MAOIs; glaucoma; stenosing peptic ulcer; symptomatic prostatic hypertrophy; bladder neck obstruction; pyloroduodenal obstruction; elderly, debilitated patients; predisposition to urinary retention.
Precautions: Pregnancy; children under 2 years; driving a car or operating machinery; patients with a history of bronchial asthma, increased intra-ocular pressure, hyperthyroidism, cardiovascular disease, or hypertension due to its atropine-like action; lower respiratory tract symptoms including acute asthma.
Interactions: •MAOIs (enhance the anticholinergic effects of antihistamines).
•Alcohol and other CNS depressants such as hypnotics, sedatives, tranquillisers.
Adverse effects: CNS effects such as drowsiness (often transient); integumentary reaction such as urticaria and excessive perspiration; effects on special senses such as blurred vision, tinnitus; cardiovascular effects such as hypotension, anaphylactic shock, tachycardia; haematological effects such as leucopenia, agranulocytosis; effects on digestive system such as epigastric distress, anorexia; effect on respiratory system such as nasal stuffiness; others such as fatigue, rigors, headache.
Advice to patients: See Label 2 in Appendix 6. May cause drowsiness; may stimulate appetite, avoid alcohol and other CNS depressants; may impair judgement and coordination.
Nursing considerations: •Administer drug with food or milk, if GI upset occurs.
•Coffee or tea can reduce drowsiness.
•Relieve dry mouth with chewing gum, frequent sips of water or ice chips.
•Raise bed rails, institute safety measures, assist with ambulation.
Dose: *In allergy and pruritus*, Adult, by mouth, 4-20 mg daily in 3-4 divided doses or as often as necessary; up to a max. 32 mg daily.
Child (7-14 years), usually 4 mg 2-3 times a day according to the patient's weight and response; up to a max. 16 mg a day; 2-6 years, initially 2 mg 2-3 times a day according to the patient's weight and response; up to a max. 12 mg a day.
In vascular headache and migraine, Treatment and prophylaxis, initially 4 mg, repeated if necessary after an hour; not exceeding 8 mg within a 4-to 6-hour period.
Maintenance, 4 mg every 4 to 6 hours.
As an appetite stimulant, Adult and adolescent, usually 12 mg a day; higher doses are not recommended.
Child (7-14 years), a max. 12 mg a day.
2-6 years, a max. 8mg a day.
Note: Daily dosage to be taken as a singe dose once a day in the evening or alternatively in divided doses.

OTC **CYPRIGOLD®** *(Therapeutic)*
Syrup, Cyproheptadine HCl 2 mg, L-lysine 50 mg liquid glucose 1.5 g per 5 ml.
Pack - 100 ml; 200 ml.
Dose: By mouth, Adult, 4 mg 3 times daily.
Child, 2 mg 3 times daily.

OTC **CYPRON®** *(Orange Drugs)*
Caplet, Cyproheptadine 4 mg
4 mg - 3 x 10 (strips).

OTC **PERIACTIN®** *(Bolax/BPP)*
Tablet, Cyproheptadine HCl 4 mg; white, half–scored tab. marked 'MSD 62'.
4 mg - 100.
Syrup, Cyproheptadine HCl 2 mg; yellow coloured syrup.

Pack - 200 ml.

OTC **TAVO-APPETI**® *(Justeen)*
Tablet, Cyproheptadine HCl BP 4 mg.
Pack – 2 x 10's.

LORATIDINE

Therapeutic category: Antihistamine, H_1 Blocker, Non-sedating.
Indications: Allergic rhinitis such as sneezing, rhinorrhea and itching; also chronic urticaria other allergic dermatologic disorders.
Contra-indications: Hypersensitivity to loratidine or other components of the preparation.
Precautions: Severe liver impairment; safety and efficacy in children below 12 years not established; pregnancy, nursing mothers.
Interactions: Alcohol, erythromycin, ketoconazole, procarbazine, other antihistamines.
Adverse effects: Headache, fatigue, somnolence, dry mouth, nasal dryness, dyspnea, palpitations, anxiety, depression.
Advice to patients: Drink plenty of water; may cause dry mouh, sedation, and can impair judgement and coordination.
Dose: Adult and child above 12 years, by mouth, 10 mg once daily on an empty stomach.

POM **CLARITINE**® *(Supreme)*
Tablet, Loratidine 10 mg.
10 mg - 10.

POM **LORFAST**® *(Interpharma)*
Tablet, Loratidine 10 mg.
10 mg - 3 x 10's.

PROMETHAZINE

Therapeutic category: Antihistamine, H_1 Blocker; Antiemetic; Sedative.
Pharmacology: Promethazine is a long-acting antihistamine with additional anti-emetic effects.
Indications: Symptomatic treatment of allergic conditions of the respiratory tract and skin such as sensitisation reactions to drugs or foreign proteins, anaphylactic reactions; prevention and treatment of nausea and vomiting especially motion sickness.
Contra-indications: Hypersensitivity to promethazine or any component; narrow-angle glaucoma.
Precautions: Pregnancy, road users.
Contra-indications: Hypersensitivity to promethazine or any component; narrow-angle glaucoma.
Interactions: Alcohol, CNS depressants, MAOIs.
Adverse effects: Drowsiness, dizziness, disorientation, photosensitive skin reactions.
Advice to patients: See Label 2 in Appendix 6. May cause drowsiness, impair judgement and coordination; may cause photosensitivity, sunscreening agent and protective clothing may be used; avoid excessive sunlight; notify physician of involuntary movements or feelings of restlessness.
Nursing considerations: •Give with food or milk to reduce GI distress; food may slightly reduce absorption.
•Give I.M. deep into a large muscle mass and rotate injection sites. Avoice S.C route.
•I.V. dose must be diluted to a max. concentration of 25-50 mg/9 ml and infused at max. rate of 25 mg/2 minute. Rapid I.V. administration may cause a transient fall in B.P.
•Coffee or tea may reduce drowsiness; give chewing gum or ice chips to relieve dry mouth.
Dose: By mouth, 25 mg at bedtime; increased to 50-75 mg at bedtime if necessary.
Allergy: 10-20 mg 2-3 times daily.
Child (6 months - 1 year), 5-10 mg daily; 1-5 years, 5-15 mg daily; 5-10 years, 10-25 mg daily; or the lower dose twice daily.
By deep i.m. injection or slow i.v. injection, see lit.

POM **Promethazine** *(EDL 3.1)*
Tablets, Promethazine HCl 10 mg, 25 mg.
Syrup, Promethazine HCl 5 mg per 5ml.
Injection, Promethazine HCl 25 mg per ml; in 1 ml, 2 ml amps.

POM **CIMAX**® *(Beta Drugs)*
Injection, Promethazine HCl 50 mg; sterile solution of Promethazine HCl in water for injections free from dissolved air.
Pack – 2-ml x 100 amps.

POM **FAPZINE**® *(Food & Pharma)*
Syrup, Promethazine HCl 5 mg per 5 ml.
Pack - 100 ml.

POM **PHENERGAN**® *(May & Baker)*
Tablets, Promethazine HCl 10 mg (blue s-c tab. marked 'M & B'), 25 mg (blue f-c tab. marked 'PHENERGAN 25').
10 mg - 50; 500
25 mg - 50; 500.
Elixir, Promethazine HCl 5 mg per 5 ml.
Pack - 100 ml.
Injection, Promethazine HCl 25 mg per ml; in 1 ml, 2 ml amps.
1 ml x 10

RETURN

2 ml x 10

POM **PHENERIL**® *(Vitabiotics)*
Syrup, Promethazine HCl 5 mg
Pack - 60 ml.

POM **Promethazine** *(Emzor)*
Syrup, Promethazine HCl 5 mg per 5 ml.
Pack - 60 ml; 100 ml; 2 L.

POM **Promethazine** *(Leady)*
Syrup, Promethazine HCl 5 mg per 5 ml.
Pack - 100 ml; 2 L.

POM **PROTHAZIN**® *(Ranbaxy)*
Syrup, Promethazine HCl 5 mg per 5 ml.
Pack - 100 ml.

POM **RABYGAN**® *(Rajrab)*
Tablet, Promethazine HCl 25 mg; prussian blue s-c tab.
25 mg - 500.
Elixir, Promethazine HCl 5 mg per 5 ml.
Pack - 100 ml; 2 L.

8.2 Sympathomimetic

ADRENALINE

Synonym: Epinephrine

Indications: Severe anaphylactic reaction; severe angioedema; cardiac arrest (section 5.4).

Precautions: Hyperthyroidism, hypertension, diabetes mellitus, heart disease, arrhythmias, cerebrovascular disease; second stage of labour; elderly; **interactions**: Appendix 1.

Adverse effects: Tachycardia and arrhythmias, hypertension, tremor, anxiety, sweating, nausea, vomiting, weakness, hyperglycaemia, dizziness, pulmonary oedema have all been reported; headache common.

Nursing considerations: •Read the labels to make sure you are using correct concentration, route and dosage.
•Shake before using; rotate IM/SC inj sites; massage after injection.
•Monitor injection site for tissue damage.
•Warn patient to avoid the use of OTC Adrenaline inhalation products; beta$_2$-adrenergic agents for inhalation are preferred.

Dose: CAUTION: DIFFERENT DILUTIONS OF EPINEPHRINE INJECTION ARE USED FOR DIFFERENT ROUTES OF ADMINISTRATION.

Anaphylaxis, by intramuscular or subcutaneous injection of 1:1000 epinephrine injection, see Steps in the Management of Anaphylaxis for doses.

Anaphylaxis, by slow intravenous injection of 1:10 000 epinephrine injection. This route should be reserved for severely ill patients when there is doubt about the adequacy of circulation and absorption from the intramuscular site, see Steps in the Management of Anaphylaxis for doses.

POM **Adrenaline** *(WMF 3.1)*
Injection (Solution for injection), Adrenaline (as hydrochloride or hydrogen tartrate) 1 mg/1 ml; in 1-ml ampoule.

POM **Adrenaline** *(EDL 3.7)*
Injection, Adrenaline (as Acid tartrate or HCl) 1 mg per ml (1 in 1000); in 1ml amp.

8.3 Corticosteroids

DEXAMETHASONE

Indications: Adjunct in the emergency treatment of anaphylaxis; short-term suppression of inflammation in allergic disorders; for other indications see section 10.3.

Contra-indications: Untreated systemic infection (unless condition life-threatening); administration of live virus vaccines.

Precautions: Increased susceptibility to and severity of infection; activation or exacerbation of tuberculosis, amoebiasis, strongyloidiasis; risk of severe chickenpox in non-immune patient (varicella-zoster immunoglobulin required if exposed to chickenpox); avoid exposure to measles (normal immunoglobulin possibly required if exposed); diabetes mellitus; peptic ulcer; hypertension; for further precautions relating to long-term use of corticosteroids see section 10.3.

Adverse effects: Nausea, dyspepsia, malaise, hiccups; hypersensitivity reactions including anaphylaxis; perineal irritation after intravenous administration; for adverse effects associated with long-term corticosteroid treatment see section 10.3.

Dose: *Allergy (short-term use)*, by mouth, ADULT and CHILD, usual range 0.5–10 mg daily as a single dose in the morning.

Anaphylaxis, by slow intravenous injection or infusion, ADULT 0.5–20

mg; CHILD 200–500 micrograms/kg.

POM **Dexamethasone** *(WMF 3.1)*
Tablets, Dexamethasone 500 micrograms, 4 mg [not on WHO Model List].
Injection (Solution for injection), Dexamethasone phosphate (as sodium salt) 4 mg/ml; in 1-ml ampoule.

HYDROCORTISONE

Indications: Adjunct in the emergency treatment of anaphylaxis; inflammatory skin conditions (section 15.2); inflammatory bowel disease (section 4.7); adrenocortical insufficiency (section 10.3)
Contra-indications: Not relevant to emergency use but for contra-indications relating to long-term use see section 10.3.
Precautions: Not relevant to emergency use but for precautions relating to long-term use see section 10.3.
Adverse effects: For adverse effects associated with long-term corticosteroid treatment see section 10.3.
Dose: *Anaphylaxis*, by slow intravenous injection as a single dose, see Steps in the Management of Anaphylaxis (above).

POM **Hydrocortisone** *(WMF 3.1)*
Injection (Powder for solution for injection), Hydrocortisone (as sodium succinate); in 100-mg vial.

PREDNISOLONE

Prednisolone is representative corticosteroid. Various drugs can serve as alternatives.
Indications: Short-term suppression of inflammation in allergic disorders; longer-term suppression (section 10.3); malignant disease (section 12.2.2); eye (section 13.2)
Contra-indications: Untreated systemic infection; administration of live virus vaccines.
Precautions: Increased susceptibility to and severity of infection; activation or exacerbation of tuberculosis, amoebiasis, strongyloidiasis; risk of severe chickenpox in non-immune patient (varicella–zoster immunoglobulin required if exposed to chickenpox); avoid exposure to measles (normal immunoglobulin possibly required if exposed); diabetes mellitus; peptic ulcer; hypertension; for further precautions relating to long-term use of corticosteroids see section 10.3.
Adverse effects: Nausea, dyspepsia, malaise, hiccups; hypersensitivity reactions including anaphylaxis; for adverse effects associated with long-term corticosteroid treatment see section 10.3.
Dose: *Allergy* (short-term use), by mouth, ADULT and CHILD , initially up to 10–20 mg daily as a single dose in the morning (in severe allergy up to 60 mg daily as a short course of 5–10 days).

POM **Prednisolone** *(WMF 3.1)*
Tablets, Prednisolone 5 mg, 25 mg.

9. Anti-infective drugs

RETURN

9.1 Antibacterial drugs
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9.1 Antibacterial drugs

9.1.1 Beta-lactam drugs
9.1.2 Other antibacterials
9.1.3 Antileprosy drugs
9.1.4 Antituberculosis drugs

9.1.1 Beta-lactam drugs

9.1.1.1 Penicillins
9.1.1.2 Cephalosporins and imipenem with cilastatin

Beta-lactam drugs

Beta-lactam antibiotics including penicillins, cefalosporins and carbapenems share a common structure; they are bactericidal, their mechanism of action resulting from inhibition of peptidoglycan, a mucopeptide in bacterial cell walls. **Benzylpenicillin** and **phenoxymethylpenicillin** are active against susceptible strains of Gram-positive bacteria and Gram-negative bacteria, spirochaetes, and actinomycetes, but are inactivated by penicillinase and other beta-lactamases. **Benzathine benzylpenicillin** and **procaine benzylpenicillin** are long-acting preparations which slowly release benzylpenicillin on injection. A range of

penicillins with improved stability to gastric acid and penicillinases have been produced by substitution of the 6-amino position of 6-aminopenicillanic acid. **Cloxacillin** is an isoxazoyl penicillin which is resistant to staphylococcal penicillinase. Broad-spectrum penicillins such as **ampicillin** are acid-stable and active against Gram-positive and Gram-negative bacteria, but are inactivated by penicillinase. Beta-lactamase inhibitors such as **clavulanic acid** are often necessary to provide activity against beta-lactamases produced by a wide range of both Gram-negative and Gram-positive bacteria.

Cefalosporins are classified by generation, with the first generation agents having Gram-positive and some Gram-negative activity; the second generation drugs have improved Gram-negative activity and the third generation cefalosporins have a wider spectrum of activity, although may be less active against Gram-positive bacteria than first generation drugs, but they are active against Gram-negative Enterobacteriaceae and *Pseudomonas aeruginosa*.

Carbapenems are semisynthetic derivatives of *Streptomyces cattleya*. They have a broad spectrum of activity and are stable to most penicillinases. They should be reserved for severe infections resistant to other antibiotics.

Penicillins may cause encephalopathy due to cerebral irritation. This rare, but serious adverse effect may result from very high doses or in severe renal failure. Penicillins should not be given by intrathecal injection because they can cause encephalopathy which may be fatal.

HYPERSENSITIVITY

The most important adverse effect of penicillins is hypersensitivity which causes rashes and, occasionally anaphylaxis, which can be fatal. A careful history should be taken with regard to previous allergic reactions. If rash develops, another antimicrobial should be substituted. Allergic reactions to penicillins occur in 1–10% of exposed individuals, while anaphylactic reactions occur in fewer than 0.05% of treated patients. Individuals with a history of anaphylaxis, urticaria, or rash immediately after penicllin administration are at risk of immediate hypersensitivity to a penicillin. These individuals should not receive a penicillin, a cefalosporin or another beta-lactam antibiotic. Patients who are allergic to one penicillin will be allergic to them all because the hypersensitivity is related to the basic penicillin structure and about 10% of penicillin-sensitive patients will be allergic to cefalosporins and other beta-lactams. Individuals with a history of a minor rash (a non-confluent rash restricted to a small area of the body) or a rash occurring more than 72 hours after penicillin administration are possibly not allergic to penicillin and in these individuals a penicillin should not be withheld unnecessarily for a serious infection; however, the possibility of an allergic reaction should be borne in mind and facilities should be available for treating anaphylaxis.

9.1.1.1 Penicillins

Benzylpenicillins and phenoxymethylpenicillin

Benzylpenicillin remains an important and useful antibiotic but it is inactivated by bacterial beta-lactamases. It is effective for many streptococcal (including pneumococcal) , gonococcal and meningococcal infections and also for anthrax, diphtheria, gas gangrene, leptospirosis, tetanus and treatment of Lyme disease in children. Pneumococci, meningococci and gonococci often have decreased sensitivity to penicillin and benzylpenicillin is no longer the first choice for pneumococcal meningitis. Benzylpenicillin is given by injection as it is inactivated by gastric acid and absorption from the intestinal tract is low.

Depot preparations are used when therapeutic concentrations need to be sustained for several hours. **Benzathine benzylpenicillin** or **procaine benzylpenicillin** provides a tissue depot from which the drug is slowly absorbed over a period of 12 hours to several days. They are the preferred choice for the treatment of syphilis or yaws.

Phenoxymethylpenicillin is suitable for oral administration; it has a similar spectrum of activity but is less effective than benzylpenicillin. It should not be used for serious infections because absorption can be unpredictable and plasma concentrations variable.

Ampicillin, amoxicillin, amoxicillin

with clavulanic acid and cloxacillin

Ampicillin is active against certain Gram-positive and Gram-negative organisms. It is used to treat a wide range of infections including otitis media, respiratory-tract and urinary-tract infections, and gonorrhoea due to susceptible bacteria. However, ampicillin is inactivated by penicillinases including those produced by *Staphylococcus aureus* and by common Gram-negative bacilli such as *Escherichia coli*; many strains of *Haemophilus influenzae*, *Moraxella catarrhalis*, *Neisseria gonorrhoeae*, and *Salmonella* and *Shigella* spp. are resistant. There are geographical variations in the incidence of resistance and an awareness of local patterns is important. In some areas, oral use should be restricted to treatment of *Shigella* infections; it is given in an oral dose of 1 g every 6 hours for 7–10 days.

Amoxicillin has a similar spectrum of activity to ampicillin, but is also inactivated by penicillinases. However, it is better absorbed after oral administration than ampicillin and higher plasma and tissue levels are achieved. Amoxicillin is preferred to ampicillin for the treatment of some infections including otitis media and respiratory-tract and urinary-tract infections.

Clavulanic acid is a beta-lactamase inhibitor. It has no significant antibacterial activity but in combination with **amoxicillin** widens amoxicillin's spectrum of activity and allows its use against amoxicillin-resistant strains of bacteria. It is used in respiratory-tract, genito-urinary and abdominal infections, cellulitis, animal bites, and dental infections.

Cloxacillin is used to treat infections due to penicillinase-producing staphylococci which are resistant to benzylpenicillin. It is acid-stable and may therefore be given by mouth as well as by injection.

These antibiotics may also be administered with an aminoglycoside to increase their spectrums of activity. The penicillin and aminoglycoside should not be mixed before or during administration, because loss of aminoglycoside activity can occur on mixing.

BENZYLPENICILLIN

Synonym: Penicillin G; Crystalline Penicillin.
Therapeutic category: Penicillin Antibiotic

Indications: Pneumonia; throat infections; otitis media; Lyme disease in children; streptococcal endocarditis; meningococcal disease; necrotizing enterocolitis; necrotizing fasciitis; leptospirosis; neurosyphilis; anthrax; actinomycosis; brain abscess; gas gangrene; cellulitis; osteomyelitis.

Contra-indications: Penicillin hypersensitivity (see notes above); avoid intrathecal route (see notes above).

Precautions: History of allergy (see notes above); renal failure (Appendix 4); heart failure; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reactions, haemolytic anaemia, interstitial nephritis (see also notes above); diarrhoea, antibiotic-associated colitis; neutropenia, thrombocytopenia, coagulation disorders, central nervous system toxicity, including convulsions, coma, and encephalopathy (associated with high dosage, or severe renal failure); electrolyte disturbances; Jarisch-Herxheimer reaction (during treatment for syphilis and other spirochaete infections, probably due to release of endotoxins); inflammation, phlebitis or thrombophlebitis at injection sites.

Advice to patients: Report any rash or shortness of breath.

Nursing considerations: •Determine whether the patient is allergic to penicillins prior to administration.
•Obtain specimen for C&S test; therapy may begin pending test results.
•Dosage should be modified in renal impairment.
•Tell patient to report any rash, fever or chills; fever, eosinophilia are common allergic reactions; very slow absorption time makes allergic reactions difficult to treat.
•Large doses and prolonged therapy may give rise to superimposed infection; teach patient symptoms namely sore throat, fever fatigue and to report such symptoms.
•Encourage patient to take adequate fluids if diarrhoea occurs.

Dose: *Mild to moderate infections due to sensitive organisms*, by intramuscular injection or by slow intravenous injection or by intravenous infusion, ADULT 0.6–2.4 g daily in 2–4 divided doses, with higher doses in severe infections and duration of treatment depending on disease (see also below); neonate 50

mg/kg daily in 2 divided doses; infant 1 to 4 weeks, 75 mg/kg daily in 3 divided doses; CHILD 1 month to 12 years, 100 mg/kg daily in 4 divided doses, with higher doses in severe infections (see also below).
Bacterial endocarditis, by slow intravenous injection or by intravenous infusion, ADULT up to 7.2 g daily in 6 divided doses.
Meningococcal disease, by slow intravenous injection or by intravenous infusion, ADULT up to 14.4 g daily in divided doses; premature infant and neonate 100 mg/kg daily in 2 divided doses; infant 150 mg/kg daily in 3 divided doses; CHILD 1 month to 12 years, 180–300 mg/kg daily in 4–6 divided doses.
Suspected meningococcal disease (before transfer to hospital), by intramuscular injection or by slow intravenous injection , ADULT and CHILD over 10 years, 1.2 g; CHILD under 1 year, 300 mg; CHILD 1 to 9 years, 600 mg.
Neurosyphilis, by slow intravenous injection, ADULT 1.8–2.4 g every 4 hours for 2 weeks.
Congenital syphilis, by intramuscular injection or by slow intravenous injection, CHILD up to 2 years, 30 mg/kg daily in 2 divided doses for 10 days; CHILD over 2 years, 120–180 mg/kg (to a maximum of 1.44 g) daily in divided doses for 14 days.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

Note: Administer I.M by deep injection in the upper outer quadrant of the buttock; administer injection around-the-clock to promote less variation in peak and trough levels; while I.M route is preferred route of administration, large doses should be administered by continuous I.V. infusion; determine volume and rate of fluid administration required in a 24-hour period, add appropriate daily dosage to this fluid.

POM **Benzylpenicillin** *(WMF 6.2.1.1)*
Injection (Powder for solution for injection), Benzylpenicillin sodium 600-mg vial (1 million units); 3-g vial (5 million units).

POM **Benzylpenicillin** *(EDL 6.8)*
Injection, Benzylpenicillin (as sodium or potassium salt) 0.6 g (1 million units), 3 g (5 million units); powder in vials.

POM **BENYCIN®** *(Beta Drugs)*
Injection, Benzylpenicillin potassium 0.125 g (200,000 i.u.)/vial; 0.25 g (400,000 i.u.)/vial; 0.313 g (500,000 i.u.)/vial; 0.5 g (800,000 i.u.)/vial; 0.625 g (1,000,000 i.u.)/vial; white sterile crystalline powder, which is very soluble in water.

POM **CRYSGEN®** *(Geneith)*
Injection, Benzylpenicillin sodium 1 mega unit.

POM **Crystalline Penicillin G** *(Doyin)*
Injection, Crystalline penicillin G potassium 0.6 g (1 million units); powder in vial.
Pack - 50.

POM **SACOPEN®** *(GoldMoore)*
Injection, Benzylpenicillin (as potassium) 0.12 g (200,000 i.u), 0.24 g (400,000 i.u), 0.3 g (500,000 i.u), 0.48 g (800,000 i.u), 0.6 g (1000,000 i.u), 1.2 g (2000,000 i.u), 3.0 g (5000,000 i.u).

BENZATHINE PENICILLIN

Synonym: Penicillin G Benzathine; Benzathine benzylpenicillin.
Therapeutic category: Penicillin Antibiotic.
Indications: Streptococcal pharyngitis; diphtheria carrier state; syphilis and other treponemal infections (yaws, pinta, bejel); rheumatic fever prophylaxis.
Contra-indications: Penicillin hypersensitivity (see notes above); intravascular injection; neurosyphilis.
Precautions: History of allergy (see notes above); renal failure (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.
Adverse effects: Hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reaction, haemolytic anaemia, interstitial nephritis (see also notes above); neutropenia, thrombocytopenia, coagulation disorders and central nervous system toxicity (associated with high dosage or severe renal failure); Jarisch-Herxheimer reaction (during treatment for syphilis and other spirochaete infections, probably due to release of endotoxins); rarely, non-allergic (embolic-toxic) reactions; pain and inflammation at injection site.
Nursing considerations: •Before giving drug, ask patient if he has had any allergic reactions to this drug or penicillins generally; scratch test may be done

to assess allergy; obtain specimen for C&S test, therapy may begin pending test results.
•Administer by deep IM inj in large muscle mass; aspirate to avoid intravascular inj. Shake well before injection.
•Never give I.V - inadvertent I.V. administration has caused instant cardiac arrest and death.
•Tell patient to report any rash, fever or chills; fever, eosinophilia are common allergic reactions; very slow absorption time makes allergic reactions difficult to treat.
•Large doses and prolonged therapy may give rise to superimposed infection; teach patient symptoms namely sore throat, fever fatigue and to report such symptoms.
•Encourage patient to have extra fluid intake if diarrhoea occurs.

Dose: *Streptococcal pharyngitis; primary prophylaxis of rheumatic fever*, by deep intramuscular injection , ADULT and CHILD over 30 kg, 900 mg as a single dose; CHILD under 30 kg, 450–675 mg as a single dose.
Secondary prophylaxis of rheumatic fever, by deep intramuscular injection, ADULT and CHILD over 30 kg, 900 mg once every 3–4 weeks; CHILD under 30 kg, 450 mg once every 3–4 weeks.
Early syphilis, by deep intramuscular injection, ADULT 1.8 g as a single dose, divided between 2 sites.
Late syphilis, by deep intramuscular injection, ADULT 1.8 g, divided between two sites, once weekly for 3 consecutive weeks.
Congenital syphilis (where no evidence of CSF involvement), by deep intramuscular injection, CHILD up to 2 years, 37.5 mg/kg as a single dose.
Yaws, pinta, and bejel, by deep intramuscular injection, ADULT 900 mg as a single dose; CHILD 450 mg as a single dose.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

How to Use: For deep intramuscular injection. For i.m. injections suspend the content of the 600,000 I.U. (0.6 M.U.)vial in at least 2 ml of water for injections, that of the 1.2 M.U. vial in at least 3 ml of water for injections and that of the 2.4 M.U. vial in at least 5 ml of water for injections.
Shake vigorously for 20 secnds and apply immediately using a needle of at least 0.9 mm strenght. Withdraw no more than one dose. Only use freshly prepared suspensions. Before injecting the dose, aspirate to be sure needle bevel is not in a blood vessel. When repeating doses, vary the injection site.
Administer by deep intramuscular injection into the outer, upper quadrant of the buttock or into Hochstetter's ventrogluteal field. In children the midlateral aspect of the thigh (quadriceps femoris muscle) is preferable. Only use the deltoid muscle for injections, if its muscle mass is well developed; keep well away from the radial nerve.
The maximal volume tolerated at a given injection site is 5 ml. Consequently, no more than 5 ml of the injectable suspension should be applied at any one site.

POM **Benzathine penicillin** *(WMF 6.2.1.1)*
Injection (Powder for solution for injection), Benzathine penicillin, 1.8-g vial (equivalent to benzylpenicillin 1.44 g, 2.4 million units).

POM **Benzathine Penicillin** *(EDL 6.8)*
Injection, Benzathine penicillin 1.2 m.u., 2.4 m.u.; powder for reconstitution in vials.

POM **PENADUR L–A®** *(Wyeth/Delpitano)*
Injection, Benzathine penicillin 0.6 m.u., 1.2 m.u., 2.4 m.u.; powder for reconstitution in vials.

POM **RETARPEN®** *(Carrot-Top)*
Injection, Benzathine penicillin 0.6 m.u., 1.2 m.u., 2.4 m.u.; powder for reconstitution in vials.
Pack - Single packs of 1 vial (+ solvent); Hospital packs.

Dose: Treatment of syphilis
Congenital syphilis in neonates or infants (without neurological involvement): 1 dose of 1.2 M.U. injected at 2 sites
Primary, Secondary, Latent syphilis:
Primary - 1 dose of 2.4 M.U. injected at 2 sites
Secondary - 2 doses of 2.4 M.U. injected at 2 sites; Repeat treatment if clinical symptoms recur or if laboratory tests are persistently positive.
Late (tertiary, seropositive) - 1 to 2 doses of 2.4 M.U. weekly for 3 to 5 weeks.
Treatment of Yaws
Children under 12 years: 1 dose of 0.6 M.U.
Adults: 1 to 2 doses of 1.2 M.U.
Contacts and persons with latent infections are given half of these doses.
Other infections
Children under 12 years: 1 dose of 0.6 M.U. at intervals of 3 days or daily,

depending on the severity of the disease. Alternatively, 1 dose of 1.2 M.U. at intervals of 2 to 4 weeks.
Adults: 1 dose of 1.2 -2.4 M.U. once a week.
Prophylaxis
Prevention of recurrent rheumatic fever, rheumatic endocarditis, chorea, poststreptococcal glomerulonephritis and erysipela: Children under 12 years: 1 dose of 0.6 M.U. at intervals of 14 days or 1 dose of 1.2 M.U. at intervals of 4 weeks.
Adults: 1 to 2 doses of 1.2 M.U. at intervals of 4 weeks.
Prevention of scarlet fever in contacts: Children under 12 years: 1 dose of 0.6 - 1.2 M.U. at weekly intervals.
Adults: 2 doses of 1.2 M.U. or 1 dose of 2.4 M.U.

Note: To prevent complications, patients with streptococcal disease should receive treatment for at least 10 days.
This can generally be ensured with a single injection of 0.6 M.U. in children under the age of 12 years, with a single injection of 1.2 M.U. in children over the age of 12 years and with a single injection of 2.4 M.U. in adults.
Do not apply more than 50 mg of Povidone (equivalent to 2.4 M.U. Retarpen) at one injection site. Inject higher single doses at different sites.

PROCAINE PENICILLIN FORTIFIED

Synonym: Penicillin G Procaine; Aqueous Procaine Penicillin G, APPG; Procaine Benzylpenicillin.
Therapeutic category: Penicillin Antibiotic.
Indications: Syphilis; anthrax; childhood pneumonia; diphtheria carrier state; cellulitis; mouth infections; bites.
Contra-indications: Hypersensitivity to penicillins (see notes above); intravascular injection.
Precautions: History of allergy (see notes above); renal failure (Appendix 4); **interactions**: Appendix 1.
Adverse effects: Hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reaction, haemolytic anaemia, interstitial nephritis (see also notes above); neutropenia, thrombocytopenia, coagulation disorders and central nervous system toxicity (associated with high doses and severe renal failure); Jarisch-Herxheimer reaction (during treatment for syphilis and other spirochaete infections, probably due to release of endotoxins); rarely, non-allergic (embolic-toxic) reactions; pain and inflammation at injection site
Advice to patients: Notify physician if skin rash, itching, hives, or severe diarrhoea occurs.
Nursing considerations: •Before administration, confirm that patient is not allergic to penicillins.
•Obtain specimen for C&S test; therapy may begin pending test results.
•Give deep I.M. into a large muscle mass using the upper outer quadrant of buttocks in adults and midlateral thigh in small children. Avoid S.C route. Do not massage injection site. Rotate the injection site.
•Never give I.V. - inadvertent I.V. administration has caused death, due to CNS toxicity from procaine.
•Tell patient to report any rash, fever or chills; rash is the most common allergic reaction; allergic reactions are difficult to treat due to slow absorption rate.
•Large doses and prolonged therapy may cause superimposed infection; teach patient symptoms namely sore throat, fever fatigue and to report such symptoms.
•Renal and haematologic systems should be evaluated periodically during prolonged therapy.
•Encourage patient to have extra fluid intake if diarrhoea occurs.
Dose: *Infections due to sensitive organisms*, by deep intramuscular injection, ADULT 0.6 to 1.2 g daily.
Pneumonia, by deep intramuscular injection, CHILD 50 mg/kg daily for 10 days.
Syphilis, by deep intramuscular injection, ADULT 1.2 g daily for 10 to 15 days, or up to 3 weeks in late syphilis.
Congenital syphilis, by deep intramuscular injection, CHILD up to 2 years, 50 mg/kg daily for 10 days.

See also under the individual preparations below.
RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Procaine penicillin** *(WMF 6.2.1.1)*
Injection (Powder for solution for injection), Procaine penicillin 1-g vial (1 million units), 3-g vial (3 million units).

POM **Procaine Penicillin Fortified** *(EDL 6.8)*
Injection, Procaine Penicillin 0.3 m.u (300 mg), benzylpenicillin 0.1 m.u (60 mg); Procaine penicillin 3 m.u (3 g), benzylpenicillin 1 m.u. (600 mg).

POM **GLOPEN®** *(GoldMoore)*
Injection, Procaine penicillin 3,000,000 I.U,

penicillin potassium (or sodium) 1,000,000 I.U.
Pack - 4,000,000 I.U. in vials

POM **LIFEFORT®** *(Justeen)*
Injection, Procaine Benzylpenicillin 4 m.u.
Pack – 1 x 10's.

POM **NIXA-G®** *(Beta Drugs)*
Injection, Procaine penicillin 3,000.000 I.U., penicillin potassium (or sodium) 1,000.000 I.U.; in 4,000.000 I.U. vials.

POM **Procaine Penicillin Fortified** *(Doyin)*
Injection, Procaine penicillin 3 m.u. (3 g), benzylpenicillin 1 m.u. (600 mg); ten dose vial.
4 m.u. (4,000,000 units) - 100.
When suspended in 8.2ml of water for injection or sterile isotonic sodium chloride solution, each ml contains 400,000 units of Procaine penicillin fortified (300,000 units of Procaine Penicillin G plus 100,000 units of Potassium Penicillin G).

Dose: By I.M. injection only (solution should be at room temperature), 400,000 units (1 ml) once every 24 hours; increased in severe infections to 400,000 - 800,000 units (1-2 ml) every 12-24 hours. Treatment should be continued for at least 48 hours after the temperature has returned to normal and other evidences of infection have disappeared. The treatment of streptococcal infections should be continued for 10 dadys to prevent the development of rheumatic fever or glomerunephritis.
Primary or secondary syphilis and latent syphilis with negative spinal fluid, 800,000 (2 ml) daily for 6 days (total of 4,800,000 units).
Late syphilis (including symptomatic and asymptomatic neurosyphilis), 800,000 units (2 ml) daily for 10-15 days (total of 8,000,000 to 12,000,000 units).
Congenital syphilis (early or late), 10,000 units/kg daily for 10 days.
Syphilis in pregnancy, treatment should correspond to the stage of disease.

Note: **Method of Preparation of suspension** - One dose vial (400,000 units) should be dissolved in 0.9ml solvent to form 1ml suspension. Ten dose vial (4,000,000 units) should be dissolved in 8.2 ml solvent to form 10 ml suspension. Water for injection or sterile isotonic Sodium chloride solution is the recommended solvent.

To prepare suspension - Draw up required amount of diluent into a sterile syringe. Insert diluent with vial in an inverted position. Shake vigorously until all diluent has been added and suspension is smooth and uniform. Shake well each time before withdrawing dose.
To withdraw dose- Insert air to break vaccum. Withdraw dose in clean syringe without tight fitting plunger. After removing needle from vial, clear needle by drawing small amount of air. Use 20 gauge needle.

POM **Procaine Penicillin Fortified** *(Neimeth)*
Injection, Penicillin G Procaine crystalline 3 m.u., buffered penicillin G potassium crystalline 1 m.u; powder in vial.
4 m.u. - 50.

POM **PROMACIN®** *(Geneith)*
Injection, Procaine penicillin 3 M.I.U., Benzylpenicillin 1 M.I.U.

POM **REMPEN®** *(Strides Vital)*
Injection, Fortified procaine penicillin 4 MU; in vials.
Pack – 100's.

PHENOXYMETHYLPENICILLIN

Synonym: Penicillin V
Therapeutic category: Oral penicillin antibiotic.
Indications: Streptococcal pharyngitis; otitis media; erysipelas; mouth infections; secondary prophylaxis of rheumatic fever; post-splenectomy prophylaxis.
Contra-indications: Hypersensitivity to penicillins (see notes above); serious infections (see notes above).
Precautions: History of allergy (see notes above); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.
Adverse effects: Hypersensitivity reactions including urticaria, joint pain, rash, angioedema, anaphylaxis (see notes above); nausea and diarrhoea.
Advice to patients: See Labels 9 and 23 in Appendix 6. Take on an empty stomach 1 hour before or 2 hours after meals; take until gone, do not skip doses; report any rash or shortness of breath; shake liquid well before use.
Nursing considerations: •Obtain history of allergic reactions from patient.
•Obtain specimen for C&S test; therapy may begin pending test results.
•Give on an empty stomach for best absorption; and to minimise GI distress, may be given 1-2 hours before or 2-3 hours after meals with a full glass of water NOT juice (Acid inactivates the drug).
•Tell patient to report any rash, fever or chills; rash is the most common allergic reaction.
•Large doses and prolonged therapy may cause su-

perimposed infection; advise patient to report sore throat, fever and fatigue which indicate superinfection.
•Encourage patient to take adequate fluids if diarrhoea occurs
•Renal and haematologic systems should be evaluated periodically during prolonged therapy.

Dose: *Infections due to sensitive organisms*, by mouth, ADULT 500 mg every 6 hours increased up to 1 g every 6 hours in severe infections; CHILD up to 1 year, 62.5 mg every 6 hours; CHILD 1–5 years, 125 mg every 6 hours; CHILD 6–12 years, 250 mg every 6 hours.
Secondary prophylaxis of rheumatic fever, by mouth, ADULT 500 mg twice daily; CHILD 1–5 years, 125 mg twice daily; CHILD 6–12 years, 250 mg twice daily.

POM **Phenoxymethylpenicillin** *(WMF 6.2.1.1)*
Tablets, Phenoxymethylpenicillin (as potassium salt) 250 mg.
Oral suspension (Powder for oral suspension), Phenoxymethylpenicillin (as potassium salt) 250 mg/5 ml.

POM **Phenoxymethyl Penicillin** *(EDL 6.8)*
Tablet, Phenoxymethylpenicillin (as potassium salt) 250 mg.
Suspension, Phenoxymethylpenicillin 250 mg per 5 ml.

AMOXICILLIN

Synonym: Amoxycillin
Therapeutic category: Penicillin Antibiotic.
Indications: Urinary-tract infections, upper respiratory-tract infections, bronchitis; pneumonia; otitis media; dental abscess; osteomyelitis; Lyme disease in children; endocarditis prophylaxis; post-splenectomy prophylaxis; gynaecological infections; gonorrhoea; Helicobacter pylori eradication (section 4.1).
Contra-indications: Hypersensitivity to penicillins (see notes above).
Precautions: History of allergy (see notes above); renal impairment (Appendix 4); erythematous rashes common in glandular fever, chronic lymphatic leukaemia, and possibly HIV infection; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.
Adverse effects: Nausea and vomiting, diarrhoea; rashes (hypersensitivity or toxic response; may be serious reaction—discontinue treatment); hypersensitivity reactions including urticaria, angioedema, anaphylaxis, serum sickness-like reactions, haemolytic anaemia, interstitial nephritis (see also notes above); rarely, antibiotic-associated colitis; neutropenia, thrombocytopenia, coagulation disorders; rarely, central nervous system disorders including convulsions associated with high doses or impaired renal function.
Advice to patients: See Label 9 in Appendix 6. Report diarrhoea promptly; entire course of medication (10-14 days) should be taken to ensure eradication of organism; should be taken in equal intervals around-the-clock to maintain adequate blood levels; may interfere with oral contraceptives; females should report symptoms of vaginitis; paediatric drops may be placed on child's tongue or added to formula, milk, etc.
Nursing considerations: •Obtain specimens for culture and sensitivity before the first dose (therapy may begin pending test results); ensure patient is not allergic to penicillins.
•Give with food to prevent GI distress; administer around-the-clock (in equal interval) rather than 3 times/day to promote less variation in peak and trough serum levels. Shake suspension well before each dose.
•Monitor closely for signs of superinfection especially with large doses and prolonged therapy.
•Advise patient to report immediately if rash, fever, or chills occur. Rash is the most common allergic reaction.
•Advise patient to report diarrhoea; may be symptom of pseudomembranous colitis which can be life-threatening.

Dose: *Infections due to sensitive organisms*, by mouth, ADULT and CHILD over 10 years, 250 mg every 8 hours, doubled in severe infections; CHILD up to 10 years, 125 mg every 8 hours, doubled in severe infections.
Severe or recurrent purulent respiratory-tract infections, by mouth, ADULT 3 g every 12 hours.
Pneumonia, by mouth, adult 0.5–1 g every 8 hours.
Dental abscess (short course), by mouth, ADULT 3 g repeated once after 8 hours.
Urinary-tract infections (short course), by mouth, ADULT 3 g repeated once after 10–12 hours.
Chlamydia, by mouth, 500 mg every 8 hours for 7 days.
Gonorrhoea (short course), by mouth, ADULT 3 g as a single dose (with probenecid 1 g).
Otitis media (short course), by mouth, CHILD aged 3–10 years, 750 mg

twice daily for 2 days.

Note: Except for gonorrhoea and for other short-course therapies, treatment should be continued for a minimum of 48-72 hours after patient becomes asymptomatic or evidence of bacterial eradication has been obtained. In stuborn or severe infections, large doses and prolonged therapy may be required. A minimum of 10 days of treatment is recommended for any infection caused by haemolytic streptococci to prevent the occurrence of acute rheumatic fever or glomerulonephritis.

POM **Amoxicillin** *(WMF 6.2.1.2)*
Capsules, Amoxicillin 250 mg, 500 mg.
Oral suspension (Powder for oral suspension), Amoxicillin 125 mg/5 ml.

POM **Amoxicillin** *(EDL 6.8)*
Capsule, Amoxicillin 250 mg.
Suspension, Amoxicillin 125 mg per 5 ml.
Injection, Amoxicillin 250 mg, 500 mg; powder in vials.

POM **AMAXIN®** *(Dana)*
Capsule, Amoxicillin (as trihydrate) BP 250 mg.
250 mg - 10 x 10's (in blister).
Syrup, Amoxicillin (as trihydrate) BP 125 mg per 5 ml.
Pack - 100 ml.

POM **AMOXICAP®** *(Hovid)*
Capsules, Amoxicillin (as trihydrate) 250 mg, 500 mg.
250 mg - 10 x 10 (blister)
500 mg - 10 x 10 (blister)

POM **AMOXIGRAN®** *(Hovid)*
Suspension, Amoxicillin (as trihydrate) 125 mg per 5 ml, 250 mg per 5 ml; granules for reconstitution.
125 mg/5 ml - 100 ml
250 mg/5 ml - 100 ml

POM **AMOXIL®** *(GSK)*
Capsule, Amoxicillin (as trihydrate) 250 mg; maroon/gold cap. marked with cap name and strength.
250 mg - 16; 100.
Syrup, Amoxicillin (as trihydrate) 125 mg per 5 ml in a sucrose-free sorbitol base; powder for reconstitution.
Pack - 100 ml.
Injection, Amoxicillin (as sodium salt) 250 mg, 500 mg; powder in vials.
250 mg - 10
500 mg - 10.

POM **AMOXITAB®** *(Hovid)*
Tablet, Amoxicillin (as trihydrate) 125 mg; flavoured tab.
125 mg - 100; 1000; 10 x 10 (blister).

POM **AMOXIVAL®** *(NGC)*
Capsule, Amoxicillin (as trihydrate) 250 mg.
250 mg - 10 x 10.
Syrup, Amoxicillin (as trihydrate) 125 mg per 5 ml.
Pack - 100 ml.

POM **Amoxicillin** *(Afrab-Chem)*
Suspension, Amoxicillin (as trihydrate) 125 mg per 5 ml, 250 mg per 5 ml; dry powder for oral reconstitution.
125 mg/5 ml - 100 ml.
250 mg/5 ml - 100 ml.

POM **Amoxicillin** *(Drugfield)*
Capsule, Amoxicillin 250 mg.
Syrup, Amoxicillin 125 mg per 5 ml; dry powder for reconstitution.

POM **Amoxicillin** *(Emzor)*
Capsule, Amoxicillin 250 mg.
Suspension, Amoxicillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.

POM **AMOXYDAR®** *(Supreme)*
Capsule, Amoxicillin 250 mg, 500 mg.
250 mg - 500.
500 mg - 500.

POM **BARBIMOX®** *(Juhel)*
Syrup, Amoxicillin (as tryhydrate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.

POM **DAMOXICILLIN®** *(David)*
Capsule, Amoxicillin (as trihydrate)250 mg.
250 mg - 100
Syrup, Amoxicillin (as tryhydrate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **DRIMOX®** *(Fidson)*
Capsules, Amoxicillin (as trihydrate) 250 mg, 500 mg.
250 mg - 10 x 10.
500 mg - 10 x 10.
Syrup, Amoxicillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **IPCAMOX**® *(IPCA)*
Capsules, Amoxicillin (as trihydrate) BP 250 mg, 500 mg.
250 mg - 10's; 500's; 1000's.
500 mg - 10's; 500's; 1000's.
Syrup, Amoxicillin (as tryhydrate) BP 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **JAWAMOX**® *(Jawa)*
Capsule, Amoxicillin 500 mg.
500 mg - 10 x 10's.
Syrup, Amoxicillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.

POM **KEZZ AMOXICILLIN**® *(Kezz)*
Capsule, Amoxicillin (as trihydrate) BP 500 mg.
500 mg - 10 x 10's.

POM **MAXMOX**® *(GoldMoore)*
Capsules, Amoxycillin (as trihydrate) BP 250 mg, 500 mg.
250 mg - 10 x 10's.
500 mg - 10 x 10's.

POM **MOCKS**® *(Sam)*
Capsules, Amoxicillin (as trihydrate) 250 mg, 500 mg.
250 mg - 10 x 10.
500 mg - 10 x 10.

POM **MOXY**® *(Food & Pharma)*
Syrup, Amoxicillin (as trihydrate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml

POM **MOXYCARE**® *(Ulticare-Lyka)*
Suspension, Amoxicillin (as trihydrate) 125 mg per 5 ml.
Pack - 100 ml.

POM **MOXYLIN**® *(Dizpharm)*
Capsule, Amoxicillin (as trihydrate) 250 mg.
250 mg - 100
Suspension, Amoxicillin (as trihydrate) 125 mg per 5 ml.
Pack - 60 ml.

POM **NOXIL**® *(Geneith)*
Capsule, Amoxicillin 500 mg.
500 mg – 10's (in blister).

POM **RANOXYL**® *(Ranbaxy)*
Capsules, Amoxicillin (as trihydrate) BP 250 mg, 500 mg.
250 mg - 10 x 10's; 1000's.
500 mg - 10 x 10's; 1000's.
Suspension, Amoxicillin USP 125 mg, 250 mg per 5 ml.
Pack - 60 ml; 100 ml.

POM **TECMOX**® (*Panvij Biotec*)
Capsules, Amoxicillin (as trihydrate) 250 mg, 500 mg; maroon/yellow caps marked with brand name and strenght.
250 mg - 10 x 10; 1000.
500 mg - 10 x 10; 1000.
Suspension, Amoxicillin (as trihydrate) 125 mg per 5 ml; light orange coloured, viscous, flavoured, oily suspension.

POM **TYMOXYL**® *(Titan)*
Capsule, Amoxicillin (as trihydrate) 250 mg.
250 mg - 10 x 10.
Syrup, Amoxicillin (as trihydrate) 125 mg per 5 ml; powder for reconstitution.
Pack - 100 ml.

POM **VITAMOX**® *(Strides Vital)*
Capsules, Amoxicillin (as trihydrate) 250 mg, 500 mg; maroon/yellow caps marked with brand name and strength.
250 mg - 10 x 10's.
500 mg - 10 x 10's.

POM **WINPEN**® *(Interpharma)*
Capsules, Amoxicillin (as trihydrate) 250 mg, 500 mg.
250 mg - 10 x 10's.
500 mg - 10 x 10's.
Suspension, Amoxicillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.

AMOXICILLIN plus CLAVULANIC ACID

Synonym: Amoxycillin with clavulanic acid.
Therapeutic category: Penicillin Antibiotic.
Indications: Infections due to beta-lactamase producing bacteria (where Amoxicillin alone not appropriate) including respiratory-tract infections, genito-urinary and abdominal infections, cellulitis, animal bites, severe dental infections, and surgical prophylaxis.
Contra-indications: Hypersensitivity to penicillins (see notes above); history of penicillin- or Amoxicillin with clavulanic acid-associated jaundice or hepatic dysfunction.
Precautions: History of allergy (see notes above); renal impairment (Appendix 4); erythematous rashes common in glandular fever, chronic lymphatic leukaemia, and

possibly HIV infection; hepatic impairment (Appendix 5); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Nausea and vomiting, diarrhoea; rashes (hypersensitivity or toxic response—may be serious, discontinue treatment); hypersensitivity reactions including urticaria, angioedema, anaphylaxis, serum sickness-type reaction, haemolytic anaemia, interstitial nephritis (see also notes above); rarely, antibiotic-associated colitis; neutropenia, thrombocytopenia, coagulation disorders; dizziness, headache, convulsions (particularly with high doses or in renal impairment); hepatitis, cholestatic jaundice; erythema multiforme (including Stevens-Johnson syndrome), toxic epidermal necrolysis, exfoliative dermatitis, vasculitis reported; superficial staining of teeth with suspension; phlebitis at injection site.

Advice to patients: See label 9 in Appendix 6.

See also under Amoxicillin.

Nursing considerations: •Two 250 mg tablets are not equivalent to one 500 mg tablet (both tablet sizes contain equivalent clavulanate, i.e., 125 mg); potassium content: 0.16 mEq of potassium per 31.25 mg of clavulanic acid.

•*See also under Amoxicillin*.

Dose: NOTE: ALL DOSES EXPRESSED AS AMOXICILLIN.

Infections due to susceptible beta-lactamase producing organisms, by mouth, ADULT and CHILD over 12 years, 250 mg every 8 hours, doubled in severe infections; CHILD under 1 year, 20 mg/kg daily in 3 divided doses; 1–6 years, 125 mg every 8 hours; 6–12 years, 250 mg every 8 hours.

Severe dental infections, by mouth, ADULT 250 mg every 8 hours for 5 days.

Infections due to susceptible beta-lactamase producing organisms, by intravenous injection over 3–4 minutes, ADULT and CHILD over 12 years, 1 g every 8 hours, increased to 1 g every 6 hours in severe infections; neonate and premature infant 25 mg/kg every 12 hours; infant up to 3 months, 25 mg/kg every 8 hours; CHILD 3 months to 12 years, 25 mg/kg every 8 hours increased to 25 mg/kg every 6 hours in more severe infections.

Surgical prophylaxis, by intravenous injection , ADULT 1 g at induction, with up to 2–3 further doses of 1 g every 8 hours if increased risk of infection).

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

See below under the proprietary preparations.

POM **Amoxicillin plus Clavulanic acid** *(WMF 6.2.1.2)*

Tablets, Amoxicillin (as trihydrate) 500 mg with clavulanic acid (as potassium salt) 125 mg.

Oral suspension (Powder for oral suspension), Amoxicillin (as trihydrate) 125 mg with clavulanic acid (as potassium salt) 31 mg [not included on WHO Model List].

Oral suspension (Powder for oral suspension), Amoxicillin (as trihydrate) 250 mg with clavulanic acid (as potassium salt) 62 mg [not included on WHO Model List].

Injection (Powder for solution for injection), Amoxicillin (as sodium salt) 0.5 g or 1 g with clavulanic acid (as potassium salt) 100 mg or 200 mg respectively [not included on WHO Model List].

POM **Amoxicillin plus Clavulanic acid** *(EDL 6.8)*

Tablet or Capsule, Amoxicillin (as trihydrate) 250 mg, Clavulanic acid (as potassium salt) 125 mg.

Suspension, Amoxicillin (as trihydrate) 125 mg, clavulanic acid (as potassium salt) 31.25 mg; powder for oral susp.

Injection, Amoxicillin (as trihydrate) 500 mg, clavulanic acid (as potassium salt) 125 mg; powder for i.v. Injection in vial.

POM **AMOKSIKLAV®** *(Taylek)*

Tablet (375 mg), Amoxicillin (as trihydrate) 250 mg, clavulanic acid (as potassium salt) 125 mg. 375 mg - 15; 20; 21.

Tablet (625 mg), Amoxicillin (as trihydrate) 500 mg, clavulanic acid (as potassium salt) 125 mg. 625 mg - 10; 15; 16; 20; 21.

Suspension (156.25 mg/5 ml), Amoxicillin (as trihydrate)125 mg, clavulanic acid (as potassium salt) 31.25 mg per 5 ml; powder for reconstitution.

Dose: By mouth, child (7-12 years), 10 ml 3 times daily; 2-7 years, 5ml 3 times daily; 9 months - 2 years, 2.5 ml 3 times daily before or with meals.

Exact children's doses are based on body weight, usually 20-40 mg/kg b.wt per day divided in 3 equal doses depending on severity of infection.

Treatment must not exceed 14 days without medical re-examination.

Reconstitution - Shake well the bottle containing the powder, add 86 ml of water in two portions (or first to 2/3 and then to the mark) each time shaking well.

Suspension forte (312.5 mg/5ml), Amoxicillin (as trihydrate) 250 mg, clavulanic acid (as potassium salt) 62.5 mg per 5ml; powder for reconstitution.

Dose: By mouth, child (7-12 years), 5 ml 3 times daily; 2-7 years, 2.5 ml 3 times daily; 9 months - 2 years, use the normal suspension (156.25 mg/5 ml). Exact children's doses are based on body weight, usually 20-40 mg/kg but per day divided in 3 equal doses depending on the severity of infection. Treatment must not exceed 14 days without medical re-examination.

Reconstitution - Shake well the bottle containing the powder, add 85 ml of water in two portions (or first to 2/3 and then to the mark) each time shaking well.

Injection, Amoxicillin 500 mg, clavulanic acid 100 mg.

POM **AUGMENTIN®** *(GSK)*

Tablet (375 mg), Amoxicillin (as trihydrate) 250 mg, clavulanic acid (as potassium salt)125 mg; white oval f-c tab. marked 'AUGMENTIN' on one side.

Pack - 21.

Dose: *Mild to moderate infections*, Adult and Children over 12 years, 375 mg tab. 3 times a day; *Severe infections*, 625 mg tab. 3 times a day or 2 375 mg tabs 3 times a day.

Suspension (156 mg), Amoxicillin (as trihydrate) 125 mg, clavulanic acid (as potassium salt) 31.25 mg; sugar-free fruit flavoured powder for reconstitution with aspartame.

Pack - 100 ml.

Dose: Child: usually 25 mg/kg/day in divided doses every 8 hours as follows:
Under 1 year (e.g., 7.5 kg), 2 ml 3 times a day; 1-6 years (10-18 kg), 5 ml 3 times a day; over 6 years (18-40 kg), 10 ml 3 times a day.

Injection, Amoxicillin (as sodium salt) 500 mg, clavulanic acid (as potassium salt) 100 mg; powder in vial.

POM **AUGMENTIN® BD** *(GSK)*

Tablet (625 mg), Amoxicillin (as trihydrate) 500 mg, clavulanic acid (as potassium salt)125 mg; white oval f-c tab. marked 'AUGMENTIN'.

Dose: *Mild to moderate infections*, Adult and Children over 12 years, 625 mg 2 times a day; *Severe infections*, 1 g tab. 2 times a day.

Tablet (1 g), Amoxicillin (as trihydrate) 875 mg, clavulanic acid (as potassium salt) 125 mg; white oval f-c tab. marked AC either side of a break line on one side and AC only on the other side.

Dose: See under 625 mg tablet above.

Syrup (228 mg/5 ml), Amoxicillin (as trihydrate) 200 mg, clavulanic acid (as potassium salt) 28.5 mg per 5 ml; aspartame-containing powder for suspension.

Dose: *Mild to moderate infections*, Child (2-6 years or 13-21 kg), 5 ml twice daily; 7-12 years (22-40 kg), 10ml twice daily. *Severe infections*, double the above doses.

Syrup (457 mg/5 ml), Amoxicillin (as trihydrate) 400 mg, clavulanic acid (as potassium salt) 57 mg per 5 ml; aspartame-containing powder for suspension.

Dose: *Mild to moderate infections*, Child (2 months to 2 years), 0.15 ml/kg twice daily; 2-6 years (13-21 kg), 2.5ml twice daily; 7-12 years (22-40 kg), 5 ml twice daily. *Severe infections*, double the above doses.

Note: Not recommended for children under 2 months old. To minimise potential gastrointestinal intolerance, administer at the start of a meal. Absorption is optimised when taken at the start of a meal. Duration of therapy should be appropriate to the indication and should not exceed 14 days without review.

POM **ENHANCIN®** *(Ranbaxy)*

Tablet, (375 mg), Amoxicillin 250 mg, clavulanic acid 125 mg; f-c tab.

375 mg - 20.

Tablet, (625 mg), Amoxicillin 500 mg, clavulanic acid 125 mg; f-c tab.

625 mg - 20.

Suspension (156.25 mg), Amoxicillin USP 125 mg, clavulanic acid 31.25 mg per 5 ml; powder for reconstitution.

Pack - 30 ml; 60 ml; 75 ml; 100 ml.

Suspension (312.5 mg), Amoxicillin USP 250 mg, clavulanic acid 62.5 mg per 5 ml; powder for reconstitution.

Pack - 30 ml; 60 ml; 75 ml; 100 ml.

Injection (300 mg), Amoxicillin (as sodium salt) Ph. Eur. 250 mg, clavulanic acid (as potassium salt) USP 50 mg; powder in vial.

300 mg - 5 ml vial

Injection (1.2 g), Amoxicillin (as sodium salt) Ph. Eur. 1 g, clavulanic acid (as potassium salt) USP 200 mg; powder in vial.

1.2 g - 20 ml vial

POM **RAPICLOX**® *(IPCA)*
Tablet, (375 mg), Amoxicillin 250 mg, clavulanic acid 125 mg; f-c tab.
375 mg - 3's; 21's.
Tablet, (625 mg), Amoxicillin 500 mg, clavulanic acid 125 mg; f-c tab.
625 mg - 3's; 21's.

AMPICILLIN

Synonym: Aminobenzylpencillin.
Therapeutic category: Penicillin Antibiotic.
Indications: Mastoiditis; gynaecological infections; septicaemia; peritonitis; endocarditis; meningitis; cholecystitis; osteomyelitis.
Contra-indications: Hypersensitivity to penicillins (see notes above).
Precautions: History of allergy (see notes above); renal impairment (Appendix 4); erythematous rashes common in glandular fever, acute or chronic lymphocytic leukaemia, and cytomegalovirus infection; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.
Adverse effects: Nausea and vomiting, diarrhoea; rashes (hypersensitivity or toxic response—may be serious reaction, discontinue treatment); hypersensitivity reactions including urticaria, angioedema, anaphylaxis, serum sickness-like reaction, haemolytic anaemia, interstitial nephritis (see also notes above); rarely, antibiotic-associated colitis; neutropenia, thrombocytopenia, coagulation disorders
Advice to patients: See labels 9 and 23 in Appendix 6.
Nursing considerations: •Ask patient about allergy to penicillins; obtain specimen for C&S test; give orally on an empty stomach (i.e., 1 hour prior to, or 2 hours after meals) to increase total absorption; with a full glass of water. Shake suspension well before each dose.
•Avoid I.M or I.V. use except in severe infection or when patient can't take oral dose.
•Give I.V. intermittently to prevent vein irritation.
•Mix with sterile water and give directly I.V.; alternatively, mix with 0.9% NS; solutions for I.V. infusion will be inactivated by dextrose at room temperature.
•Administer around-the-clock (in equal interval) rather than 4 times/day to promote less variation in peak and trough serum levels.
•Ampicillin and gentamicin should not be mixed in the same I.V. tubing or administered concurrently.
•Monitor closely for signs of superinfection especially with large doses and prolonged therapy namely fever, sore throat, fatigue, diarrhoea.
•Advise patient to report immediately if rash, fever, or chills occur. Rash is the most common allergis reaction.
Dose: *Severe infections due to sensitive organisms*, by intramuscular, by slow intravenous injection or by intravenous infusion, ADULT 500 mg every 4–6 hours; CHILD under 10 years, half the adult dose
Meningitis, by slow intravenous injection, ADULT 1–2 g every 3–6 hours (maximum 14 g daily); CHILD 150–200 mg/kg daily in divided doses.
Listerial meningitis (in combination with another antibacterial), by intravenous infusion, adult 2 g every 4 hours for 10–14 days; infant under 1 month, 50 mg/kg every 6 hours; 1–3 months, 50–100 mg/kg every 6 hours; child 3 months–12 years, 100 mg/kg every 6 hours (maximum 12 g daily).
RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

Dosage for oral Ampicillin
By mouth, Adult and Child over 20 kg, usually 250-500 mg 4-6 hourly; to be given at least 30 minutes before or 2 hours after meals.
Respiratory tract, genitourinary or gastrointestinal tract infections, 250-500 mg every 6 hours in equally spaced doses; may increased in severe or chronic infections.
Gonorrhoea, 3.5 g as a single oral dose with Probenecid 1 g given simultaneously.

POM **Ampicillin** *(WMF 6.2.1.2)*
Injection (Powder for solution for injection), ampicillin (as sodium salt) 500-mg vial, 1-g vial.

POM **Ampicillin** *(EDL 6.8)*
Capsule, Ampicillin 250 mg, 500 mg.
Suspension, Ampicillin 125 mg per 5 ml.
Injection, Ampicillin 250 mg, 500 mg.

POM **ALPHAPIN**® *(GoldMoore)*
Suspension, Ampicillin (as trihydrate) BP 125 mg per 5 ml.

POM **AMPEN**® *(Dizpharm)*
Capsule, Ampicillin 250 mg.
250 mg - 1000.
Suspension, Ampicillin 125 mg per 5 ml.
Pack - 60 ml.

Injection, Ampicillin (as sodium salt) 250 mg, 500 mg; powder in vials.

POM **AMPICAP®** *(Hovid)*
Capsules, Ampicillin (as trihydrate) 250 mg, black and scarlet cap. marked 'HD' on one end and 'AP 250' on the other; 500mg.
250 mg - 10 x 10 (blister)
500 mg - 10 x 10 (blister).

POM **AMPICARE®** *(Ulticare-Lyka)*
Capsule, Ampicillin (as trihydrate) 250 mg.
250 mg - 1000.
Suspension, Ampicillin (as trihydrate) 125 mg per 5 ml.
Pack - 60 ml.

POM **AMPICEE®** *(Ranbaxy)*
Capsule, Ampicillin (as trihydrate) 250 mg.
250 mg - 10 x 10; 10 x 100; 1000.
Suspension, Ampicillin (as trihydrate) 125 mg per 5 ml.
Pack - 60 ml.

POM **Ampicillin** *(Chemo-Pharma)*
Capsule, Ampicillin 250 mg
Suspension, Ampicillin 125 mg per 5 ml
Pack - 60 ml.

POM **Ampicillin** *(Doyin)*
Capsule, Ampicillin 250 mg.
250 mg - 100; 1000.
Suspension, Ampicillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.
Injection, Ampicillin 500 mg; in vials.
500 mg - 100.

POM **Ampicillin** *(Mopson)*
Syrup, Ampicillin (as trihydrate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.

POM **Ampicillin** *(Sam)*
Capsule, Ampicillin 250 mg
250 mg - 1000
Suspension, Ampicillin 125 mg per 5 ml
Pack - 60 ml

POM **AMPITAB®** *(Hovid)*
Tablets, Ampicillin (as trihydrate) 125 mg (orange scored tab. marked 'HOVID'); 250 mg (yellow scored tab. marked 'HOVID'); 500 mg (yellow tab. with shallow convex faces). All the tablets are flavoured.
125 mg - 1000; 10 x 10 (blister)
250 mg - 100; 1000; 10 x 10 (blister)
500 mg - 1000.

POM **AMPIVAL®** *(NGC)*
Capsule, Ampicillin (as trihydrate) 250 mg.
250 mg - 10 x 10.
Syrup, Ampicillin 125 mg per 5 ml.
Pack - 100 ml.

POM **AMPOTA®** *(L.B.S.)*
Injections, Ampicillin (as sodium salt) 250 mg, 500 mg; in vials.
Pack - 50.

POM **AMPY-250®** *(Diamond Remedies)*
Capsule, Ampicillin (as trihydrate) 250 mg.
Pack - 50.

POM **AMTEC®** (*Panvij Biotec*)
Capsules, Ampicillin (as trihydrate) 250 mg, 500 mg; black/scarlet caps marked with brand name and strenght.
250 mg - 10 x 10; 1000
500 mg - 10 x 10; 1000
Suspension, Ampicillin (as trihydrate) 125 mg per 5 ml; yellow coloured, viscous, flavoured, oily suspension.
Pack - 100 ml.

POM **BARBICILLIN®** *(Juhel)*
Capsule, Ampicillin (as trihydrate) 250 mg.
250 mg - 100; 1000.
Suspension, Ampicillin (as trihydrate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **DANACILLIN®** *(Dana)*
Capsule, Ampicillin (as trihydrate) BP 250 mg.
250 mg - 10 x 10's.
Syrup, Ampicillin (as trihydrate) BP 125 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.

POM **EMCILLIN®** *(Emzor)*
Capsule, Ampicillin (as trihydrate) 250 mg, 500 mg; red/black caps marked 'EMZOR' and cap strength.
250 mg - 20; 1000
500 mg - 20; 1000
Suspension, Ampicillin (as trihydrate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.

POM **EVAPICILLIN®** *(David)*
Capsule, Ampicillin (as trihydrate)250 mg
250 mg - 100
Syrup, Ampicillin (as trihydrate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **FAPCILLINE**® *(Food & Pharma)*
Capsule, Ampicillin 250 mg.
250 mg - 100; 500; 1000.
Syrup, Ampicillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **GLOCILLIN**® *(GoldMoore)*
Capsules, Ampicillin (as trihydrate) BP 250 mg, 500 mg.
250 mg - 10 x 10's (in blister).
500 mg - 10 x 10's (in blister).
Injection, Ampicillin (as sodium salt) BP 500 mg.

POM **JAWACILIN**® *(Jawa)*
Syrup, Ampicillin 125 mg per 5 ml; dry powder for reconstitution.
Pack -100 ml.

POM **MAXICILLIN**® *(GoldMoore)*
Capsules, Ampicillin (as trihydrate) BP 250 mg, 500 mg.
250 mg - 10 x 10's
500 mg - 10 x 10's.

POM **MIRACILLIN**® *(Mirapharm)*
Suspension, Ampicillin (as trihydrate) 125 mg per 5 ml.

POM **NAMPICILLIN** ®*(NASDMU)*
Capsule, Ampicillin (as trihydrate) 250 mg; black/maroon cap. marked 'NAMPI 250 mg'.
Pack - 100; 1000.

POM **NOCILLIN**® *(Geneith)*
Capsule (250 mg), Ampicillin 250 mg.
250 mg – 10's (in blister)
Capsule (500 mg), Ampicillin 500 mg.
500 mg – 10's (in blister); 1000's

POM **OMNIPEN**® *(Wyeth/Delpitano)*
Capsule, Ampicillin 250 mg, 500 mg.
Pack - 100, 500.
Suspension, Ampicillin 125 mg per 5 ml.
Pack - 60 ml.
Injection, Ampicillin (as sodium salt) 250 mg, 500 mg; in vials.
250 mg - 10
500 mg - 10.

POM **RAJAMPI**® *(Rajat)*
Capsule, Ampicillin (as trihydrate) BP 250 mg.
Pack – 10 x 10's (in blister)

POM **REICHLIN**® *(Medreich)*
Capsules, Ampicillin (as trihydrate) BP 250 mg, 500 mg; black and red capsule marked 'REICHLIN'.
Pack - 10 x 100.
Suspension, Ampicillin (as trihydrate) BP 125 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.

POM **ROSCILLIN**® *(Ranbaxy)*
Capsules, Ampicillin (as trihydrate) 250 mg, 500 mg.
250 mg - 10's; 20's; 500's; 1000's.
500 mg - 10's; 20's; 500's; 1000's.

POM **VITACILLIN**® *(Strides Vital)*
Capsules, Ampicillin (as trihydrate) 250 mg, 500 mg; red/black caps marked with brand name and strenght.
250 mg - 10 x 10's.
500 mg - 10 x 10's.
Dry Syrup, Ampicillin (as trihydrate) 125 mg per 5 ml; dry powder for reconstitution in amber bottle.
Pack - 100 ml.
Injections, Ampicillin 0.5 g, 1 g; in vials.
0.5 g - 50's
1 g - 50's.

AMPICILLIN plus CLOXACILLIN

Therapeutic category: Penicillin Antibiotic:
Pharmacology: Ampicillin, an aminopenicillin and cloxacillin, an isoxazolyl penicillin have an identical mode of action i.e., they inhibit bacterial cell wall synthesis. This results in the weakening of the bacterial cell wall and cell lysis. Ampicillin is susceptible to degradation by ß-lactamases and is therefore inactive against strains producing this enzyme. The combination displays synergy against some ß-lactamase producing organisms as cloxacillin protects ampicillin from enzymatic destruction by ß-lactamases by binding them. Most staphylococci and many strains of *E.coli*, *H. influenzae*, *M. catarrhalis*, *N.gonorrhoeae*, *Salmonella* and *Shigella* are resistant to ampicillin as beta-lactamases produced by these strains inactivate ampicillin. Cloxacillin forms a relatively stable enzyme substrate complex with beta-lactamase and competitively inhibits the activity of beta-lactamases; thus cloxacillin when given in combination with ampicillin protects the latter from the destruction by beta-lactamase. The sparing of ampicillin by this mechanism increases the availability of ampicillin at the site of infection. This serves to retain the broad antibacterial spectrum of ampicillin against Gram-positive as well as Gram-negative organisms including those that produce beta-lactamase.

Indications: Infections of the respiratory tract, ear, nose and throat (ENT), urinary tract, gastro-intestinal tract, skin and soft-tissue; septicaemia, pelvic infections, endocarditis and orthopaedic infections.
Contra-indications: History of hypersensitivity to penicillins, cephalosporins, penicillin derivatives or penicillamine.
Precautions: History of GI disease especially antibiotic associted colitis (ampicillin like other penicillins may cause pseudomembranous colitis). Ampicillin may cause skin rash in patients with infectious mononucleosis. Renal impairment.
Interactions:
•Bacteriostatic antibiotics such as tetracyclines, erythromycin or sulphonamides may antagonise the bactericidal effect of penicillin (avoid co-administration).
•Probenecid decreases renal tubular secretion of penicillins resulting in increased and more prolonged penicillin concentrations.
•Allopurinol (increased incidence pof skin rash).
•Oral contraceptives (decreased efficacy of oral contraceptives due to reduction in enterohepatic circulation of oestrogens. Advise patient to use alternative or additional method of contraception while taking ampicillin).
Adverse effects: GI reactions such as nausea, vomiting, diarrhoea, pseudomembranous colitis, cholestatic jaundice; neutropenia; anaphylaxis, serum sickness-like reactions, skin rash, hives, itching; oral candidiasis.
Advice to patients: See label 9 in Appendix 6.
Nursing considerations: •See under Ampicillin.
Dose: By mouth, 0.5-1 g 6 hourly or more frequently according to the severity of the infection.
By I.M. Injection, 0.5-1 g 6 hourly
By I.V. Injection, 0.5-1 g 4-6 hourly; up to 12 g by I.V. infusion.
Child: 1 month - 2 years, by mouth, 1/4 adult dose; 2-10 years, 1/2 adult dose.
Neonates: Oral drops, 0.6 ml (90 mg) susp. 4 hourly.
By I.M. Injection, 75 mg 8 hourly
By I.V. Injection, 75 mg 8 hourly.

POM **Ampicillin plus Cloxacillin** *(EDL 6.8)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg.
Suspension, Ampicillin 125 mg, cloxacillin 125 mg per 5 ml.
Neonatal drops, Ampicillin 60 mg, cloxacillin 30 mg per 0.6 ml.
Neonatal injection, Ampicillin 50 mg, cloxacillin 25 mg; per vial.
Injection, Ampicillin 250 mg, cloxacillin 250 mg; powder in vial.

POM **AMLOC®** *(Titan)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg. 500 mg - 10 x 10.

POM **AMPICLOX®** *(GSK)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg. 500 mg - 12; 100.
Syrup, Ampicillin 125 mg, cloxacillin 125 mg per 5 ml.
Pack - 60 ml; 100 ml.
Neonatal drops, Ampicillin 60 mg, cloxacillin 30 mg per 0.6 ml.
Pack - 8 ml.
Injection, Ampicillin 250 mg (as sodium salt), cloxacillin 250 mg (as sodium salt); powder in vial.
Pack - 10.
Neonatal Injection, Ampicillin 50 mg (as sodium salt), cloxacillin 25 mg (as sodium salt); powder in single dose vial.
Pack - 10.

POM **AMPIXAL®** *(Dizpharm)*
Capsule, Ampicillin (anhydrous) 250 mg, cloxacillin (as sodium salt) 250 mg.
500 mg - 100.
Suspension, Ampicillin (anhydrous) 125 mg, cloxacillin (as sodium salt) 125 mg per 5 ml.
Pack - 60 ml.
Injection, Ampicillin (as sodium salt) 250 mg, cloxacillin (as sodium salt) 250 mg; in vial.

POM **AMPY-CLOXA®** *(Diamond Remedies)*
Capsule, Ampicillin (trihydrate) 250 mg, cloxacillin (as sodium salt) 250 mg.

POM **BARBICLOX®** *(Juhel)*
Capsule, Ampicillin (anhydrous) 250 mg, cloxacillin (as sodium salt) 250 mg.
500 mg - 100; 1000.
Syrup, Ampicillin (anhydrous) 125 mg, cloxacillin (as sodium salt) 125 mg per 5 ml.
Pack - 60 ml; 100 ml.

POM **CAPICLOX®** *(Ulticare-Lyka)*
Capsule, Ampicillin (as trihydrate) 250 mg, Cloxacillin (as sodium salt) 250 mg.
500 mg - 100.
Suspension, Ampicillin (as trihydrate) 125 mg, Cloxacillin (as Sodium salt) 125 mg per 5 ml.
Pack - 60 ml; 100 ml.

POM **CHEMOCLOX®** *(Chemo-Pharma)*
Capsule, Ampicillin (as trihydrate) 250 mg, Cloxacillin (as sodium salt) 250 mg.
Suspension, Ampicillin (as trihydrate) 125 mg,

Cloxacillin (as Sodium salt) 125 mg per 5 ml.
Pack - 60 ml.

POM **COMPI-CLOX**® *(Drugfield)*
Neonatal drops, Ampicillin 60 mg, cloxacillin 30 mg per 0.5 ml.
Syrup, Ampicillin 125 mg, cloxacillin 125 mg per 5 ml; dry powder for reconstitution.

POM **DAMOXICLOX**® *(David)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg.
500 mg - 100
Syrup, Ampicillin 125 mg, cloxacillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **DANACLOX**® *(Dana)*
Capsule, Ampicillin (as trihydrate) BP 250 mg, cloxacillin BP 250 mg.
Pack - 10 x 10's.
Syrup, Ampicillin (as trihydrate) BP 125 mg, cloxacillin BP 125 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.

POM **DONACLOX**® *(Doyin)*
Capsule, Ampicillin (as trihydrate) 250 mg, cloxacillin (as sodium salt) 250 mg.
Syrup, Ampicillin (as ttrihydrate) 125 mg, cloxacillin (as sodium salt) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.
Injection, Ampicillin 250 mg, cloxacillin 250 mg; in 500 mg vial.

POM **EMZOCLOX**® *(Emzor)*
Capsule, Ampicillin (as trihydrate) 250 mg, cloxacillin (as sodium salt) 250 mg; pink/black cap marked 'EMZOR' and '500'.
500 mg - 10 x 2; 10 x 50; 10 x 100; 1000.
Suspension, Ampicillin (as trihydrate) 125 mg, cloxacillin (as sodium salt) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.

POM **FAPCLOX**® *(Food & Pharma)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg.
500 mg - 100
Suspension, Ampicillin 125 mg, cloxacillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **FECLOX**® *(Fidson)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg.
500 mg - 100.
Suspension, Ampicillin 125 mg, cloxacillin 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml; 100 ml.

POM **GENICLOX**® *(Geneith)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg.
500 mg – 10's (in blister).

POM **JAWACLOX**® *(Jawa)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg.
500 mg - 10 x 10's
Syrup, Ampicillin 250 mg, cloxacillin 250 mg per 5 ml; dry powder for reconstitution.
Pack - 100 ml.
Neonatal drops, Ampicillin 60 mg, cloxacillin 30 mg per 0.6 ml.
Pack - 8 ml.
Injection, Ampicillin 250 mg, cloxacillin 250 mg; in vial.
Pack - 10's; 50's.

POM **MAXACLOX**® *(GoldMoore)*
Capsule, Ampicillin (as trihydrate) BP 250 mg, cloxacillin (as sodium salt) BP 250 mg.
Pack - 10 x 10's (in blister).

POM **PENCLODAR**® *(Supreme)*
Capsule, Ampicillin 250 mg, cloxacillin 250 mg.
500 mg - 16.

POM **PLOX**® *(Sam)*
Capsule, Ampicillin 250 mg, Cloxacillin 250 mg.
500 mg - 10 x 10

POM **RIAMCLOX-500**® *(GoldMoore)*
Capsule (250 mg), Ampicillin (as trihydrate) BP 250 mg, cloxacillin (as sodium) BP 250 mg.
Pack - 10's; 1000's.

POM **ROSCILOX**® *(Ranbaxy)*
Capsule, Ampicillin (as trihydrate) 250 mg, cloxacillin (as sodium salt) 250 mg.
500 mg - 25 x 4's; 24 x 10's; 500's.
Suspension, Ampicillin (as trihydrate) 125 mg, cloxacillin (as sodium salt) 125 mg per 5 ml.
Pack - 60 ml.
Injection, Ampicillin 250 mg, cloxacillin 250 mg; in vial.
Pack - 1.

POM **VALCLOX**® *(NGC)*
Capsule, Ampicillin (anhydrous) 250 mg, cloxacillin (as sodium salt) 250 mg.
500 mg - 10 x 10.
Syup, Ampicillin (anhydrous) 125 mg, cloxacillin (as sodium salt) 125 mg per 5 ml.

Pack - 100 ml.

POM **VITACLOX**® *(Strides Vital)*
Capsule, Ampicillin (as trihydrate) 250 mg, cloxacillin (as sodium salt) 250 mg; black/maroon cap. marked 'VITACLOX'
500 mg - 10 x 10.
Injection, Ampicillin 250 mg, cloxacillin 250 mg; in 500 mg vial.
Pack - 50's.

CLOXACILLIN

Cloxacillin is a representative penicillinase-resistant penicillin. Various drugs such as dicloxacillin can serve as alternatives.

Therapeutic category: Penicillin antibiotic.

Indications: Infections due to beta-lactamase-producing staphylococci including impetigo, cellulitis and other soft-tissue infections; staphylococcal endocarditis, septicaemia, pneumonia and osteomyelitis.

Contra-indications: Hypersensitivity to penicillins (see notes above).

Precautions: History of allergy (see notes above); renal and hepatic impairment (Appendices 4 and 5); heart failure; pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Nausea and vomiting, diarrhoea; hypersensitivity reactions including urticaria, fever, joint pain, rashes, angioedema, anaphylaxis, serum sickness-like reactions, haemolytic anaemia, interstitial nephritis (see also notes above); neutropenia, thrombocytopenia, coagulation disorders; antibiotic-associated colitis; hepatitis and cholestatic jaundice—may be delayed in onset; electrolyte disturbances; pain, inflammation, phlebitis or thrombophlebitis at injection sites.

Advice to patients: See Labels 9 and 23 in Appendix 6. Take 1 hour before or 2 hours after meals;take the entire medication as prescribed, do not skip doses.

Nursing considerations: •Find out if patient is allergic to penicillins; obtain specimen for C&S test; therapy may begin pending test result.
•Administer around-the-clock (in equal interval) to lessen peak and trough levels.
•Oral dose may cause GI upset and food may interfere with absorption, so give 1 to 2 hours before meals or 2 to 3 hours after. Shake suspension well before each dose.
•Advise patient to take each dose with a full glass of water, not fruit juice or carbonated beverage, because acid will inactivate the drug.
•Large dose and prolonged therapy may give rise to superinfection; advise patient to report sore throat, fever and fatigue which indicate superinfection.
•Advise patient to report immediately if rash, fever, or chills occur. Rash is the most common allergic reaction.

Dose: *Infections due to susceptible beta-lactamase-producing staphylococci*, by mouth, ADULT 500 mg 4 times daily, doubled in severe infection; by intramuscular injection, 250 mg every 4–6 hours, doubled in severe infection; by slow intravenous injection or intravenous infusion, 1–2 g every 6 hours; CHILD up to 2 years, quarter adult dose; CHILD 2–10 years, half adult dose.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Cloxacillin** *(WMF 6.2.1.2)*
Capsules, Cloxacillin (as sodium salt) 500 mg.
Oral solution (Powder for oral solution), Cloxacillin (as sodium salt) 125 mg/5 ml.
Injection (Powder for solution for injection), Cloxacillin (as sodium salt) 500-mg vial.

POM **Cloxacillin** *(EDL 6.8)*
Capsule, Cloxacillin 250 mg.
Suspension, Cloxacillin 125 mg per 5 ml.
Injection, Cloxacillin 250 mg, 500 mg.

POM **CLOXACAP**® *(Hovid)*
Capsules, Cloxacillin (as trihydrate) 250 mg, 500 mg.
250 mg - 10 x 10 (blister)
500 mg - 10 x 10 (blister).

POM **Cloxacillin** *(Emzor)*
Capsule, Cloxacillin 250 mg
250 mg - 100.
Suspension, Cloxacillin 125 mg per 5 ml
Pack - 60 ml.

POM **CLOXALIN**® *(Dizpharm)*
Capsule, Cloxacillin (as sodium salt) 250 mg.
250 mg - 100.
Syrup, Cloxacillin (as sodium salt) 125 mg per 5 ml.
Pack - 60 ml.
Injection, Cloxacillin (as sodium salt) 250 mg; in vial.

POM **ORBENIN**® *(GSK)*
Capsule, Cloxacillin (as sodium salt) 250 mg; black/orange cap. marked with cap. name and strength.
250 mg - 12, 100.
Syrup, Cloxacillin (as sodium salt) 125 mg per

5 ml; powder for reconstitution.
Pack - 100 ml.
Injection, Cloxacillin 250 mg; powder in vial.
Pack - 10.

FLUCLOXACILLIN

Therapeutic category: Penicillin Antibiotic.
Indications: Treatment of infections caused by Gram-positive organisms including penicillinase-producing staphylococci. They include skin and soft tissue infections, bone infections, respiratory tract/ENT infections and other infections such as endocarditis, meningitis, septicaemia.
Contra-indications: History of penicillin hypersensitivity; should not be administered subconjunctivally or as eye drops.
Adverse effects: Occasional rashes, transient diarrhoea or indigestion.
Advice to patients: See labels 9 nd 23 in Appendix 6.
Nursing considerations: See under Cloxacillin.
Dose: Adult, by mouth, 250 mg every 8 hours; increased to 500 mg every 6 hours in severe infections.
Doses to be taken ½-1 hour before meals.
By slow i.m. injection, 250 mg every 8 hours; increased to 500 mg every 6 hours in severe infections.
Add 1.5 ml water for injection to the 250 mg vial.
By slow i.v. injection or infusion (3-4 minutes), 250-500 mg every 4-6 hours; may be increased up to 8 g daily in severe infections.
Dissolve 250-500 mg in 5-10 ml water for injection.
Child, *by any route*, 0-2 years: ¼ adult dose; 2-10 years: ½ adult dose.
Alternatively, for children, 25-50 mg/kg daily in divided doses; increased in severe infections.

POM **FLOXAPEN®** *(GSK)*
Capsules, Flucloxacillin (as sodium salt) 250 mg, 500 mg.
Syrup,Flucloxacillin (as sodium salt) 125 mg, 250 mg per 5 ml; powder for preparing fruit flavoured syrup.
Injection, Flucloxacillin (as sodium salt) 250 mg, 500 mg; powder in vials.

SULTAMICILLIN

Synonym: Ampicillin plus Sulbactam.
Therapeutic category: Penicillin Antibiotic.
Pharmacology: Sultamicillin is a double ester in which ampicillin and the beta-lactamase inhibitor sulbactam are linked via a methylene group. Sulbactam does not possess any useful antibacterial activity but is an irreversible inhibitor of beta-lactamases. Ampicillin is bactericidal and acts against sensitive organisms during the stage of active multiplication by the inhibition of biosynthesis of cell wall mucopeptide.
Indications: Upper respiratory tract infections such as otitis media; lower respiratory tract infections such as bacterial pneumonia;, urinary tract infections and pyelonephritis; skin and soft tissue infections and gonococcal infections. Perioperative prophylaxis of infections, intra-abdominal infections including peritonitis, endometritis and pelvic cellulitis, bacterial septicaemia.
Contra-indications: Allergy to any of the penicillins.
Precautions: Overgrowth of nonsusceptible organisms; periodic checks for organ system dysfunction including renal, hepatic and haemopoietic systems.
Adverse effects: GI disturbances; dermatological reactions; drowsiness, malaise, headache.
Advice to patients: See labels 9 and 23 in Appendix 6.
Nursing considerations: •See under Ampicillin.
•Give IM deep in large muscle after reconstituting in sterile water.
•Allow reconstituted solution for IV inj to stand until foaming stops to allow visual inspection for complete for complete solution.
•Teach patient to report signs of superinfection including fever, vaginal itching, loose, foul-smelling stools.
Dose: By mouth, Adult, 375-750 mg twice daily, usually for 5-14 days.
Child (less than 30 kg), 50 mg/kg daily in 2 divided doses.
Child (over 30 kg), adult dose.
By IM or IV injection, Adult, usually 1.5 g to 3 g 6-8 hourly; Child, infant and neonate: 150 mg/kg daily.
Perioperative prophylaxis, 1.5 g to 5 g at the induction of anaesthesia; may be repeated 6 hourly for a total of 24 hours.
Note: The reconstituted solution for injection should be allowed to stand to allow any foaming to dissipate to permit visual inspection for complete dissolution. The reconstituted oral suspension must be stored under refrigeration and discarded after 14 days.

POM **Sultamicillin** *(EDL 6.8)*
Tablet, Ampicillin 220 mg, sulbactam 147 mg.
Suspension, Ampicillin 147 mg, sulbactam 98 mg.

POM **UNASYN®** *(Pfizer)*

Tablet, Sultamicillin 375 mg.
375 mg - 10's; 50's.
Suspension, Sultamicillin 250 mg per 5 ml; powder for oral suspension.
Pack - 60 ml.
Injection, Sulbactam 500 mg, ampicillin 1000 mg; dry powder in vial.
Pack - 10.

9.1.1.2 Cefalosporins and imipenem with cilastatin

Ceftazidime and **ceftriaxone** are third generation cefalosporins. Ceftriaxone is used for serious infections such as septicaemia, pneumonia and meningitis; it is used as a reserve antimicrobial to treat meningitis due to *Streptococcus pneumoniae* in some areas where penicillin resistance is found. Ceftazidime is active against *Pseudomonas aeruginosa* and other Gram-negative bacteria; it is used in the treatment of pseudomonas infections and in some areas is restricted to use only where gentamicin resistance is high.

Imipenem is a broad-spectrum antibiotic. As it is partially inactivated by enzymatic activity in the kidney, it is administered with **cilastatin** which inhibits the renal metabolism of imipenem. It is active against many aerobic and anaerobic Gram-positive and Gram-negative bacteria; in some areas it is reserve agent for the treatment of infections due to *Acinetobacter spp.* and *Ps aeruginosa*, which are resistant to other more usual treatments.

CEFACLOR

Therapeutic category: Oral Cephalosporin antibiotic (Second Generation).

Indications: Bactericidal antibiotic which is active against both Gram-positive and Gram-negative organisms including coagulase-positive, coaguluase-negative and penicillinase-producing strains of staphyloccoci and beta-lactamase-producing, ampicillin-resistant strains of haemophilus influenza among others. Indicated in both lower and upper respiratory tract infections such as acute and chronic bronchitis, pharyngitis, tonsillitis, pneumonia, sinusitis, etc.; skin and soft tissue infections such as carbuncules, boils, impetigo; genito-urinary tract infections such as cystitis, pyelonephritis, etc.; bone and joint infections such as osteomyelitis; gonococcal urethritis.

Contra-indications: Hypersensitivity to cephalosporin antibiotics.

Precautions: Hypersensitivity to penicillin; pregnancy (use only if the benefits outweigh the risks).

Interactions:
•Loop diuretics, aminoglycosides (increased nephrotoxicity).

Adverse effects: Hypersensitivity reactions in about 1.5% of patients; pruritus, urticaria and positive Coomb's test in less than 1 in 200 patients. GI disturbances including diarrhoea rarely occur (about 1 in 70).

Nursing considerations: •Obtain specimen for C&S tests before first dose; therapy may begin pending test results.
•Before administration, confirm that patient is not allergic to cephalosporins or penicillins.
•Administer capsule with meals if needed to decrease GI symptoms.
•Reconstituted oral suspension should be stored in a refrigerator and should be used within 14 days; keep tightly closed and shake well before using.
•Dosage adjustment is necessary in renal impairmemt.
•Tell patient to take the entire medication as pescribed, even after he feels better; to report any skin rash, persistent diarrhoea.
•Large doses or prolonged therapy may cause super-infection; monitor for signs and ask patient to report same.
•Monitor urine output; decreasing amount of urine may indicate nephrotoxicity, notify physician

Dose: By mouth, Adult, *Bronchitis and pneumonia*, usually 750 mg in 2-3 divided doses daily.
Sinusitis, 10-day treatment is recommended.
For more severe infections,or those caused by less susceptible organisms, the dose may be doubled.
Do not exceed total daily dosage of 4 g.
Acute gonococcal urethritis in male and female, a single dose of 3 g combined with Probenecid 1 g.
CHILD: Usually 20 mg/kg/day in 2 divided doses; may be doubled in more severe infections or those caused by less susceptible organisms.

Note: Dosage adjustment in renal impairment may not be necessary.

POM **CECLOR**® *(CHI/Eli Lilly)*
Capsules, Cefaclor (as monohydrate) 250 mg, 375 mg; white and purple caps.
250 mg - 15.
375 mg - 10.
Suspension, Cefaclor (as monohydrate) 187 mg per 5 ml; strawberry flavoured granules for reconstitution.

Pack - 50 ml multidose plastic bottle.

POM **VERCEF**® *(Ranbaxy)*
Capsule, Cefaclor USP 250 mg.
250 mg - 5 x 3's (in blister)
Suspension (125 mg), Cefaclor USP 125 mg per 5 ml; granules for reconstitution.
Pack - 100 ml.
Suspension (250 mg), Cefaclor USP 250 mg per 5 ml; granules for reconstitution.
Pack - 100 ml.

CEFOTAXIME

Therapeutic category: Cephalosporin antibiotic (Third Generation).
Indications: Infections of the respiratory tract; kidneys; urinary tract and reproductive organs including gonorrhoea; bones, joints, soft tissues and skin such as infected burns and wounds; ear, nose and throat. Abdominal Infections; infections in gynaecology and obstetrics; septicaemia, endocarditis, meningitis. Treatment or prophylaxis of infections in patients with reduced resistance.
Contra-indications: Known allergy to cephalosporins.
Precautions: Penicillin hypersensitivity, severe renal failure, pregnancy, breast feeding.
Interactions: •Loop diuretics, aminoglycosides (increased nephrotoxicity).
•Probenecid may decrease cephalosporin elimination.
Adverse effects: See under Cefuroxime.
Nursing considerations: •Give IV after diluting in NS, D_5W, or sterile H_2O for inj as ordered; confirm that patient is not allergic to cephalosporins or penicillins prior to use.
•Check injection site for induration, sterile abscess and tissue sloughing; change site every 3 days.
•Do not admix with aminoglycosides in same bottle/bag.
•Teach patient to report sore throat, easy bruising, bleeding, joint pain; may be signs of blood dyscrasias.
•Decreasing amount of urine may indicate nephrotoxicity, notify physician; discontinue drug if severe diarrhoea occurs, may indicate pseudomembranous colitis.
•Observe for signs and symptoms of anaphylaxis during first dose.
•Monitor closely for signs of superinfection.
Dose: Adult, by i.m. or i.v. injection, 1 g 12 hourly; up to a max. 12 g daily in 3-4 doses.
Gonorrhoea (males and females), 1 g I.M. as single dose.
Premature babies and Newborns: 50 mg/kg daily in 2 doses.
Infants and children: 50-100 mg/kg daily in 2-4 doses; up to a max. 200 mg/kg daily in 3-4 doses.

POM **Cefotaxime** *(EDL 6.8)*
Injection, Cefotaxime (as sodium salt) 500 mg, 1 g; powder in vials.

POM **CEFOMIC**® *(L.B.S.)*
Injections, Cefotaxime (as sodium salt) 500 mg, 1 g; powder in vials with water for injection as diluent.
Pack - 1.

POM **CEFOTAMAX**® *(Strides Vital)*
Injection, Cefotaxime 1 g.
Pack – 1 g (in vial)

POM **CLAFORAN**® *(May & Baker)*
Injections, Cefotaxime (as sodium salt) 500 mg, 1 g; powder in vials with water for injection.

POM **FOTARAN**® *(Pharmabox)*
Injection, Cefotaxime sodium USP 1 g; white or light-yellowish crystalline powder in vial + 4 ml water for injection in ampoule.
Pack – 1's; 5; 10's; 20's; 50's; 100's (plus water for injection in amouples)

POM **NICOL**® *(Justeen)*
Injection, Cefotaxime USP 1 g.
Pack – 1's.

POM **ORITAXIM**® *(Interpharma)*
Injection, Cefotaxime 1 g.
Pack – 1's.

POM **REFTAX**® *(Ranbaxy)*
Injections, Cefotaxime (as sodium salt) Ph. Eur. 1 g, 2 g; powder for reconstitution in vials.
1 g - 10's
2 g - 10's.

POM **TAX-O-BID**® *(Saingenes)*
Injections, Cefotaxime USP 125 mg, 250 mg, 500 mg, 1 g; in clear glass vials with coloured-off seal.

POM **ZETAX**® *(Justeen)*
Injection, Cefotaxime USP 1 g.
Pack - 1's.

CEFTAZIDIME

Ceftazidime is a complementary antibacterial drug for use only when there is significant resistance to other drugs on the WHO Model List.
Therapeutic category: Cephalosporin antibiotic (Third Generation).
Indications: Infections due to sensitive

bacteria, especially those due to *Pseudomonas spp.* and including those resistant to aminoglycosides.

Contra-indications: Cefalosporin hypersensitivity (see section 9.1.1); porphyria.

Precautions: Penicillin sensitivity (see section 9.1.1); renal impairment (Appendix 4); pregnancy and breastfeeding (but appropriate to use, see Appendices 2 and 3); false positive urinary glucose (if tested for reducing substances) and false positive Coombs' test; **interactions**: Appendix 1

Adverse effects: Diarrhoea, nausea, vomiting, abdominal discomfort, headache; rarely, antibiotic-associated colitis (particularly with higher doses); allergic reactions including rashes, pruritus, urticaria, serum sickness-like reaction, fever and arthralgia, and anaphylaxis; erythema multiforme, toxic epidermal necrolysis reported; transient hepatitis, cholestatic jaundice; eosinophilia and blood disorders (including thrombocytopenia, leukopenia, agranulocytosis, aplastic anaemia, and haemolytic anaemia); reversible interstitial nephritis; nervousness, sleep disturbances, confusion, hypertonia, and dizziness.

Nursing considerations: •See under Cefotaxime.

Dose: *Infections due to susceptible organisms*, by deep intramuscular injection or by intravenous injection or intravenous infusion, ADULT 1 g every 8 hours or 2 g every 12 hours, or in severe infections (including immunocompromised), 2 g every 8–12 hours or 3 g every 12 hours (ELDERLY usual maximum 3 g daily); neonate and infant up to 2 months, 25–60 mg/kg daily in 2 divided doses; CHILD over 2 months, 30–100 mg/kg daily in 2–3 divided doses (intravenous route recommended for children).

Pseudomonal lung infection in cystic fibrosis, by deep intramuscular injection or by intravenous injection or intravenous infusion, ADULT with normal renal function, 100–150 mg/kg daily in 3 divided doses

Infections in immunocompromised, cystic fibrosis, or meningitis, by intravenous injection or intravenous infusion, CHILD over 2 months up to 150 mg/kg daily in 3 divided doses (maximum 6 g daily).

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. INTRAMUSCULAR DOSES OVER 1 G DIVIDED BETWEEN MORE THAN ONE SITE.

POM **Ceftazidime** *(WMF 6.2.1.3)*
Injection (Powder for solution for injection), ceftazidime (as pentahydrate) 250-mg vial.

POM **Ceftazidime** *(EDL 6.8)*
Injection, Ceftazidime 0.5 g, 1 g, 2 g; powder in vials.

POM **BESTUM®** *(Zoomota)*
Injection, Ceftazidime 1 g; white powder for reconstitution in vials.
Pack – 1's (in vial) + 10 ml diluent

POM **FORTUM Monovial®** *(GSK)*
Injections, Ceftazidime (as pentahydrate) 500 mg, 1 g; white to faintly yellow powder in vials which effervesces on dissolution.
Pack - 1; 5.

POM **K-ZIDIME®** *(Justeen)*
Injection, Ceftazidime USP 1 g.
Pack - 1's.

POM **ORZID®** *(Saingenes)*
Injections, Ceftazidime USP 250 mg, 500 mg, 1 g; powder for reconstitution in vials.

CEFTRIAXONE

Ceftriaxone is a representative third-generation cefalosporin antibiotic. Various drugs can serve as alternatives.

Ceftriaxone is a complementary antibacterial drug for use only when there is significant resistance to other drugs on the WHO Model List.

Therapeutic category: Cephalosphorin antibiotic (Third Generation).

Indications: Serious infections due to sensitive bacteria, including septicaemia, pneumonia, and meningitis; surgical prophylaxis; prophylaxis of meningococcal meningitis; gonorrhoea.

Contra-indications: Cefalosporin hypersensitivity (see section 9.1.1); porphyria; neonates with jaundice, hypoalbuminaemia, acidosis or impaired bilirubin binding.

Precautions: Penicillin sensitivity (see section 9.1.1); severe renal impairment (Appendix 4); hepatic impairment if accompanied by renal impairment (Appendix 5); premature neonates; may displace bilirubin from serum albumin; treatment longer than 14 days, renal failure, dehydration or concomitant total

parenteral nutrition—risk of ceftriaxone precipitation in gallbladder; pregnancy and breastfeeding (but appropriate to use, see Appendices 2 and 3); false positive urinary glucose (if tested for reducing substances) and false positive Coombs' test; **interactions**: Appendix 1.

Adverse effects: Diarrhoea, nausea and vomiting, abdominal discomfort, headache; antibiotic-associated colitis (particularly with higher doses); allergic reactions including rashes, pruritus, urticaria, serum sickness-like reactions, fever and arthralgia, and anaphylaxis; erythema multiforme, toxic epidermal necrolysis reported; transient hepatitis and cholestatic jaundice; eosinophilia and blood disorders (including thrombocytopenia, leukopenia, agranulocytosis, aplastic anaemia, and haemolytic anaemia); reversible interstitial nephritis, hyperactivity, nervousness, sleep disturbances, confusion, hypertonia and dizziness; calcium ceftriaxone precipitates in urine (particularly in very young, dehydrated, or those who are immobilized) or in gall bladder—consider discontinuation if symptomatic; rarely prolongation of prothrombin time, pancreatitis.

Nursing considerations: •See under Cefotaxime.

Dose: *Infections due to susceptible organisms*, by deep intramuscular injection, by intravenous injection (over at least 2–4 minutes) or by intravenous infusion, ADULT 1 g daily; severe infections 2–4 g daily; infant and CHILD under 50 kg 20–50 mg/kg daily; up to 80 mg/kg daily in severe infections (doses of 50 mg/kg and over by intravenous infusion only); by intravenous infusion (over 60 minutes), neonates 20–50 mg/kg daily (maximum 50 mg/kg daily).

Uncomplicated gonorrhoea, by deep intramuscular injection, ADULT 125 mg as a single dose.

Surgical prophylaxis, by deep intramuscular injection or by intravenous injection (over at least 2–4 minutes), ADULT 1 g at induction.

Colorectal surgery (with antibacterial active against anaerobes), by deep intramuscular injection or by intravenous injection (over at least 2–4 minutes), or by intravenous infusion, 2 g as a single dose.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. INTRAMUSCULAR DOSES OVER 1 G DIVIDED BETWEEN MORE THAN ONE SITE. ADMINISTER BY INTRAVENOUS INFUSION OVER 60 MINUTES IN NEONATES (SEE ALSO CONTRAINDICATIONS).

Note: For I.M. injection, 0.25 g or 0.5 g Ceftriaxone is dissolved in 2 ml, and 1 g Ceftriaxone is dissolved in 3.5 ml, of 1% lidocaine solution and administered by deep intragluteal injection. It is recommended that not more than 1 g be injected on either side. Lidocaine solution must never be administered intravenously. For I.V. injection, 1 g Ceftriaxone is dissolved in 10 ml of sterile water for injection lasting 2 to 4 mins. Intravenous doses of 50 mg or more per kg should be given by infusion over at least 30 minutes.

POM **Ceftriaxone** *(WMF 6.2.1.3)*
Injection (Powder for solution for injection), Ceftriaxone (as sodium salt) 250-mg vial.

POM **AXONE®** *(Interpharma)*
Injection, Ceftriaxone 1000 mg.
Pack - 1's.

POM **CEFIN®** (*Pharmabox)*
Injection (500 mg), Ceftriaxone (as sodium salt) USP 500 mg; white to light yellow powder for reconstitution + 5 ml water for injection.
500 mg - 1's; 5's; 10's; 20's; 100's
Injection (1 g), Ceftriaxone (as sodium salt) USP 1 g; white to light yellow powder for reconstitution + 10 ml water for injection.
1 g - 1's; 5's; 10's; 20's; 100's

POM **CEFOGRAM®** *(Saingenes)*
Injections, Ceftriaxone (as sodium salt) USP 250 mg, 500 mg, 1 g; powder for reconstitution.

POM **CEFTRIAXON®** *(Strides Vital)*
Injection, Ceftriaxone 1 g.
Pack – 1 g (in vial)

POM **OFRAMAX®** (*Ranbaxy)*
Injections, Ceftriaxone (as sodium salt) USP 250 mg, 500 mg, 1 g; powder for reconstitution.
250 mg - 10's
500 mg - 10's
1 g - 10's.

POM **ONECEF®** *(Justeen)*
Injections, Ceftriaxone USP 250 mg, 1 g.
Pack - 1's.

POM **POWERCEF** *(Zoomota)*
Injections: Ceftriaxone (as Sodium salt) USP 250 mg, 500 mg, 1 g; white powder for reconstitution in vials.
250 mg – 1's (in vial) + 5 ml diluent + 5 ml syringe/needle
500 mg – 1's (in vial) + 5 ml diluent + 5 ml syringe/needle
1 g – 1's (in vial) + 10 ml diluent + 10 ml syringe/needle

POM **ROCEPHIN®** *(Swipha)*
I.M. Injection, Ceftriaxone 250 mg + 2 ml Lidocaine 1%; 500 mg + 2 ml lidocaine 1%; 1g + 3.5 ml lidocaine 1%.
I.V. Injection, Ceftriaxone 1 g + 10 ml water for injection.

POM **TRIXONE®** *(L.B.S.)*
I.M. Injection, Ceftriaxone 500 mg + 2 ml lidocaine 1%; 1 g + 3.5 ml lidocaine 1%.
I.V. Injection, Ceftriaxone 500 mg + 5 ml water for injection; 1 g + 10 ml water for injection.
Pack - 1.

POM **UNOCEF®** *(Korlyns)*
Injection (250 mg), Ceftriaxone (as Sodium salt) 250 mg; white to yellowish crystalline powder for injection in 10 ml vial.
Pack – 250 mg x 25's.
Injection (500 mg), Ceftriaxone (as Sodium salt) 500 mg; white to yellowish crystalline powder for injection in 10 ml vial.
Pack – 500 mg x 25's.
Injection (1000 mg), Ceftriaxone (as Sodium salt) 1000 mg; white to yellowish crystalline powder for injection in 10 ml vial.
Pack – 1000 mg x 25's.

POM **XAPO®** *(Justeen)*
Injections, Ceftriaxone USP 1 g.
Pack - 1's.

CEFUROXIME

Therapeutic category: Cephalosporin antibiotic (Second Generation).
Indications: Cefuroxime is resistant to most beta-lactamases and is active against a wide range of Gram-positive and Gram-negative organisms. Indications include: Respiratory tract infections such as acute and chronic bronchitis; upper respiratory tract infections such as ear, nose and throat infections; Genito-urinary tract infections such as pyelonephritis; skin and soft-tissue infections such as impetigo; Bone and joint infections such as osteomyelitis; obstetric and gynaecological infections such as pelvic inflammatory diseases; Gonorrhoea and other infections such as septicaemia and meningitis.
Also as prophylactic against infection in abdominal, pelvic, orthopaedic, cardiac, pulmonary, oesophageal and vascular surgery where there is increased risk from infection.
Contra-indications: Hypersensitivity to cephalosporin antibiotics.
Precautions: Hypersensitivity to penicillins, pregnancy, breast feeding.
Interactions: •Loop diuretics, aminoglycosides(increased nephrotoxicity).
Adverse effects: Hypersensitivity reactions, GI disturbances, positive coomb's test, candidosis, pain at injection site, transient increase of liver enzyme levels, headache.
Advice to patients: See Labels 9, 21 and 25 in Appendix 6. Report prolonged diarrhoea; entire course of medication (10-14 days) should be taken to ensure eradication of organism; should be taken in equal intervals around-the-clock to maintain adequate blood levels; may interfere with oral contraceptives; females should report symptoms of vaginitis.
Nursing considerations: •Obtain specimens for C&S tests prior to the first dose; administer around-the-clock to promote less variation in peak and trough serum levels.
•Cefuroxime axetil tablet may be crushed to aid swallowing but it has a bitter taste that is too difficult to mask, even with food.
•Give deep I.M. into a large muscle mass, such as gluteus or lateral aspect of thigh.
•Total daily dosage is the same for I.M. or I.V. administration and depends on susceptibility of organisms and severity of infection.
•*See also under Cefaclor*.
Dose: By mouth (Cefuroxime axetil), usually 250 mg 2 times daily doubled in *bronchitis* and *pneumonia*; *urinary tract infections*, 125 mg 2 times daily; *uncomplicated gonorrhoea*, single dose of 1 g.
Child over 5 years: 125 mg 2 times daily doubled in *otitis media* if necessary.
Adult: By i. m. or i.v. injection, usually 750 mg 3 times daily increased to 1.5 g 3 times daily i.v. if necessary.
Child: 30-100 mg/kg/day in 3-4 divided doses (2-3 divided doses in neonates).
Gonorrhoea, single dose of 1.5 g (2 x 750 mg i. m. in two sites).
See lit. for details.

POM **Cefuroxime** *(EDL 6.8)*
Tablet, Cefuroxime 125 mg, 250 mg, 500 mg.
Injection, Cefuroxime 250 mg, 750 mg.

RETURN

POM **CEFOGEN**® *(Interpharma)*
Injection, Cefuroxime 750 mg.
750 mg - 1's.

POM **CEROXIM**® *(Ranbaxy)*
Tablets, Cefuroxime (as Cefuroxime axetil) USP 125 mg, 250 mg, 500 mg; f-c tablets.
Pack – 10's; 5 x 10's.

POM **SPIZEF**® *(Saingenes)*
Injections, Cefuroxime (as Sodium salt) USP 250 mg, 750 mg; in clear glass vial with coloured flip-off seal.

POM **ZINACEF**® *(GSK)*
Injection, Cefuroxime (as sodium salt) 250 mg, 750 mg; white to faintly yellow powder in vials.
750 mg - 5.

POM **ZINNAT**® *(GSK)*
Tablets, Cefuroxime (as cefuroxime axetil) 125 mg, 250 mg, 500 mg; white f-c capsule-shaped tabs. marked 'GLAXO' and '125', '250' and '500' respectively.
Pack - 10; 50.
Suspension, Cefuroxime (as cefuroxime axetil) 125 mg per 5 ml; granules for oral suspension in multidose bottle.

CEPHALEXIN

Therapeutic category: Cephalosporin antibiotic(First Generation).
Indications: Cephalexin is a bactericidal antibiotic which is active against a wide range of gram-positive and gram-negative organisms. Indicated for the following conditions, when caused by susceptible bacteria: Respiratory tract infections; Ear, nose and throat infections; Urinary tract infections; Gynaecological and obstetric infections; skin, soft-tissue and bone infections; Gonorrhoea and in dental procedures (as temporary replacement of penicillin prophylaxis in patients with heart disease who are undergoing dental treatment).
Contra-indications, Precautions, etc: See under cefuroxime.
Advice to patients: See label 9 in Appendix 6. See also under Cefuroxime.
Nursing considerations: •Obtain specimens for C&S tests prior to the first dose.
•Administer on an empty stomach (i.e, 1 hour prior to, or 2 hours after meals) to increase total absorption; may give with meals to reduce GI upset if needed.
•Reconstituted oral suspension should be stored in a refrigerator and should be used within 14 days; keep tightly closed and shake well before using.
•Give around-the-clock in equal intervals to promote less variation in peak and trough serum concentrations.
•Teach patient to report sore throat, easy bruising, bleeding, joint pain; may be signs of blood dyscrasias.
•Persistent diarrhoea may be sign of pseudomembranous colitis; notify physician.
•With prolonged therapy monitor renal, hepatic, and haematologic functions periodically.
Dose: By mouth, 250 mg 6hourly or 500 mg 8-12 hourly; increased to 1 g 8 hourly or 1.5 g 6 hourly in severe or deep-seated infections.
Child: usually 25-60 mg/kg/day increased to 100 mg/day (max. 4g/day) in chronic, severe or deep-seated infections.
0-1 year, 25-60 mg/kg/day; 1-2 years, 62.5-125 mg 4 times daily or 125-250 mg twice daily; 3-6 years, 125-250 mg 4 times daily or 250-500 mg twice daily; 7-12 years, 250-500mg 4 times daily or 500 mg-1 g twice daily.
Note: For most acute infections, treatment should continue for at least two days after signs have returned to normal and symptoms have subsided, but in chronic, recurrent or complicated *urinary tract infection* and *Syhilis*, treatment for two weeks (giving 1 g twice daily) is recommended.
For *gonorrhoea*, a single dose of 3 g with 1 g probenecid for males or 2 g with 0.5 g probenecid for females is usually effective. Concurrent administration of probenecid delays excretion of cephalexin and raises the serum levels by 50-100%.

POM **CEFAMOR**® *(Interpharma)*
Capsule, Cephalexin 500 mg.
500 mg - 5 x 20's.
Suspension, Cephalexin BP 125 mg per 5 ml; dry granules for oral suspension.
Pack - 100 ml.

POM **CEFORAL**® *(Dizpharm)*
Capsule, Cephalexin 250 mg.
250 mg - 20; 100; 500; 1000.
Suspension, Cephalexin 125 mg per 5 ml.
Pack - 60 ml.

POM **CELEXIN**® *(Hovid)*
Tablets, Cephalexin 250 mg, 500 mg; f-c tabs.
250 mg - 40; 100.
500 mg - 40; 100.
Suspension, Cephalexin 125 mg per 5 ml; dry granules for oral susp.

POM **CEPHAXIN**® *(Fidson)*
Capsules, Cephalexin 250 mg, 500 mg.
Suspension, Cephalexin 125 mg per 5 ml.
Pack - 60 ml; 100 ml.

POM **CEPOREX**® *(GSK)*
Tablet, Cephalexin 500 mg; pink f-c tab.
Suspension, Cephalexin 125 mg or 250 mg per 5 ml; dry granule for oral, orange-flavoured and coloured suspension.

POM **KEFLEX**® *(CHI/Eli Lilly)*
Capsules, Cephalexin 250 mg; white and green cap.
250 mg - 15.
Suspension, Cephalexin 125 mg per 5 ml; strawberry flavoured granules for reconstitution.
Pack - 100 ml.

POM **SPORIDEX**® *(Ranbaxy)*
Capsules, Cephalexin BP 250 mg, 500 mg.
250 mg - 24 x 10's; 24 x 20's (blister).
500 mg - 24 x 10's; 24 x 20's (blister).
Suspension (125 mg), Cephalexin USP 125 mg mg per 5 ml.
Pack - 60 ml; 100 ml.
Suspension (250 mg), Cephalexin USP 250 mg per 5 ml.
Pack - 60 ml; 100 ml.
Paediatric Drops, Cephalexin USP 100 mg per ml.
Pack - 10 ml.

IMIPENEM plus CILASTATIN

Imipenem with cilastatin is a complementary antibacterial combination for use only when there is significant resistance to other drugs on the WHO Model List.

Indications: Severe aerobic and anaerobic Gram-positive and Gram-negative infections in hospital (not indicated for CNS infections), including infections caused by resistant Pseudomonas and Acinetobacter spp.

Contra-indications: Hypersensitivity to beta-lactam antibiotics (see section 9.1.1).

Precautions: Renal impairment (Appendix 4); CNS disorders, such as epilepsy; pregnancy (Appendix 2); breastfeeding (Appendix 3).

Adverse effects: Nausea, vomiting, diarrhoea; antibiotic-associated colitis; taste disturbances; tooth or tongue discoloration, hearing loss; blood disorders, positive Coombs' test; allergic reactions (see section 9.1.1) including rash, pruritus, urticaria, erythema multiforme (Stevens-Johnson syndrome), fever, anaphylactic reactions, rarely toxic epidermal necrolysis, exfoliative dermatitis; myoclonic activity, convulsions, confusion, and mental disturbances; slight increase in liver enzymes and bilirubin, rarely hepatitis; increases in serum creatinine and blood urea; red coloration of urine in children; erythema, pain and induration, and thrombophlebitis at injection sites.

Dose: NOTE: ALL DOSES ARE IN TERMS OF IMIPENEM.

Infections due to susceptible organisms, by intravenous infusion, ADULT 1–2 g daily (in 3–4 divided doses); less susceptible organisms, ADULT up to 50 mg/kg daily (maximum 4 g daily) in 3–4 divided doses; CHILD over 3 months, 60 mg/kg daily (maximum 2 g daily) in 4 divided doses; child over 40 kg, adult dose.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. THE INTRAMUSCULAR PREPARATION MUST NOT BE ADMINISTERED INTRAVENOUSLY. THE INFUSION PREPARATION MUST NOT BE ADMINISTERED INTRAMUSCULARLY.

POM **Imipenem plus Cilastatin** *(WMF 6.2.1.3)*
Injection (Powder for solution for intramuscular injection), Imipenem (as monohydrate) 500 mg with cilastatin (as sodium salt) 500 mg.
Infusion (Powder for solution for intravenous infusion), Imipenem (as monohydrate) 250 mg or 500 mg with cilastatin (as sodium salt) 250 mg or 500 mg, respectively.

9.1.2 Other antibacterials

9.1.2.1 Chloramphenicol
9.1.2.2 Quinolones
9.1.2.3 Tetracyclines
9.1.2.4 Macrolides
9.1.2.5 Aminoglycosides
9.1.2.6 Metronidazole
9.1.2.7 Nitrofurantoin
9.1.2.8 Spectinomycin
9.1.2.9 Sulfonamides and trimethoprim
9.1.2.10 Clindamycin
9.1.2.11 Vancomycin

9.1.2.1 Chloramphenicol

Chloramphenicol is a potent broad-spectrum antibiotic. It is associated with serious haematological adverse effects and should be reserved for the treatment of severe infections, particularly those caused by *Haemophilus influenzae* and

typhoid fever. The oily suspension should be reserved for use in situations of catastrophic epidemics of meningococcal meningitis occurring mainly in sub-Saharan Africa, during which the medical services are overwhelmed by the epidemic and in which the overwhelming scale of the epidemic precludes any other form of antimicrobial therapy.

CHLORAMPHENICOL

Indications: Severe life-threatening infections, particularly those caused by *Haemophilus influenzae*, and typhoid fever; also, cerebral abscess; mastoiditis; relapsing fever; gangrene; granuloma inguinale; listeriosis; severe melioidosis; plague; psitticosis; tularaemia; Whipple disease; septicaemia; empirical treatment of meningitis.

Contra-indications: Pregnancy (Appendix 2); porphyria.

Precautions: Avoid repeated courses and prolonged use; reduce dose in hepatic impairment (Appendix 5) and severe renal impairment (Appendix 4); blood counts required before and during treatment; monitor plasma concentrations in neonates (see below); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Bone marrow depression—reversible and irreversible aplastic anaemia (with reports of leukaemia), anaemia, leukopenia and thrombocytopenia; nocturnal haemoglobinuria; peripheral neuritis and optic neuritis; nausea, vomiting, diarrhoea, dry mouth, stomatitis, glossitis; headache, depression; hypersensitivity reactions including, rashes, fever, angioedema and rarely anaphylaxis; grey syndrome (vomiting, greenish diarrhoea, abdominal distension, hypothermia, pallid cyanosis, irregular respiration, circulatory collapse) may follow excessive doses in neonates with immature hepatic metabolism; also reported in infants born to mothers treated in late pregnancy.

Advice to patients: Take on empty stomach; take with food if GI upset occurs, at evenly spaced intervals (every 6 hours around-the-clock); notify physician of persistent sore throat, tiredness, or unusual bleeding or bruising.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.

•Administer around-the-clock in equal intervals to promote less variation in peak and trough serum levels.

•For I.V. use, give slowly over at least 60 seconds and check injection site for signs of irritation or phlebitis.

•Encourage adequate intake of fluids.

•Observe closely for superinfection by nonsusceptible organisms.

Dose: *Infections due to susceptible organisms (not susceptible to other antimicrobials)*, by mouth or by intravenous injection or intravenous infusion, ADULT and CHILD 50 mg/kg daily in 4 divided doses; up to 100 mg/kg daily in divided doses *in severe infections such as meningitis, septicaemia, and haemophilus epiglottitis* (reduce high doses as soon as clinically indicated); infant under 2 weeks 25 mg/kg daily in 4 divided doses, 2 weeks to 1 year 50 mg/kg daily in 4 divided doses. *Epidemics of meningococcal meningitis*, by intramuscular injection (of oily injection), ADULT 3 g as a single dose, repeated after 48 hours if necessary; INFANT 1–8 weeks 250 mg as a single dose, 2–11 months 500 mg as a single dose; CHILD 1–2 years 1 g as a single dose, 3–5 years 1.5 g as a single dose, 6–9 years 2 g as a single dose, 10–14 years 2.5 g as a single dose, over 15 years as for adult; dose repeated after 48 hours if necessary.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. THE OILY INJECTION IS FOR INTRAMUSCULAR USE ONLY (SEE NOTES ABOVE).

NOTE: PLASMA CONCENTRATION MONITORING REQUIRED IN NEONATES AND PREFERRED IN THOSE UNDER 4 YEARS OF AGE AND IN HEPATIC IMPAIRMENT; RECOMMENDED PEAK PLASMA-CHLORAMPHENICOL CONCENTRATION (APPROX. 1 HOUR AFTER INTRAVENOUS INJECTION OR INFUSION) 15–25 MG/LITRE; PRE-DOSE 'TROUGH' CONCENTRATION SHOULD NOT EXCEED 15 MG/LITRE.

POM **Chloramphenicol** *(WMF 6.2.2.1)*
Capsules, Chloramphenicol 250 mg.
Oral suspension, Chloramphenicol (as palmitate) 150 mg/5 ml.
Injection (Powder for solution for injection), Chloramphenicol (as sodium succinate) 1-g vial.
Oily injection (Suspension for injection), Chloramphenicol (as sodium succinate) 500 mg/ml, 2-ml ampoule.

POM **Chloramphenicol** *(EDL 6.8)*
Capsule, Chloramphenicol 250 mg.
Suspension, Chloramphenicol (as palmitate)

125 mg per 5 ml.
Injection, Chloramphenicol (as sodium succinate) 1 g; powder in vial.

POM **CAFON-250®** *(Beta Drugs)*
Capsule, Chloramphenicol BP 250 mg; white or slight yellow, odourless powder in capsule.
Pack – 10 x 10's (in blister); 1000's (in tin).

POM **CHLOMACOL®** *(Geneith)*
Capsule, Chloramphenicol 250 mg.
250 mg – 10's; 1000's.

POM **CHLORAF®** *(Afrab-chem)*
Suspension, Chloramphenicol (as palmitate) 125 mg per 5 ml.
Pack - 60 ml; 100 ml.

POM **Chloramphenicol** *(Doyin)*
Capsule, Chloramphenicol 250 mg.
250 mg - 12; 100
Syrup, Chloramphenicol (as palmitate) 125 mg per 5 ml.
Pack - 60 ml.
Injection, Chloramphenicol (as sodium succinate) 0.5 g, 1 g; lyophilised powder for reconstitution in vials.
Pack - 50.
Note: **Parenteral Administration** - For the preparation of I.V. injection, the substance is dissolved by adding distilled water, 0.5 g in 1.3-2 ml and 1 g in 2.5-4 ml. The diluted solution may be added to saline or 5% Dextrose solution and administered by drop-wise infusion.

POM **Chloramphenicol** *(Emzor)*
Capsule, Chloramphenicol palmitate 250 mg; white cap. marked 'EMZOR' and '250'.
250 mg - 1000.

POM **CLOFENCOL®** *(Dana)*
Suspension, Chloramphenicol (as palmitate) BP 125 mg per 5 ml.
Pack - 60 ml.

POM **DALCOL®** *(Justeen)*
Capsule, Chloramphenicol BP 250 mg.
250 mg – 1 x 10's.

POM **NAMPHENICOL®** *(NASDMU)*
Capsule, Chloramphenicol 250 mg; cream coloured cap. marked 'NAMPHE 250 mg'.
Pack - 500.

POM **RICHPHENICOL®** *(GoldMoore)*
Injection, Chloramphenicol (as sodium succinate) BP 1 gm.
Pack - 1 g in vial.

9.1.2.2 Quinolones

Ciprofloxacin is active against both Gram-positive and Gram-negative bacteria. It is particularly active against salmonella, shigella, campylobacter, neisseria, *Bacillus anthracis* and pseudomonas. It is also active against chlamydia and some mycobacteria. Most anaerobic organisms are not susceptible. Ciprofloxacin is used with doxycycline and metronidazole to treat pelvic inflammatory disease. **Nalidixic acid** is an older quinolone effective in uncomplicated urinary-tract infections and, in the treatment of shigella in areas where it remains susceptible.

CIPROFLOXACIN

Ciprofloxacin is a representative quinolone antibacterial. Various drugs can serve as alternatives.

Therapeutic category: Broad-spectrum quinolone antibiotic.

Indications: Gastroenteritis—including cholera, shigellosis, travellers' diarrhoea, campylobacter and salmonella enteritis; typhoid; gonorrhoea; chancroid; legionnaires' disease; meningitis (including meningococcal meningitis prophylaxis); respiratory-tract infections—including pseudomonal infections in cystic fibrosis, but not pneumococcal pneumonia; urinary-tract infections; bone and joint infections; septicaemia; anthrax; skin infections; prophylaxis in surgery.

Contra-indications: History of tendon disorders related to quinolone use.

Precautions: History of epilepsy or conditions that predispose to seizures, G6PD deficiency, myasthenia gravis (risk of exacerbation), pregnancy (Appendix 2), breastfeeding (Appendix 3), children or adolescents (see below); avoid exposure to excessive sunlight (discontinue if photosensitivity occurs); rarely, tendon damage—discontinue at first sign of pain or inflammation and rest affected limb; hepatic impairment (Appendix 5); renal failure (Appendix 4); avoid excessive alkalinity of urine and ensure adequate fluid intake as risk of crystalluria; **interactions**: Appendix 1.

USE IN CHILDREN: CIPROFLOXACIN CAUSES ARTHROPATHY IN THE WEIGHT-BEARING JOINTS OF IMMATURE ANIMALS AND IS THEREFORE GENERALLY NOT RECOMMENDED IN CHILDREN AND GROWING ADOLESCENTS.

HOWEVER, THE SIGNIFICANCE OF THIS EFFECT IN HUMANS IS UNCERTAIN AND IN SOME SPECIFIC CIRCUMSTANCES SHORT-TERM USE OF CIPROFLOXACIN IN CHILDREN MAY BE JUSTIFIED. CIPROFLOXACIN IS USED FOR PSEUDOMONAL INFECTIONS IN CYSTIC FIBROSIS (FOR CHILDREN OVER 5 YEARS), AND FOR TREATMENT AND PROPHYLAXIS OF ANTHRAX.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Nausea, vomiting, dyspepsia, abdominal pain, flatulence, diarrhoea (rarely antibiotic-associated colitis), dysphagia, tremor, hyperglycaemia, headache, dizziness, sleep disorders, rash (rarely erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis), and pruritus; vasculitis, erythema nodosum, petechiae, haemorrhagic bullae; less frequently anorexia, increase in blood urea and creatinine; drowsiness, restlessness, asthenia, depression, confusion, hallucinations, convulsions, paraesthesia; photosensitivity, hypersensitivity reactions including fever, urticaria, angioedema, arthralgia, myalgia, and anaphylaxis; blood disorders (including eosinophilia, leukopenia, thrombocytopenia), altered prothrombin time; disturbances in vision, taste, hearing and smell, tinnitus; tenosynovitis; tachycardia, oedema, syncope, hot flushes and sweating; also isolated reports of tendon inflammation and damage (especially in the elderly and in those taking corticosteroids), haemolytic anaemia, renal failure, interstitial nephritis, and hepatic dysfunction (including hepatitis and cholestatic jaundice); if psychiatric, neurological or hypersensitivity reactions (including severe rash) occur discontinue.

Advice to patients: See Label 6,9, and 25 in Appendix 6. May be taken with food to minimize upset to stomach; avoid antacids containing magnesium or aluminium, or products containing zinc or iron within 4 hours before or 2 hours after dosing; may cause dizziness or drowsiness; drink fluid liberally.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.

•Administer oral dose preferably 2 hours after a meal (food does not affect absorption but may delay peak serum levels); may administer with food to minimize GI upset.

•Advise patient not to take antacid within 2 hr of using medication.

•Give plenty of fluids to maintain proper hydration and urine output.

•Administer by slow IV infusion over 60 minutes to reduce the risk of venous irritation (burning, pain, erythema and swelling); final concentration for administration should not exceed 2 mg/ml.

•Prolonged use may result in overgrowth of nonsusceptible organisms; monitor patient for symptoms.

•Advise patient not to drive or operate machinery if dizziness occurs.

Dose: *Infections due to susceptible organisms*, by mouth, ADULT 250–750 mg twice daily.

Acute uncomplicated cystitis, by mouth, ADULT 100 mg twice daily for 3 days.

Gonorrhoea, chancroid, shigellosis, or cholera, by mouth, 500 mg as a single dose.

Pseudomonal lower respiratory-tract infection in cystic fibrosis, by mouth, ADULT 750 mg twice daily; CHILD 5–17 years (see Precautions) up to 20 mg/kg twice daily (maximum 1.5 g daily).

Surgical prophylaxis, by mouth, ADULT 750 mg 60–90 minutes before procedure.

Prophylaxis of meningococcal meningitis, by mouth, ADULT 500 mg as a single dose.

Further dosage information

By mouth, Adult, *Bone/joint infections*, 500-750 mg twice daily for 4-6 weeks; *Infectious diarrhoea*, 500 mg every 12 hours for 5-7 days.

Typhoid fever, 500 mg every 12 hours for 10 days;

By I.V. infusion (over 30-60 minutes), Adult, *Urinary tract infection*, 200-400 mg every 12 hours for 7-14 days

Child: Not recommended except where benefit outweighs risk. See lit. for details.

POM **Ciprofloxacin** *(WMF 6.2.2.2)*

Tablets, Ciprofloxacin (as HCl) 100 mg [not included on WHO Model List], 250 mg.

POM **Ciprofloxacin** *(EDL 6.8)*

Tablet, Ciprofloxacin HCl 250 mg, 500 mg.

Injection (I.V.), Ciprofloxacin lactate 2 mg per ml; in 50 ml, 100 ml vials.

POM **BISO®** *(Silva Hill)*

Tablets, Ciprofloxacin HCl 250 mg; 500 mg (white, oblong, f-c tab.).

250 mg -10 x 10.

500 mg - 10 x 10.

POM **CIFRAN®** (*Ranbaxy)*

Tablets, Ciprofloxacin (as HCl) USP 250 mg,

500 mg; both are f-c tabs.
250 mg - 5 x 10's; 5 x 20's; 10 x 10's (blister)
500 mg - 5 x 10's; 5 x 20's; 10 x 10's (blister).
Infusion (i.v.), Ciprofloxacin (as lactate) USP 2 mg per ml; in 100 ml plastic bottle.
Pack - 100 ml.

POM **CIFRAN OD®** *(Ranbaxy)*
Tablets, Ciprofloxacin Ph. Eur. 500 mg, 1000 mg; extended release f-c tablets.
500 mg – 2 x 5's (in blister)
1000 mg – 2 x 5's (in blister).

POM **CIPENTEX®** *(Titan)*
Tablets, Ciprofloxacin HCl 250 mg; 500 mg.
250 mg -10 x 10.
500 mg - 10 x 10.

POM **CIPOCIL®** *(Justeen)*
Tablet, Ciprofloxacin 500 mg.
Pack – 1 x 10's.

POM **CIPRO®** *(Afrab-Chem)*
Tablets, Ciprofloxacin HCl 250 mg, 500 mg, 750 mg.
250 mg - 10's
500 mg - 10's
750 mg - 10's.

POM **CIPRO-J®** *(Juhel)*
Caplet, Ciprofloxacin 500 mg; white scored caplet marked 'Cipro/500' on one side and 'Juhel' on the reverse.
500 mg – 10's (in blister); 100's (in tins).

POM **CIPROBIOTIC®** *((Fill Pharma))*
Tablets, Ciprofloxacin HCl USP 250 mg, 500 mg, 750 mg; film-coated tabs.
250 mg - 1 x 10's
500 mg - 1 x 10's
750 mg - 1 x 10's.

POM **CIPRODAC®** *(Interpharma)*
Tablet (250 mg): Ciprofloxacin HCl U.S.P. 291.5 mg equivalent to Ciprofloxacin 250 mg.
Pack - Blister of 10's.
Tablet (500 mg): Ciprofloxacin HCl U.S.P. 683 mg equivalent to Ciprofloxacin 500 mg.
Pack - Blister of 10's.
Infusion: Ciprofloxacin USP 200 mg, Sodium chloride BP 0.9% w/v, Water for injection BP q.s.
Pack - Bottle of 100 ml.

POM **CIPRODAR®** *(Supreme)*
Tablets, Ciprofloxacin HCl 250 mg, 500 mg.
250 mg - 10
500 mg - 3.

POM **CIPROF 500®** *(Diamond Remedies)*
Caplet, Ciprofloxacin 500 mg; white caplet marked 'CF 500' on one side and 'TWL' on the reverse.
500 mg - 10.

POM **Ciprofloxacin** *(Dana)*
Infusion, Ciprofloxacin 200 mg per 100 ml of water for injection.
Pack - 100 ml x 40's.

POM **CIPROGEM®** *(Gemini)*
Tablet, Ciprofloxacin (as HCl) 250 mg; laquer-coated tab.
250 mg. - 10; 100.

POM **CIPROPAN®** (*Panvij Biotec*)
Tablets, Ciprofloxacin (as HCl) 250 mg, 500 mg; both are white to off-white f-c tabs marked 'CIPROPAN' on one side and the tab. strenght on the reverse.
250 mg - 10; 10 x 10.
500 mg - 4 x10; 10 x 10.

POM **CIPROPOL®** *(St. Michael)*
Tablets, Ciprofloxacin HCl 250 mg, 500 mg.
250 mg - 10 (Blister).
500 mg - 10 (Blister).

POM **CIPROTAB®** *(Fidson)*
Tablets, Ciprofloxacin (as HCl) 250 mg, 500 mg
Pack - 10.
Infusion (i.v.), Ciprofloxacin 2 mg per ml.
Pack - 100 ml.

POM **CIPROVAL®** *(NGC)*
Tablets, Ciprofloxacin (as HCl) 500 mg.
500 mg - 10; 100.

POM **CYPLOX®** *(Medreich)*
Tablets, Ciprofloxacin (as HCl) 250 mg.

POM **DEPMAX®** *(Dana)*
Tablets, Ciprofloxacin (as HCl) 250 mg, 500 mg; f-c tabs.
250 mg - 10 x 10's (in blister).
500 mg - 10 x 10's (in blister).

POM **ELCIP®** *(GoldMoore)*
Tablets, Ciprofloxacin (as HCl) USP 250 mg, 500 mg; f-c tabs.
250 mg - 2 x 10's.
500 mg - 1 x 10's.

POM **SIPROSAN®** *(Tyonex)*
Tablet, Ciprofloxacin (as HCl) 500 mg; f-c tab.
500 mg - 14 (in blister).

POM **ULTRAFLOX®** *(Sam)*
Tablet, Ciprofloxacin 250 mg.
250 mg - 10
Caplet, Ciprofloxacin 500 mg.
500 mg - 10.

POM **UNIFLOX I.V.®** *(Unique)*
Infusion, Ciprofloxacin 200 mg per 100 ml of water for injection.
Pack - 100 ml.

POM **UROXIN®** *(Unison)*
Tablets, Ciprofloxacin (as HCl) 250 mg, 500 mg; f-c tabs.
250 mg - 10 (in blister).
500 mg - 10 (in blister).

POM **VITAPRO®** *(Strides Vital)*
Tablet, Ciprofloxacin HCl 500 mg; white capsule shaped tab. marked 'VITAPRO' on one side and scored on the reverse.
500 mg - 1 x 10's.

NALIDIXIC ACID

Indications: Urinary-tract infections; shigellosis.
Precautions: History of epilepsy or conditions that predispose to seizures, G6PD deficiency, myasthenia gravis (risk of exacerbation), pregnancy (Appendix 2), breastfeeding (Appendix 3); avoid exposure to excessive sunlight (discontinue if photosensitivity occurs); rarely tendon damage—discontinue at first sign of pain or inflammation and rest affected limb; porphyria; hepatic impairment (Appendix 5); renal impairment (Appendix 4); false positive urinary glucose (if tested for reducing substances); monitor blood counts, renal and liver function if treatment exceeds 2 weeks; **interactions**: Appendix 1.
Adverse effects: Nausea, vomiting, dyspepsia, abdominal pain, diarrhoea (rarely antibiotic-associated colitis), headache, dizziness, weakness, sleep disorders, rash (rarely erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis), and pruritus; less frequently anorexia, increase in blood urea and creatinine; metabolic acidosis; drowsiness, restlessness, asthenia, depression, confusion, hallucinations, convulsions, paraesthesia, raised intracranial pressure, cranial nerve palsy; photosensitivity, hypersensitivity reactions including fever, urticaria, angioedema, arthralgia, myalgia, and anaphylaxis; blood disorders (including eosinophilia, leukopenia, thrombocytopenia); disturbances in vision, taste, hearing and smell; also isolated reports of tendon inflammation and damage (especially in the elderly and in those taking corticosteroids); haemolytic anaemia, renal failure, interstitial nephritis, and hepatic dysfunction (including hepatitis and cholestatic jaundice); if psychiatric, neurological or hypersensitivity reactions (including severe rash) occur discontinue.
Dose: *Urinary-tract infections*, by mouth, ADULT 1 g every 6 hours for 7 days, reduced in chronic infections to 500 mg every 6 hours; CHILD over 3 months, maximum 50 mg/kg daily in divided doses, reduced in prolonged treatment to 30 mg/kg daily.
Shigellosis, by mouth, ADULT 1 g every 6 hours for 5 days; CHILD over 3 months, 15 mg/kg every 6 hours for 5 days.
PATIENT ADVICE: TAKE ON AN EMPTY STOMACH, PREFERABLY ONE HOUR BEFORE A MEAL.

POM **Nalidixic acid** *(WMF 6.2.2.2)*
Tablets, Nalidixic acid 250 mg, 500 mg.

NORFLOXACIN

Therapeutic category: Quinolone antibiotic.
Pharmacology: Norfloxacin, like Ciprofloxacin and Ofloxacin, is a quinoline antibiotic with broad-spectrum activity. It is bactericidal against many gram-positive and gram-negative organisms. It acts mainly by inhibitng DNA gyrase. See also under Ciprofloxacin.
Indications: Broad spectrum bactericidal agent for urinary tract infections; acute bacterial gastroenteritis; gonococcal urethritis, pharyngitis, proctitis or cervicitis; typhoid fever; prophylaxis of sepsis in neutropaenic patients, bacterial gastroenteritis.
Contra-indications: Hypersensitivity to norfloxacin or to other quinolone antibacterials.
Precautions: Reduce dose in renal impairment; pregnancy, breast-feeding; not recommended for prepubertal children; history of convulsions.
Interactions: Probenecid, nitrofurantion, theophylline, cyclosporine, sucralfate.
Adverse effects: GI, neuropsychiatric and skin reactions including nausea, headache, dizziness, rash, and diarrhoea.
Advice to patients: See Labels 6 and 9 in Appendix 6. Tablets should be taken at least 1 hour before or 2 hours after a meal with a glass of water; patients receiving norfloxacin should

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be well hydrated; take all the medication, do not skip doses; do not take with antacids.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.
•Give 1 hr before or 2 hr after meals.
•Antacids and iron products may hinder absorption.
•Encourage patient to increase fluid intake to avoid crystallization in kidneys.
•Advise patient to avoid hazardous activities which require alertness and good coordination.
•Assist with ambulation if dizziness occurs.
•Advise limited intake of foods and drugs that contain alcohol, milk, dairy products, vegetables, sodium bicarbonate and antacids.

Dose: Treatment, by mouth, 400 mg 2 times daily: *UTI*, 7-10 days; *Uncomplicated acute cystitis*, 3-7 days; *Chronic relapsing UTI*, up to 12 weeks; *Acute bacterial gastroenteritis*, 5 days.
Acute gonococcal urethritis, pharyngitis, proctitis or cervicitis, 800 mg as a single dose.
Typhoid fever, 400 mg 3 times daily for 14 days.
Prophylaxis: *Sepsis of profound Neutropenia*, 400 mg 3 times daily; *Bacterial gastroenteritis*, 400 mg daily, 24 hours before arrival and 48 hours after leaving endemic areas.

POM **Norfloxacin** *(EDL 6.8)*
Tablet, Norfloxacin 100 mg.

POM **BROADIFLOX®** *(Sam)*
Tablet, Norfloxacin 400 mg.
400 mg - 10.

POM **NORBACTIN®** *(Ranbaxy)*
Tablet, Norfloxacin USP 400 mg.
400 mg - 5 x 10's; 10 x 10's.

POM **NORFEN®** *(Interpharma)*
Tablet, Norfloxacin 400 mg; f-c tab.
400 mg - 10's.

POM **NOROXIN®** *(Bolax/BPP)*
Tablet, Norfloxacin 100 mg.

POM **NORXIN®** *(Pharmabox)*
Tablet (200 mg), Norfloxacin USP 200 mg; orange coloured capsule containing white powder.
200 mg - 10's; 100's; 500's
Tablet (400 mg), Norfloxacin USP 400 mg; blue cap and white body capsule containing white powder.
400 mg - 10's; 100's; 500's

OFLOXACIN

Therapeutic category: Quinolone Antibiotic.

Indications: Bacterial infections due to ofloxacin sensitive pathogens: respiratory tract infections including ENT infections; infections of soft tissue and skin; infections of the abdominal cavity including the pelvis, minor bacterial enteritis; infections of the kidneys, urinary tract and genital organs including gonorrhoea.

Contra-indications: Hypersensitivity to ofloxacin or other quinolone-carboxylic acid derivative; epileptics, children and adolescents in the growth phase, pregnancy, breast feeding.

Interactions:
•Preparations containing divalent or trivalent cations such as antacids, haematinics (cause attenuation of the ofloxacin effect).
•See also under Ciprofloxacin.

Adverse effects: Allergic reactions, haemorrhages, CVS disturbances, pain in joints and muscles, blood dyscrasias, GI disturbances; transient rise of serum creatinine, liver enzymes and bilirubin levels.

Advice to patients: See Labels 6,9 and 11 in Appendix 6. Report any skin rash or allergic reactions; avoid excessive sunlight; do not take with food; do not take within 2 hours of any products including antacids which contain zinc, magnesium, or aluminium.

Nursing considerations: •See under Ciprofloxacin.

Dose: By mouth, Adult, usually 200 mg 2 times daily; may be increased up to 300-400 mg 2 times daily in severe infections.
Uncomplicated urinary tract infections, 100 mg 2 times daily for 3 days; increased to 7 days in complicated urinary tract infections.
Osteomylitis, 200 mg 3 times daily.
Lower respiratory -tract infections, 400 mg daily preferably in the morning; increased if necessary to 400 mg twice daily.
Skin and soft-tissue infections, 400 mg twice daily.
Uncomplicated gonorrhoea, 400 mg as a single dose.
Non-gonococcal urethritis and cervicitis, 400 mg daily in single or divided doses.
In renal impairment (creatinine clearance between 50 and 20 ml/min.), initially 200 mg, then 100 mg 24 hourly; less than 20 ml/min., initially 200 mg, then 100 mg 48 hourly.

POM **Ofloxacin** *(EDL 6.8)*

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Tablet or Capsule, Ofloxacin 200 mg.

POM **APO-OFLOX**® *(Lahams)*
Tablet, Ofloxacin 200 mg; light yellow, oval, f-c tab. marked 'APO-200'.
200 mg - 100.

POM **DROVID**® *(Tyonex)*
Tablet, Ofloxacin 200 mg; f-c tab.
200 mg - 10 (in blister).
Dose: By mouth, Adult, usually 200-800 mg daily.
Respiratory tract infection, 200 mg every 12 hours; *Genitourinary tract infection*, 200 mg every 12 hours; *Skin and skin structure infections*, 200 mg every 12 hours; *Intra-abdominal infections including small pelvis*, 200 mg every 12 hours; *Acute, uncomplicated urethral and cervical gonorrhoea*, 400 mg as a single dose. *Typhoid fever*, 400 mg once daily or 200 mg every 12 hours for up to 10 days; Bone and joint infections, 400 mg once daily for up to 5 weeks; *Post-surgical infections*, 400 mg once daily.
In renal failure, doses should be adjusted as follows:
Above 30 ml/min, 400 mg in 24 hours;
100-30 ml/min., 200 mg in 24 hours;
Less than 10 ml/min, 100 mg in 24 hours.

POM **FLOBACIN**® *(Justeen)*
Tablet, Ofloxacin BP 200 mg.
Pack – 1 x 10's.

POM **FLOXAN**® *(Pharmabox)*
Tablet, Ofloxacin USP 200 mg; white, oval, film-coated tablets.
200 mg – 10's; 30's; 50's; 100's; 500's; 1000's.

POM **FLOXUR** *(Zoomota)*
Tablets: Ofloxacin USP 200 mg, 400 mg; white f-c tablets.
200 mg – 10's (in blister)
400 mg – 10's (in blister)

POM **GRENIS-OFLO**® *(St. Michael)*
Tablet, Ofloxacin 200 mg; f-c tab.
200 mg - 10.

POM **TARIVID**® *(May & Baker)*
Tablet, Ofloxacin 200 mg; f-c tab.
200 mg - 10.

POM **TRAFLOX**® *(NGC)*
Tablet, Ofloxacin 200 mg; f-c tab.
200 mg - 10; 100.

POM **ZANOCIN**® *(Ranbaxy)*
Tablets, Ofloxacin USP 100 mg, 200 mg; both are f-c tabs.
100 mg - 10 x 10's; 5 x 20's.
200 mg - 10 x 10's; 5 x 20's.
Tablets (OD), Ofloxacin 400 mg, 800 mg; extended release f-c tabs.
400 mg - 2 x 5.
800 mg - 2 x 5.
Infusion, Ofloxacin 2 mg per ml; in 100 ml plastic bottle.
Pack - 1.

PEFLOXACIN

Pharmacology: Pefloxacin is a synthetic fluoroquinolone antibiotic. It can be administered both orally and intravenously, and has a broad spectrum of in vitro activity against Gram-negative organisms and staphylococci. It is rapidly (approx. 20 minutes) and nearly completely (about 90%) absorbed after oral administration of 400mg. It is metabolised in the liver to norfloxacin and pefloxacin N-oxide. It is excreted in the urine as unchanged product (41.7%) and the glucuronide and N-oxide metabolites. There is no appreciable alteration in serum levels of pefloxacin, whatever the degree of renal impairment.
Indications: Complicated urinary tract infections; nosocomial lower respiratory tract infections (RTIs); septicaemia and surgical infections; gynaecological infections; soft-tissue infections; intra-abdominal infections; bone and joint infections; meningitis; ENT infections; cystitis; gonorrhoea; also in infections in immuno-compromised patients; febrile episodes in neutropenic patients; prevention of septicaemia produced by gram-negative bacilli in neutropenic cancer patients. See also under the dose.
Contra-indications: Hypersensitivity to pefloxacin and the quinolone derivatives; children up until the end of the growth period; glucose-6-phosphate-dehydrogenase deficiency; pregnancy lactation; previous history of tendinopathy with fluoroquinolone.
Precautions: Photosensitisation reaction (avoid exposure to sunlight or UV radiation during treatment); tendinitis (discontinue treatment); severe hepatic insufficiency (adjust dose).
Interactions: •Antacids containing aluminium and/or magnesium gel (absorption of pefloxacin is decreased).
•Theophylline (co-administration will prolong the serum half-life of theophylline).

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Adverse effects: Gastric pain, nausea, vomiting; allergic skin reactions and photosensitivity; muscular and/or joint pain, tendinitis, rupture of Achilles tendon; thrombocytopenia and neutropenia; neurological disorders (headaches, insomnia, myoclonia, convulsions).
Advice to patients: See Label 21 in Appendix 6.
Dose: Adult, by mouth, *Gonococcal urethritis*, 800 mg as a single dose;
Gonococcal infection in women, 400 mg twice daily for 5 days;
Prostatitis, 400 mg twice daily for not more than 30 days;
Chancroid and cystitis, 800 mg as a single dose;
Salpingitis and endometritis, 400 mg twice daily for 10 days;
Urinary tract infection (pyelonephritis), 400 mg twice daily for 10-20 days.
Typhoid fever and bacterial diarrhoea, 400 mg twice daily for 7 days; *surgical abdominal infections*, 400 mg twice daily (include ampicillin if Streptococci or metronidazole if anaerobic);
Peritonitis, 400 mg twice daily (include ampicillin I.V. if Streptococci); *Hepatic abscess*, 400 mg twice daily (include metronidazole if anaerobic).
To be taken with meals to avoid GI disturbances.
By slow I.V. injection (one hour), 400 mg, diluted in 250 ml of isotonic glucose solution, twice daily (one injection in the morning and one in the evening).

POM **ABAKTAL**® *(Taylek)*
Tablet, Pefloxacin 400 mg.
400 mg - 10; 50; 100.
Injection, Pefloxacin 400 mg per 5 ml
Pack - 5; 10.

POM **PEFLACINE**® *(May and Baker)*
Tablet, Pefloxacin 400 mg; coated tab. in pre-cut blisters.
400 mg - 50.
Injection, Pefloxacin 400 mg per 5 ml; injectable solution for infusion.
Pack - 5.

POM **PEFLOBID**® *(Interpharma)*
Tablet, Pefloxacin (as methanesulfonate dihydrate) 400 mg.
400 mg - 10 x 10's.
Infusion, Pefloxacin (as methanesulfonate dihydrate) 400 mg per 100 ml.
Pack - 5.

POM **PEFLOTAB**® *(Fidson)*
Tablet, Pefloxacin (as mesylate dihydrate) 400 mg
400 mg - 10.

POM **PEFRIN**® *(Titan)*
Tablet, Pefloxacin 400 mg.
400 mg - 10.

POM **PEMAX**® *(Pharmabox)*
Tablet, Pefloxacin (as methanesulfonate dihydrate) 400 mg; white rectangular f-c tab.
400 mg - 10's; 1000's.

SPARFLOXACIN

Therapeutic category: Quinolone antibiotic
Pharmacology: Sparfloxacin is a fluoroquinolone antibacterial agent with activity against a broad range of gram negative and gram positive organisms including *Streptococcus pneumoniae*. It prevents bacterial growth primarily by inhibiting the action of DNA gyrase.
Pharmacokinetics: Sparfloxacin is readily absorbed after oral administration. Following an oral dose of Sparfloxacin 400 mg, peak plasma concentration of about 0.6 to1.6 mg/L is achieved within 2 to 6 hours. Oral bioavailability is 90%. It penetrates extensively into the tissue. Peak concentration in bronchopulmonary tissues, alveolar macrophages and sputum exceed plasma concentration. It is about 40% bound to plasma proteins. The drug has a long elimination half life of about 15-20 hours and is excreted mainly by non-renal mechanisms.
Elimination of the drug is mainly via metabolism to its inactive acyglucuronide derivative and subsequent faecal excretion. Renal clearance of the parent drug and its glucuronide metabolite accounts for about 30 to 40% of total clearance (about 10% as unchanged drug and 20% to 30% as the glucuronide). Biliary excretion is a minor route. The presence of food has no influence on absorption or excretion of Sparfloxacin.
Indications: Community acquired pneumonia; Lower respiratory tract infections including acute exacerbations of chronic obstructive pulmonary diseases; Sinusitis; Gonococcal and non-gonococcal urethritis.
Contra-indications: Infants, children and growing adolescents because of the risk of arthropathy; history of hypersensitivity reactions to it and other quinolones; history of photosensitivity reactions; Patients with known QT prolongation and in patients receiving drugs

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known to prolong the QT interval.

Precautions: Sparfloxacin should be dicontinued if manifestations of photosensitivity (skin burning, redness, rash, itching, dermatitis, blister) appear. To minimise the risk of photosensititvity, exposure to sunlight and UV radiation must be strictly avoided during Sparfloxacin therapy and for 5 days after the end of treatment. Patients experiencing pain, inflammation or tendon rupture must stop Sparfloxacin treatment and refrain from exercise. Measures should be taken to avoid tendon rupture if this has not already occurred. Quinolones should not be used during pregnancy or while breast feeding.

Interactions: Sparfloxacin does not influence the pharmacokinetics of Theophylline but may increase plasma concentration of Digoxin and hence, patients receiving concomitant Digoxin therapy should be closely monitored.

Because Sparfloxacin has caused slight increase in the QT interval, concomitant use of agents also known to prolong the QT interval (eg. Terfenadine, Astemizole, Erythromycin, Class 1A and 111 anti-arrhythmic agents) is to be avoided.

Because absoption of Sparfloxacin is reduced by antacids containing Aluminium/Magnesium and also by Ferrous sulphate and Sucralfate, staggered drug administration is recommended. Cimetidine has no effect on Sparfloxacin disposition. Sucralfate reduces the bioavailability of Sparfloxacin whereas Cisapride accelerates absorption without affecting bioavailability.

Adverse effects: GI disturbances (diarrhoea, nausea and vomiting) and CNS effects are more common. Insomnia and other sleep disorders are the most frequent CNS adverse events. There have been some reports of convulsions during Sparfloxacin therapy. Photosensitivity occurs more frequently than with other fluoroquinolones. Tendinitis or tendon rupture has been reported during Sparfloxacin therapy. There are infrequent reports of prolonged QT interval.

Dose: Its long elimination half-life permits once daily dosage.

Lower respiratory tract infections: 400 mg as a single loading dose on day 1, followed by 200 mg once daily for 10 days.

Sinusitis: 400 mg loading dose followed by 200 mg once daily for 5 days.

Sexually transmitted diseases: *Gonococcal urethritis* - single dose of 200 mg; *Non-gonococcal urethritis* - 200 mg loading dose followed by 100 mg daily for 6 days.

Note: Elimination of Sparfloxacin is prolonged in patients with moderate to severe renal dysfunction. In patients with creatinine clearance <30 ml/min, urinary excretion and renal clearance is decreased significantly. The dosage of Sparfloxacin should therefore be adjusted accordingly with moderate to severe renal dysfunction.

Patients with severe renal insufficiency, should receive a dosage of 200 mg every alternate day (or 100 mg daily).

Sparfloxacin pharmacokinetics are unchanged in the elderly and in the presence of hepatic dysfunction. Hence, elderly patients and those with hepatic dysfunction do not require dosage adjustment.

POM **SLOXIN 200®** *(GoldMoore)*
Tablet, Sparfloxacin 200 mg; f-c tab.
Pack - 7's.

POM **SPARBACT®** *(IPCA)*
Tablet Sparfloxacin 200 mg; f-c tab.
Pack - 6's

9.1.2.3 Tetracyclines

Doxycycline is a tetracycline and is a broad-spectrum antibiotic effective for conditions caused by chlamydia, rickettsia, brucella and the spirochaete, *Borrelia burgdorferi* (Lyme disease). It is the preferred tetracycline since it has a more favourable pharmacokinetic profile than tetracycline. It is deposited in growing bone and teeth causing staining and occasionally dental hypoplasia. It should not be given to children under 8 years or pregnant women; in some countries, use in children under 12 years is contraindicated.

DOXYCYCLINE

Indications: Respiratory-tract infections, including pneumonia and chronic bronchitis; urinary-tract infections; syphilis; chlamydia, mycoplasma, and rickettsia; prostatitis; lymphogranuloma venereum; pelvic inflammatory disease (with metronidazole); Lyme disease; brucellosis (with rifampicin); leptospirosis, scrub typhus and travellers' diarrhoea; psittacosis; cholera; melioidosis; plague; anthrax; Q fever; malaria (section 9.3.1).

Contra-indications: Pregnancy (Appendix 2); children (see notes above); porphyria;

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systemic lupus erythematosus.

Precautions: Avoid exposure to sunlight or sunlamps—photosensitivity reported; renal impairment (Appendix 4); hepatic impairment (Appendix 5); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances; anorexia, erythema (discontinue treatment); photosensitivity; hypersensitivity reactions; headache and visual disturbances; hepatotoxicity, blood disorders, pancreatitis, and antibiotic-associated colitis reported; staining of growing teeth and occasional dental hypoplasia.

Advice to patients: See labels 6, 9, 11 and 27. Avoid unnecessary exposure to sunlight. Take until gone; do not skip doses.

Nursing considerations: •Obtain specimens for C&S tests prior to the first dose; administer around-the-clock in equal intervals to promote less variation in peak and trough serum levels.

•May give with meals to decrease GI upset; with a full glass of water.

•Tablets or capsules should not be taken within an hour of bed time because dysphagia may occur.

•Give drug 2 hours before or after laxative or iron products and 3 hours after antacid or kaolin-pectin products.

•Anti-emetic may be given if nausea or vomiting persists.

Dose: *Infections due to susceptible organisms*, by mouth, ADULT and CHILD over 8 years, 200 mg on first day then 100 mg daily; in severe infections, 200 mg daily

Syphilis, by mouth, 100 mg twice daily for 14 days; *late latent syphilis* 100 mg twice daily for 28 days.

Uncomplicated genital chlamydia, non-gonococcal urethritis, by mouth, 100 mg twice daily for 7 days (14 days in *pelvic inflammatory disease*).

Louse and tick-borne relapsing fevers, by mouth, 100 mg or 200 mg as a single dose.

Cholera, by mouth, ADULT 300 mg as a single dose; CHILD over 8 years, 100 mg as a single dose.

PATIENT ADVICE: CAPSULES SHOULD BE SWALLOWED WHOLE WITH PLENTY OF FLUID WHILE SITTING OR STANDING TO PREVENT OESOPHAGEAL IRRITATION. MAY BE GIVEN WITH MILK OR FOOD TO COUNTER GASTRIC IRRITATION.

Further dosage information

Acne, by mouth, 50 mg daily for 6-12 weeks or longer.

POM **Doxycycline** *(WMF 6.2.2.3)*

Capsules, Doxycycline (as HCl) 100 mg.

POM **Doxycycline** *(EDL 6.8)*
Capsule, Doxycycline HCl 100 mg.

POM **DOXIN®** *(Geneith)*
Capsule, Doxycycline 100 mg.
Pack – 10's (in blister)

POM **DOXY-200®** *(St. Michael)*
Tablet, Doxycycline (as HCl) 200 mg; scored tab.
200 mg - 8 (Blister).

POM **DOXYCAP®** *(Hovid)*
Capsule, Doxycycline (as HCl) 100 mg
100 mg - 10 x 10 (blister).

POM **DOXYDAR®** *(Supreme)*
Capsule, Doxycycline 100 mg.
100 mg - 8; 500.

POM **DOXYTAB®** *(Hovid)*
Tablet, Doxycycline (as HCl) 100 mg; f-c tab.
100 mg - 250; 1000.

POM **TENUTAN®** *(Sanofi)*
Capsule, Doxycycline HCl 100 mg
100 mg - 8; 100; 500.

POM **TETRADOX®** *(Ranbaxy)*
Capsule, Doxycycline (as HCl) BP 100 mg.
100 mg - 10 x 10's; 500's.
Tablet, Doxycycline (as Hyclate) USP 100 mg.
100 mg - 10's; 500's.

POM **VIBRAMYCIN®** *(Pfizer)*
Capsule, Doxycycline (as HCl) 100 mg; green cap. marked 'PFIZER' and 'VBM100'.
100 mg - 6; 50.

MINOCYCLINE

Therapeutic category: Tetracycline Antibiotic

Indications: Treatment of susceptible bacterial infections of both gram-negative and gram-positive organisms; acne, meningococcal carrier state.

Contra-indications, Precautions, etc: See under Tetracycline.

Advice to patients: See Labels 6, 9, 11, and 25 in Appendix 6. Avoid unnecessary exposure to sunlight; do not skip doses.

Nursing considerations: •*See under Doxycycline*.

•To be taken with adequate amount of fluid to reduce the risk of oesophageal irritation and ulceration.

Dose: By mouth, Adult, usually 200 mg initially, followed by 100 mg every 12 hours.

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Gonorrhoea, as above, for minimum of 4 days; women may require longer treatment.
Prophylaxis of asymptomatic meningococcal carrier state, 100 mg every 12 hours for 5 days.
Acne, 50 mg 1-3 times daily.

POM **MINOCIN®** *(Matbeny)*
Capsule, Minocycline HCl 50 mg, yellow/green cap. marked 'LEDERLE M45' and 'LEDERLE 50 MG'; 100 mg, opaque light green/transparent green cap. marked 'LEDERLE M46' and 'LEDERLE 100 MG'.
50 mg - 30
100 mg - 20.

OXYTETRACYCLINE

Therapeutic category: Antibiotic.
Pharmacology: It is primarily bacteriostatic and exerts its antimicrobial action by the inhibition of protein synthesis. It is active against a wide range of Gram-negative and Gram-positive organisms.
Indications, Contra-indications, etc: See under Tetracycline.
Advice to patients: See labels 7, 9, and 23 in Appendix 6.
Nursing considerations: •See under Tetracycline.
Dose: By mouth, usually 250-500 mg 4 times daily, depending on the severity of infection.
Neurosyhilis, 500 mg 4 times daily for 30 days.
Uncomplicated urethral, endocervical or rectal chlamydia infection, 500 mg 4 times daily for at least 7 days.
Nongonococcal urethritis, 500 mg 4 times daily for at least 7 days.
Acute vulgaris and rosacea, 250-500 mg daily in single or divided doses.
Note: Administer with adequate amount of fluid to reduce the risk of oesophageal irritation and ulceration. Food and some dairy products interfere with absorption. To be given 1 hour before or 2 hours after meals.

POM **Oxytetracycline** *(EDL 6.8)*
Capsule or tablet, Oxytetracycline HCl 250 mg.

POM **TERRAMYCIN®** *(Pfizer)*
Capsule, Oxytetracycline HCl 250 mg; yellow marked 'PFIZER' and 'TER 250'.
250 mg - 20.

TETRACYCLINE

Synonym: TCN.
Therapeutic category: Antibiotic
Pharmacology: Tetracyclines are broad-spectrum antibiotics and are bacteriostatic. They exert bacteriostatic effect by binding to the 30S ribosomal subunit of microorganisms, thus inhibiting protein synthesis. They are deposited in growing bone and teeth (being bound to calcium) causing staining and should not be given to children under 12 years or pregnant women.
Indications: Infections of the ear, nose and throat, respiratory tract, gastro-intestinal tract, liver, genito-urinary tract; veneral diseases.
Contra-indications: Hypersensitiviy to tetracyclines; pregnancy, children under 12 years; Kidney disease, systemic lupus erythematosus.
Precautions: Breast-feeding; overgrowth of nonsusceptible organisms. Avoid use with penicillins.
Interactions: •Milk products, calcium, magnesium, and iron salts, antacids containing aluminium hydroxide or silicate, should not be given for at least 30 mins following admin. of tetracycline due to the decrease in antibiotic absorption.
•Oral contraceptives (decrease contraceptive effectiveness and increased risk of break-through bleeding).
Adverse effects: GI disturbances; overgrowth of resistant organisms; photosensitivity and dermatological reactions.
Advice to patients: See labels 7,9, and 23 in Appendix 6. Take 1 hour before or 2 hours after meals with adequate amounts of fluid, capsules or tablets should be swallowed whole while sitting or standing; avoid taking antacids, iron, or dairy products within 2 hours of taking tetracyclines; report persistent nausea, vomiting, yellow colouring of skin or eyes, dark urine, or pale stools; avoid prolonged exposure to sunlight and U.V. light. Take until gone; do not skip doses.
Nursing considerations: •Obtain specimens for C&S tests prior to the first dose; administer around-the-clock in equal intervals to promote less variation in peak and trough serum levels.
•Administer on an empty stomach with a full glass of water; separate iron products, antacid, dairy products or kaolin/pectin by at least 2 hr.
•Give at least an hour before bedtime to prevent oesophagitis.
•Anti-emetic may be given if nausea or vomiting persists.
•Explain to the patient that effectiveness of the drug is reduced when taken with milk or other dairy products, food, antacids or iron products.
•Monitor patient for signs of superinfection.
Dose: By mouth, 250 mg 4 times daily; increased to 250 mg 6-8 times daily in severe infections.

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Not recommended for children under 12 years.

Note: To be swallowed with adequate amount of fluid while sitting or standing to prevent gastric irritation.

POM **Tetracyline** *(EDL 6.8)*
Capsule or tablet, Tetracycline HCl 250 mg.
Injection, Tetracycline 250 mg; powder in vials.

POM **LETAN-250®** *(Beta Drugs)*
Capsule, Tetracycline HCl for BP 250 mg.

POM **MAXCYCLIN®** *(GoldMoore)*
Capsule, Tetracycline (as HCl) BP 250 mg.
Pack - 10 x 10's; 1000's.

POM **NACYCLINE®** *(NASDMU)*
Capsule, Tetracycline HCl 250 mg; yellow/red cap. marked 'NACY 250 mg'.
Pack - 1000.

POM **SALMYCIN 250®** *(Strides Vital)*
Capsule, Tetracycline 250 mg.
250 mg – 10 x 10's.

POM **T-CLIN®** *(Rajat)*
Capsule, Tetracycline HCl BP 250 mg
Pack – 10's (in blister).

POM **TETRA-250®** *(Ranbaxy)*
Capsule, Tetracycline HCl 250 mg
250 mg - 10 x 10; 10 x 100; 100

POM **TETRACAP®** *(Fill Pharma)*
Capsule, Tetracycline HCl BP 250 mg
250 mg - 10 x 10 (in blister)

POM **Tetracycline** *(Doyin)*
Capsule, Tetracycline HCl 250mg
250mg - 10 x 100

POM **Tetracycline** *(Emzor)*
Capsule, Tetracycline HCl 250 mg; yellow/red cap. marked 'EMZOR'.
250 mg - 1000

POM **TETRAMAC®** *(Geneith)*
Capsule, Tetracycline 250 mg.
250 mg – 10's; 1000's.

POM **TETRASAM®** *(Sam)*
Capsule, Tetracycline HCl 250 mg
250 mg - 10 x 10 (blister)

9.1.2.4 Macrolides

Erythromycin is a macrolide; it has an antibacterial spectrum that is similar but not identical to penicillin and is used as an alternative in penicillin-allergic patients. It is effective in respiratory infections, whooping cough, legionnaires' disease and campylobacter enteritis.

Azithromycin is more active than erythromycin against some Gram-negative organisms such as *Chlamydia trachomatis*. The concentration and persistance of azithromycin is much higher in the tissue than in plasma; a single dose of azithromycin is used in the treatment of uncomplicated genital chlamydia and trachoma. Azithromycin is **not** recommended if there is a possibility of gonorrhoea because macrolide resistance emerges rapidly when it is used in this setting.

AZITHROMYCIN

Therapeutic category: Azalide antibiotic.

Indications: Uncomplicated genital chlamydial infections and trachoma.

Contra-indications: Hepatic impairment (Appendix 5).

Precautions: Renal impairment (Appendix 4); pregnancy (Appendix 2) and breastfeeding (Appendix 3); prolongation of QT interval (ventricular tachycardia reported); **interactions**: Appendix 1.

Adverse effects: See under Erythromycin (but fewer gastrointestinal effects); also anorexia, dyspepsia, constipation; dizziness, headache, drowsiness; photosensitivity; hepatitis, interstitial nephritis, acute renal failure, asthenia, paraesthesia, convulsions and mild neutropenia reported; rarely tinnitus, hepatic necrosis, hepatic failure, and taste disturbances.

Advice to patients: See labels 5, 9 and 23 for capsules, and 5 and 9 for tablets and oral suspension.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.

Dose: *Uncomplicated genital chlamydial infections or trachoma*, by mouth, ADULT over 45 kg 1 g as a single dose; under 45 kg 20 mg/kg as a single dose.

PATIENT ADVICE: NOT TO BE TAKEN AT THE SAME TIME AS ALUMINIUM- OR MAGNESIUM-CONTAINING INDIGESTION REMEDIES. CAPSULES SHOULD BE TAKEN AT LEAST 1 HOUR BEFORE OR 2 HOURS AFTER FOOD; ORAL SUSPENSION CAN BE TAKEN WITH FOOD.

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POM **Azithromycin** *(WMF 6.2.2.4)*
Capsules, Azithromycin (as dihydrate) 250 mg or 500 mg.
Oral suspension, Azithromycin (as dihydrate) 200 mg/5 ml.

POM **ZITHROMAX®** *(Pfizer)*
Capsule, Azithromycin (as dihydrate) 250 mg; white, hard gelatin cap. marked 'PFIZER' and Azithromycin '250 mg'.
250 mg - 4's; 6's; 24's.
Suspension, Azithromycin (as dihydrate) 200 mg per 5 ml; powder for oral suspension which yields on reconstitution with water a cherry/ banana flavoured suspension with a slight vanilla colour.
Pack - 15 ml.

CLARITHROMYCIN

Therapeutic category: Macrolide antibiotic.
Pharmacology: *Mechanism of Action*: Clarithromycin is a semi-synthetic derivative of erythromycin A. It exerts its antibacterial action by binding to the 50S ribosomal sub-unit of susceptible bacteria and suppresses protein synthesis. It is active against a wide variety of aerobic and anaerobic gram-positive and gram-negative organisms. The minimum inhibitory concentrations (MICs) of clarithromycin are generally two-fold lower than the MICs of erythromycin. The 14-hydroxy metabolite of clarithromycin also has antimicrobial activity.
Pharmacokinetics: Clarithromycin is well absorbed from the GIT. It undergoes substantial first pass metabolism and its systemic bioavailability is 55% after a 250 mg dose. Maximum clarithromycin plasma concentrations (C_{max}) range between were 0.62 to 0.84 mg/l and 1.77 to 1.89 mg/l following single dose administration of clarithromycin 250 and 500 mg respectively. The areas under the plasma concentration time curves (AUC) are about 4 and 11 mg/l/h for doses of 250 and 500 mg respectively. Clarithromycin undergoes rapid biotransformation to produce the microbiologically active 14 hydroxy (R) metabolite, which achieves peak plasma concentration of 0.4 and 0.8 mg/l within 3 hours of administering Clarithromycin 250 or 500 mg. Clarithromycin is widely distributed throughout the body, generally achieving higher concentrations in tissues and organs (including the lung and tonsils) than in blood. Clarithromycin is 42 to 70% bound to human plasma proteins. The primary metabolic pathways for clarithromycin are oxidative N-demethylation and hydroxylation. The principal metabolite of clarithromycin is the 14-hydroxy derivative, which mainly excreted with the parent drug via urinary mechanisms. The elimination half-life ($t_{1/2}$) for clarithromycin ranges from 2.6 to 4.4 hours. Mild to severe hepatic impairment does not significantly affect the pharmacokinetics of clarithromycin, although reduced metabolite formation may occur with severe liver impairment.
Indications: Upper respiratory tract infections - sinusitis and pharyngitis; Lower respiratory tract infections - pneumonia, acute and chronic bronchitis; Disseminated mycobacterial infections due to *Mycobacterium avium* or *Mycobacterium intracellulare*; Skin and skin structure infections.
Contra-indications: History of hypersensitivity to clarithromycin.
Precautions: Clarithromycin is principally excreted by the liver and kidney. Caution in patients with impaired hepatic and renal function. Prolonged or repeated use may result in overgrowth of non-susceptible bacteria or fungi. If super-infection occurs, discontinue and institute appropriate therapy. As with other macrolide antibiotics, the use of clarithromycin in patients concurrently taking drugs metabolised by the cytochrome P_{450} system may be associated with elevations in serum levels of these other drugs.
Warning: Monitor ECG if administered concurrently with terfenadine or astemizole. Previous history of hypersensitivity to other macrolides.
Pregnancy and Lactation: The safety of clarithromycin during pregnancy and breast feeding of infants has not been established. Clarithromycin should thus not be used during pregnancy or lactation unless the benefit outweighs the risk. Clarithromycin is secreted in the breast milk.
Paediatrics: No data for use in children below 6 months of age. Well tolerated in children above 6 months of age.
Geriatrics: No special precautions are required for the older patient provided renal and hepatic functions are not impaired.
Interactions: • Theophylline levels should be monitored in patients who are administered clarithromycin, as increased serum theophylline levels and potential theophylline toxicity may occur concomitant administration of the two drugs.
• The use of clarithromycin in patients receiving warfarin may result in a potentiation of the effects of warfarin. Prothrombin time should

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be frequently monitored in these patients. The effects of digoxin may be potentiated with concomitant administration of clarithromycin.

• Simultaneously oral administration of clarithromycin tablets and zidovudine to HIV-infected adult patients may result in decreased steady-state zidovudine concentrations.

• Macrolides have been reported to alter the metabolism of terfenadine resulting in increased levels of terfenadine. This may be associated with cardiac arrhythmias and therefore the concomitant use of terfenadine and any related non-sedating antihistamine such as astemizole with clarithromycin requires caution.

• Clarithromycin may potentiate the effects of carbamazepine due to a reduction in the rate of excretion. No effect on ethynyloestradiol or progesterone concentrations have been demonstrated and interaction with oral contraceptives is unlikely with clarithromycin.

Adverse effects: Clarithromycin is generally well tolerated. Side-effects include nausea, vomiting, diarrhoea, abdominal pain and stomatitis and headache. Rarely, allergic reactions ranging from urticaria and mild skin eruptions to anaphylaxis, Stevens-Johnson Syndrome and thrombocytopenia have occurred. Taste perversion may occur. There have been reports of transient central nervous system side-effects including anxiety, dizziness, insomnia, hallucinations and confusion, however, a cause and effect relationship has not been established.

Pseudomembranous colitis has been reported rarely with clarithromycin and may range in severity from mild to life threatening. Hepatic dysfunction, including altered liver function tests, cholestasis with or without jaundice and hepatic jaundice have been reported.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.

•Administer 12 hrly with a full glass of water; may give with food to reduce GI upset.

•Prolonged use may result in overgrowth of nonsusceptible organisms; monitor patient for symptoms such as fever, sore throat, fatigue.

Dose: *Adults and children over 12 years*: The usual dose is 250 mg twice daily for 7 days. In severe infections 500 mg twice daily for up to 14 days.

Children 6 months - 12 years: 7.5 mg per kg of body weight every 12 hours.

Note: *Renal Impairment*: Dosage adjustments are required in patients with severe renal impairment.

Creatinine clearance < 30 ml/min: 250 mg once daily for mild to moderately severe infections and 250 mg twice daily in more severe infections.

Overdosage and Treatment: Ingestion of large amounts of clarithromycin may produce allergic reactions and gastro-intestinal symptoms. Overdosage should be treated by gastric lavage and supportive measures.

POM **KLABAX**® *(Ranbaxy)*

Tablets, Clarithromycin USP 250 mg, 500 mg; f-c tablets.

250 mg - 25 x 4's

500 mg - 10 x 10's.

Suspension (125 mg), Clarithromycin 125 mg per 5 ml.

Pack - 100 ml.

Suspension (250 mg), Clarithromycin 250 mg per 5 ml.

Pack - 100 ml.

ERYTHROMYCIN

Erythromycin is a representative macrolide antibiotic. Various drugs can serve as alternatives.

Therapeutic category: Macrolide Antibiotic

Indications: Alternative to penicillin in hypersensitive patients; pneumonia; legionnaires' disease; syphilis; chancroid; chlamydia; non-gonococcal urethritis; prostatitis; lymphogranuloma venereum; campylobacter enteritis; relapsing fever; diphtheria and whooping cough prophylaxis.

Contra-indications: Hypersensitivity to erythromycin or other macrolides; porphyria.

Precautions: Hepatic impairment (Appendix 5) and renal impairment (Appendix 4); prolongation of the QT interval (ventricular tachycardia reported); pregnancy (not known to be harmful); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, abdominal discomfort, diarrhoea (and antibiotic-associated colitis); urticaria, rashes, and other allergic reactions (rarely, anaphylaxis); reversible hearing loss after large doses; cholestatic jaundice, cardiac effects (including chest pain and arrhythmias), myasthenia-like syndrome, erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis.

Advice to patients: See Label 5,9 and 25 (and only Label 9 for oral suspension) in Appendix 6. Take until gone, do not skip doses; report to physician if persistent diarrhoea occurs; drug absorption is unaffected by food.

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Nursing considerations: •Obtain specimen for C&S tests before first dose; therapy may begin pending test results.
•Administer around-the-clock in equal intervals to promote less variation in peak and trough serum levels.
•Do not crush enteric coated drug product; GI upset, including diarrhoea, is common; can give with food to decrease GI upset; give with a full glass of water, encourage adequate fluid intake if diarrhoea occurs; advise patient not to take fruit juice with medication.
•Give I.V. infusion over 60 minutes; it may be very irritating to the vein; if phlebitis/pain occur with used dilution, consider diluting further (e.g, 1:5), if fluid status of the patient will tolerate, or consider administering in larger available vein.
•Avoid IM inj or IV push.
•Monitor for symptoms of superinfection namely fever, sore throat, fatigue.
•Instruct patient to report complaints such as nausea, abdominal pain, and fever.

Dose: *Infections due to sensitive organisms*, by mouth, ADULT and CHILD over 8 years, 250–500 mg every 6 hours; up to 4 g daily in severe infections; CHILD up to 2 years, 125 mg every 6 hours, doubled in severe infections; CHILD 2–8 years, 250 mg every 6 hours, doubled in severe infections.
Early syphilis, by mouth , ADULT 500 mg 4 times daily for 14 days.
Uncomplicated genital chlamydia, non-gonococcal urethritis, by mouth, ADULT 500 mg 4 times daily for 7 days.
Severe infections, by intravenous infusion, ADULT and CHILD 50 mg/kg daily by continuous infusion or in divided doses every 6 hours.

PATIENT ADVICE: GASTRO-RESISTANT TABLETS AND CAPSULES SHOULD BE SWALLOWED WHOLE.

POM **Erythromycin** *(WMF 6.2.2.4)*
Tablets, Erythromycin (as stearate) 250 mg; erythromycin (as ethyl succinate) 500 mg.
Gastro-resistant tablets, Erythromycin 250 mg.
Gastro-resistant capsules, erythromycin 250 mg.
Oral suspension, Erythromycin (as stearate) 125 mg/5 ml; erythromycin (as ethyl succinate) 125 mg/5 ml.
Infusion (Powder for solution for infusion), erythromycin (as lactobionate) 500-mg vial.

POM **Erythromycin** *(EDL 6.8)*
Capsule or tablet, Erythromycin (as stearate or ethylsuccinate) 250 mg.
Suspension, Erythromycin (as stearate or ethylsuccinate) 125 mg per 5 ml.
Injection, Erythromycin (as lactobionate) 500 mg; powder in vial.

POM **APO-ERYTHRO-S®** *(Lahams)*
Tablets, Erythromycin stearate 250 mg, bright pink, f-c tab. marked 'APO 250'; 500 mg, white oral, f-c tab. marked 'APO 500'.
250 mg - 100
500 mg - 100.

POM **BARBIMYCIN®** *(Juhel)*
Suspension, Erythromycin (as ethylsuccinate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.

POM **ECIN®** *(Food & Pharma)*
Suspension, Erythromycin (as ethylsuccinate) 125 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.

POM **EROGRAN®** *(Hovid)*
Granules Erythromycin ethylsuccinate 200 mg.
Pack - 100 ml.

POM **EROTAB®** *(Hovid)*
Tablets, Erythromycin (as stearate) 250 mg, 500 mg; both f-c tabs.
250 mg - 10 x 10 (blister).
500 mg - 10 x 10 (blister).

POM **ERYCIN®** *(Ranbaxy)*
Suspension, Erythromycin (as ethylsuccinate) 125 mg per 5 ml.
Pack - 60 ml.

POM **ERYTHRO®** *(Fidson)*
Suspension, Erythromycin (as ethylsuccinate) 250 mg per 5 ml.
Pack - 100 ml.

POM **ERYTHRODAR®** *(Supreme)*
Tablets, Erythromycin 250 mg, 400 mg.
250 mg - 20.
400 mg - 16.

POM **ERYTHRO-TEVA®** *(Dizpharm)*
Tablets, Erythromycin (as stearate) 250 mg, 500 mg.
250 mg - 10.
500 mg - 10.
Suspension, Erythromycin (as ethylsuccinate) 125 mg, 200 mg, 400 mg per 5 ml.
Pack - 60 ml.

POM **ETOCIN®** *(Interpharma)*
Tablets, Erythromycin (as stearate) 500 mg.
500 mg - 10 x 10's.

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Syrup, Erythromycin (as ethylsuccinate) 200 mg per 5 ml; dry powder for syrup.
Pack - 100 ml.

POM **KEZZ ERYTHROMYCIN**® *(Kezz)*
Tablets, Erythromycin (as stearate) BP 500 mg; f-c tab.
500 mg - 10's (in blister).

POM **RYCIN**® *(Medreich)*
Tablets, Erythromycin (as stearate) 250 mg, 500 mg; white f-c tabs marked 'RYCIN'.

POM **MOKO ERYTHROMYCIN**® *(New Healthway)*
Suspension, Erythromycin 125 mg per 5 ml; dry powder for oral suspension.
Pack - 100 ml.

ROXITHROMYCIN

Therapeutic category: Macrolide antibiotic.
Pharmacology: Roxithromycin is a semi-synthetic macrolide. It is effective against various species of Streptococcus, Pneumococcus, Meningococcus, *Bordetella pertussis, Corynebacterium diphtheriae, Clostridium, Mycoplasma pneumonia, Chlamydia trachomatis, Haemophillus infuenzae, Vibrio cholerae, Staphylococcus aureus*, etc. It is stable in acid medium and appears in the serum 15 minutes after oral administration. The mean elimination half-life is 10.5 hours. Two tablets (300 mg) taken at 12 hour interval ensures effective plasma concentration against sensitive organisms over a 24 hour period.
Roxithromycin is only partially metabolised with more than half the active compound being excreted unchanged in faeces.
Indications: Upper and lower respiratory tract infections (including ENT infections); genital infections and sexually transmitted diseases (excluding gonococcal infections); soft tissue and structures infections; prophylaxis of meningococcal meningitis in contact subjects.
Contra-indications: Hypersensitivity to macrolides; combination with ergotamine and dihydroergotamine.
Precautions: Hepatic insufficiency (monitor hepatic function and adjust dose accordingly); hepatic impairment (no need to adjust dose as the renal excretion of the drug is low); elderly (no need to adjust dose as the drug is not accumulated); pregnancy (not recommended).
Adverse effects: Nausea, vomiting, gastric pain, diarrhoea, allergic skin rash.
Dose: By mouth, Adult, 150 mg twice daily (morning and evening).
In severe renal failure, 150 mg once daily.
To be taken before meals.

POM **RULID**® *(May & Baker)*
Tablet, Roxithromycin 150 mg; f-c tab.
150 mg - 10; 100.

SPIRAMYCIN

Therapeutic category: Macrolide antibiotic
Pharmacology: Spiramycin is a first generation macrolide antibiotic produced by *Streptomyces ambofaciens* and contains a 16-membered lactone ring. Erythromycin and roxithromycin are 14-membered-ring macrolides whereas azithromycin, an azalide, is the only 15-membered-ring macrolide in clinical use. Spiramycin exhibits and antibacterial spectrum characteristic of the macrolide family, which includes Gram-negative and Gram-positive cocci, Parvobacteriaceae, *Legionella spp., Chlamydia spp., Mycoplasma Pneumoniae*. It is inactive against Gram-negative rods (Enterobacteriaceae) Macrolides bind to the large subunit of prokaryotic ribosomes and disturb protein synthesis. Spiramycin appears to offer advantages over most other macrolides in terms of its good tolerability and lack of pharmacokinetic interactions with other drugs, as well as its relatively long half-life, which allows twice-daily administration.
Indications: Treatment of infections due to susceptible organisms including ENT, bronchopulmonary and skin infections. In certain cases, prevention of meningococcal meningitis.
Contra-indications: Known allergy to macrolides; avoid co-administration with rye ergot derivatives.
Precautions: Nausea, vomiting, diarrhoea, allergic reactions.
Dose: Adult, by mouth, one tab. 2-3 times daily.

POM **ROVAMYCIN**® *(May & Baker)*
Tablet, Spiramycin 3 M.I.U.; coated tab.
3 M.I.U - 10.

9.1.2.5 Aminoglycosides

Aminoglycosides including **gentamicin** are bactericidal and active against some Gram-positive and many Gram-negative organisms including *Pseudomonas aeruginosa*. Aminoglycosides are not

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absorbed from the gut and must therefore be given by injection for systemic infections. Excretion is mainly by the kidney and accumulation occurs in renal impairment.

Use of gentamicin should be restricted to trained health personnel and care must be taken to ensure correct dosage and duration of treatment are not exceeded, because most adverse effects are dose related. The most important adverse effects are ototoxicity and nephrotoxicity and they are most common in the elderly and in patients with renal impairment. These groups and, if possible, all patients should be monitored for ototoxicity by audiometry. If there is impairment of renal function the dose interval must be increased; in severe renal impairment, the dose should also be reduced. Serum concentration monitoring avoids both excessive and subtherapeutic concentrations and can prevent toxicity and ensure efficacy. If possible serum concentrations should be monitored in all patients, but **must** be measured in infants, the elderly, in obesity, in cystic fibrosis, in high-dosage regimens, in renal impairment, or if treatment lasts for longer than 7 days.

For most infections, doses of up to 5 mg/kg daily in divided doses are used if renal function is normal; higher doses are used occasionally for serious infections. Loading and maintenance doses are based on the patient's weight and renal function (for example, using a nomogram) with adjustments based on plasma gentamicin concentration.

GENTAMICIN

Gentamicin is a representative aminoglycoside antibiotic. Various drugs can serve as alternatives.

Therapeutic category: Aminoglycoside antibiotic

Indications: Pneumonia; cholecystitis; peritonitis; septicaemia; acute pyelonephritis; prostatitis; skin infections; pelvic inflammatory disease; endocarditis; meningitis; listeriosis; tularaemia; brucellosis; plague; surgical prophylaxis; eye (section 13.1).

Contra-indications: Myasthenia gravis.

Precautions: Renal impairment (Appendix 4), infants and elderly (dosage adjustment and monitor renal, auditory, and vestibular function, and serum-gentamicin concentrations); avoid prolonged use; conditions characterized by muscular weakness; significant obesity (monitor serum-gentamicin concentration closely and possibly reduce dose); see notes above; pregnancy (Appendix 2); **interactions**: Appendix 1.

Adverse effects: Vestibular and auditory damage, nephrotoxicity; rarely, hypomagnesaemia on prolonged therapy; antibiotic-associated colitis; also, nausea, vomiting, rash.

Advice to patients: Report any dizziness or sensations of ringing or fullness in ears.

Nursing considerations: •Obtain specimens for C&S tests prior to the first dose.

•Administer I.M. injection in large muscle area at uniform intervals to maintain blood level; rotate inj sites.

•Give IV after diluting in NS or D_5W as ordered; observe I.V. infusion site for inflammation; discontinue and apply warm compress to an inflamed site.

•Give other antibiotic drugs at least 1 hour before or after gentamicin.

•Increase fluid intake (to minimize irritation of the renal tubules) unless contraindicated.

•Provide supervised ambulation, other safety measures for patients with nausea, vomiting, dizziness, headache (vestibular dysfunction).

•Monitor renal function namely output, specific gravity, urinarysis, BUN and creatinine levels; report any signs of decreasing renal function to the physician.

•Observe for superinfection, i.e., prolonged fever and other signs of infection especially of the upper respiratory tract.

•Hearing should be tested before, during, and after treatment in patient at risk for ototoxicity; notify doctor if patient complains of tinnitus, vertigo or hearing loss.

•Bicarbonate may be ordered together with gentamicin when treating UTI to alkalinize urine; alkaline medium enhances effect of gentamicin.

Dose: *Infections due to susceptible organisms*, by intramuscular injection or by slow intravenous injection (over at least 3 minutes) or by intravenous infusion, ADULT 3–5 mg/kg daily in divided doses every 8 hours; CHILD up to 2 weeks, 3 mg/kg every 12 hours; 2 weeks–12 years, 2 mg/kg every 8 hours.

Streptococcal and enterococcal endocarditis (as part of combination therapy), by intravenous injection (over at least 3 minutes), ADULT 80 mg twice daily.

Surgical prophylaxis, by intravenous injection , ADULT 5 mg/kg as a single

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dose at induction (with clindamycin).
NOTE: ONE HOUR (PEAK) CONCENTRATIONS SHOULD NOT EXCEED 5–10 MG/LITRE; PRE-DOSE (TROUGH) CONCENTRATION SHOULD BE LESS THAN 2 MG/LITRE.
DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Gentamicin** *(WMF 6.2.2.5)*
Injection (Solution for injection), Gentamicin (as sulfate) 10 mg/ml, 2-ml vial; 40 mg/ml, 2-ml vial.

POM **Gentamicin** *(EDL 6.8)*
Injections, Gentamicin Sulfate 10 mg, 40 mg per ml; in 2 ml vials.

POM **CIDOMYCIN**® *(NGC)*
Injection, Gentamicin (as sulfate) 40 mg per ml; in 2 ml amps.
Injection (Paediatric), Gentamicin (as sulfate) 10 mg per ml; in 2 ml vial.

POM **GENTA**® *(Strides Vital)*
Injections, Gentamicin 80 mg, 280 mg per 2 ml; in ampoules.
Pack – 100's.

POM **GENTALEK**® *(Taylek)*
Injection, Gentamicin sulfate 40 mg per ml; in 2 ml amp.
Pack - 10; 50.

POM **Gentamicin** *(Doyin)*
Injection, Gentamicin 40 mg per ml; in 2 ml amp.
80 mg - 1; 100.
Dose: By I.M. injection or slow I.V. injection (over 3 mins) or I.V. infusion, Adult (above 60 kg), *systemic infections*, 80 mg every 8 hours for 7-10 days; less than 60 kg, 60 mg every 8 hours.
Urinary tract infections, as above. Alternatively, if renal function is not impaired, 160 mg/day.
Serious infections (normal kidney function), 5 mg/kg /day in equally divided doses at 6-8 hourly intervals.
Child (up to 2 weeks), 3 mg/kg every 12 hours; 2 weeks - 12 years, 2 mg/kg every 8 hours.
Note: Gentamicin sulphate, when given intravenously should be injected directly into a vein or into the drip set tubing over no less than 3 minutes. If administered by infusion, the solution may be infused over a period of ½-2 hours; and it may be diluted in 50 to 200 ml of fluid.

POM **GENTAZET**® *(Geneith)*
Injection (80 mg), Gentamicin sulfate 80 mg per 2 ml; in 2 ml ampoule.
Injection (280 mg), Gentamicin sulfate 280 mg per 2 ml; in 2 ml ampoule.

POM **GENTOCINIKA**® *(Dizpharm)*
Injection, Gentamicin (as sulfate) 80 mg per 2 ml.
Pack - 25; 100.

POM **KALMYCIN**® *(Justeen)*
Injection, Gentamicin (as sulfate) 80 mg per 2 ml.
Pack – 2 ml x 1's (in flint vials).

POM **PADEX**® *(Justeen)*
Injection, Gentamicin (as sulfate) 80 mg per 2 ml.
Pack – 1 x 100's.

POM **TAMAN**® *(Beta Drugs)*
Injection, Gentamicin BP 40 mg (40,000 units) per ml; in 2-ml glass ampoule.
Pack – 10's x 1-ml; 5's x 2-ml; 10's x 2-ml; 50's x 2-ml; 100's x 2-ml.
Injection, Gentamicin BP 280 mg per 2 ml; in 2-ml glass ampoule.

NEOMYCIN

Therapeutic category: Aminoglycoside antibiotic.
Indications: Bowel sterilisation prior to abdominal surgery; intestinal infections.
Contra-indications, Precautions, etc: See under Gentamicin.
Nursing considerations: •Avoid use in intestinal obstruction
•*See also under Gentamicin.*
Dose: By mouth, *bowel sterilisation*, 1 g 4 hourly for 6 doses or more but not exceeding 3 days. *Intestinal infections*, 50-80 mg per kg body-wt. daily in 3-4 divided doses.
See lit. for details.

POM **Neomycin** *(EDL 6.8)*
Tablet, Neomycin 500 mg.
Suspension, Neomycin 100 mg per 5 ml.

STREPTOMYCIN

Therapeutic category: Antibiotic.
Indications: Treatment of tuberculosis in combination with other drugs; other infections where patients are allergic to or have failed to respond to penicillin.
Contra-indications: Myasthenia gravis.

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Precautions: Pregnancy, renal impairment, elderly.

Interactions: Ototoxic diuretics such as frusemide. See under Gentamicin.

Adverse effects: Vestibular and auditory damage; nephrotoxicity, neuromuscular blockade, rash, nausea, vomiting, fever, headache, drowsiness.

Advice to patients: Report any unusual symptoms of hearing loss, dizziness, roaring noises, or fullness in ears.

Nursing considerations: •Obtain specimens for C&S tests prior to the first dose.

•Administer IM injection in large muscle area at uniform intervals to maintain blood level; rotate inj sites.

•IV inj is not recommended.

• *See also under Gentamicin.*

Dose: By deep I.M. injection, Adult, 15 mg/kg (max. 1 g) daily.

Note: Do not exceed cummulative dose of 100 mg due to increased incidence of adverse effects. Reduce dose in patients under 50 kg, over 40 years of age in enal impairment.

POM **Streptomycin** *(EDL 6.10)*
Injection, Streptomycin Sulphate 1 g, 5 g; powder in vials.

POM **MATOSTREP®** *(GoldMoore)*
Injections, Streptomycin (as sulfate) 1 g (1 million units), 5 g (5 million units).
Pack - 1 g; 5 g.

POM **O-STREPS®** *(Beta Drugs)*
Injections, Streptomycin (as Sulphate) 1 g (1 million units), 5 g (5 million units) per vial; white or almost white powder, freely soluble in water.

POM **Streptomycin** *(Doyin)*
Injection, Streptomycin 5 g
5 g - 100

9.1.2.6 Metronidazole

Metronidazole has high activity against anaerobic bacteria and protozoa (see also section 9.3.2). Metronidazole by the rectal route is an effective alternative to the intravenous route when oral administration is not possible.

METRONIDAZOLE

Metronidazole is a representative antibacterial and antiprotozoal drug. Various drugs can serve as alternatives.

Indications: Anaerobic bacterial infections, including gingivitis, pelvic inflammatory disease, tetanus, peritonitis, brain abscess, necrotizing pneumonia, antibiotic-associated colitis, leg ulcers and pressure sores and surgical prophylaxis; bacterial vaginosis; tissue nematode infections (section 9.4.1.3); trichomonal vaginitis, amoebiasis, and giardiasis (section 9.3.2); Helicobacter pylori eradication (section 4.1).

Contra-indications: Chronic alcohol dependence.

Precautions: Disulfiram-like reaction with alcohol; hepatic impairment and hepatic encephalopathy (Appendix 5); pregnancy (Appendix 2); breastfeeding (Appendix 3); clinical and laboratory monitoring in courses lasting longer than 10 days; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, unpleasant metallic taste, furred tongue and gastrointestinal disturbances; rarely, headache, drowsiness, dizziness, ataxia, darkening of urine, erythema multiforme, pruritus, urticaria, angioedema, and anaphylaxis; abnormal liver function tests, hepatitis, jaundice, thrombocytopenia, aplastic anaemia, myalgia, arthralgia; peripheral neuropathy, epileptiform seizures, leukopenia, on prolonged or high dosage regimens.

Dose: *Anaerobic infections* (usually treated for 7 days), by mouth, ADULT 800 mg initially then 400 mg every 8 hours or 500 mg every 8 hours; CHILD 7.5 mg/kg every 8 hours.
Anaerobic infections, by intravenous infusion over 20 minutes, ADULT 500 mg every 8 hours; CHILD 7.5 mg/kg every 8 hours.
Anaerobic infections, by rectum, adult and child over 10 years 1 g every 8 hours for 3 days, then 1 g every 12 hours; child up to 1 year, 125 mg every 8 hours for 3 days, then every 12 hours; 1–5 years 250 mg; 5–10 years 500 mg.
Bacterial vaginosis, by mouth, ADULT 2 g as a single dose or 400–500 mg twice daily for 5–7 days.
Pelvic inflammatory disease, by mouth, adult 400 mg twice daily for 14 days.
Leg ulcers and pressure sores, by mouth, ADULT 400 mg every 8 hours for 7 days
Acute ulcerative gingivitis, by mouth, 200–250 mg every 8 hours for 3 days;

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CHILD 1–3 years, 50 mg every 8 hours for 3 days; 3–7 years, 100 mg every 12 hours for 3 days; 7–10 years, 100 mg every 8 hours for 3 days.

Acute dental infections, by mouth, ADULT 200 mg every 8 hours for 3–7 days.

Antibiotic-associated colitis, by mouth, 800 mg initially then 400 mg 3 times daily for 10 days.

Surgical prophylaxis, by mouth, ADULT 400–500 mg 2 hours before surgery; up to 3 further doses of 400–500 mg may be given every 8 hours for high-risk procedures; child 7.5 mg/kg 2 hours before surgery; up to 3 further doses of 7.5 mg/kg may be given every 8 hours for high-risk procedures.

Surgical prophylaxis, by rectum, ADULT 1 g 2 hours before surgery; up to 3 further doses of 1 g may be given every 8 hours for high-risk procedures; CHILD 5–10 years 500 mg 2 hours before surgery; up to 3 further doses of 500 mg may be given every 8 hours for high-risk procedures.

Surgical prophylaxis by intravenous infusion (if rectal administration inappropriate), ADULT 500 mg at induction; up to 3 further doses of 500 mg may be given every 8 hours for high-risk procedures; CHILD 7.5 mg/kg at induction; up to 3 further doses of 7.5 mg/kg may be given every 8 hours for high-risk procedures.

PATIENT ADVICE: METRONIDAZOLE TABLETS SHOULD BE SWALLOWED WHOLE WITH WATER, DURING OR AFTER A MEAL; METRONIDAZOLE SUSPENSION SHOULD BE TAKEN ONE HOUR BEFORE A MEAL.

POM **Metronidazole** *(WMF 6.2.2.6)*
Tablets, Metronidazole 200 mg, 250 mg, 400 mg, and 500 mg.
Oral suspension, Metronidazole (as benzoate) 200 mg/5 ml.
Intravenous infusion (Solution for infusion), metronidazole 5 mg/ml, 100-ml bag.
Suppositories, Metronidazole 0.5 g, 1 g.

POM **Metronidazole** *(EDL 6.1)*
Tablet, Metronidazole 200 mg.
Oral suspension, Metronidazole (as benzoate) 200 mg per 5 ml.

See section 9.3.2 for the proprietary preparations of Metronidazole.

9.1.2.7 Nitrofurantoin

Nitrofurantoin is bactericidal *in vitro* to most Gram-positive and Gram-negative urinary-tract pathogens and it is used to treat acute and recurrent urinary-tract infections. It is also used prophylactically in chronic urinary-tract infections.

NITROFURANTOIN

Indications: Urinary-tract infections.

Contra-indications: Impaired renal function (Appendix 4); infants less than 3 months; G6PD-deficiency including breastfeeding of affected infants (Appendix 3); pregnancy, at term (Appendix 2); porphyria.

Precautions: Pulmonary disorders or hepatic impairment (Appendix 5); monitor lung and liver function on long-term therapy (discontinue if lung function deteriorates); neurological or allergic disorders; anaemia; diabetes mellitus; elderly and debilitated; vitamin B and folate deficiency; false positive urinary glucose (if testing for reducing substances); urine may be coloured yellow or brown.

Adverse effects: Dose-related gastrointestinal disorders; nausea; hypersensitivity reactions including urticaria, rash, sialadenitis, pruritus, angioedema; anaphylaxis reported; rarely, cholestatic jaundice, hepatitis, exfoliative dermatitis; erythema multiforme, pancreatitis, arthralgia; blood disorders; pulmonary reactions (pulmonary fibrosis; possible association with lupus erythematosus-like syndrome); peripheral neuropathy; benign intracranial hypertension; transient alopecia.

Advice to patients: See Label 9, 14 and 21 in Appendix 6. Take with food or milk; may discolour urine to a dark yellow or brown colour; notify physician if fever, chest pain, persistent, nonproductive cough, or difficulty in breathing occurs.

Nursing considerations: •Administer around-the-clock in equal intervals to promote less variation in peak and trough serum levels.
•Give with meals or milk to reduce GI upset.
•Continue treatment for 3 days after sterile urine specimen have been obtained.
•Observe closely for superinfection.

Dose: *Acute uncomplicated urinary-tract infections*, by mouth, ADULT 100 mg every 12 hours or 50 mg every 6 hours with food for 7 days; CHILD

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over 3 months, 3 mg/kg daily in 4 divided doses.
Severe recurrent urinary-tract infection, by mouth, ADULT 100 mg every 6 hours with food for 7 days (dose reduced to 200 mg daily in divided doses, if severe nausea).
Prophylaxis of urinary-tract infections (see Precautions), by mouth, ADULT 50–100 mg at night; CHILD over 3 months, 1 mg/kg at night.

POM **Nitrofurantoin** *(WMF 6.2.27)*
Tablets, Nitrofurantoin 50 mg [not included on WHO Model List], 100 mg.
Oral suspension, Nitrofurantoin 25 mg/5 ml [not included on WHO Model List].

POM **Nitrofurantoin** *(EDL 6.8)*
Tablets, Nitrofurantoin 50 mg, 100 mg.

9.1.2.8 Spectinomycin

Spectinomycin is active against Gram-negative organisms including *Neiserria gonorrhoea*. It is not suitable for the treatment of syphilis and patients being treated for gonorrhoea should be observed for evidence of syphilis. It should be used only when alternative therapies are inappropriate.

SPECTINOMYCIN

Indications: Uncomplicated and disseminated gonorrhoea (see notes above); adult and neonatal gonococcal conjunctivitis; chancroid.
Precautions: Renal impairment; pregnancy and breastfeeding.
Adverse effects: Nausea, dizziness, fever, urticaria; rarely, anaphylaxis; pain at injection site.
Nursing considerations: •Since Spectinomycin is ineffective in the treatment of syphilis and may mask symptoms, all patients should be tested for syphilis at the time of diagnosis and 3 months later.
•For I.M. use only; use 20G needle for the administration. The 4-g dose (10 ml) should be divided into two 5-ml injections and given one in each buttocks.
•Reconstituted solution should be used within 24 hours at room temperature; shake vial vigorously before use.
Dose: *Uncomplicated gonococcal infections and chancroid*, by deep intramuscular injection, ADULT 2 g as a single dose (may be increased to 4 g as a single dose divided between 2 injection sites in difficult to treat cases and where there is known antibiotic resistance).
Disseminated gonococcal infections, by deep intramuscular injection, ADULT 2 g twice daily for 7 days.
Neonatal gonococcal conjunctivitis, by deep intramuscular injection, neonate 25 mg/kg (maximum 75 mg) as a single dose.
RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Spectinomycin** *(WMF 6.2.2.8)*
Injection (Powder for solution for injection), Spectinomycin (as HCl), 2-g vial.

POM **Spectinomycin** *(EDL 6.8)*
Injection, Spectinomycin (as HCl) 2 g; powder in vial.

9.1.2.9 Sulfonamides and trimethoprim

The usefulness of sulfonamides is limited by an increasing incidence of bacterial resistance. For many indications they have been replaced by antibiotics that are more active and safer. **Sulfadiazine** is used in the prevention of rheumatic fever recurrence. **Sulfamethoxazole** is used in combination with **trimethoprim** because of their synergistic activity. In some countries, indications for the use of this combination have been restricted. The treatment of *Pneumocystis carinii* infections must only be undertaken with specialist supervision where there are appropriate monitoring facilities (section 9.3.5). Trimethoprim is also used alone for respiratory-tract infections and, in particular, for urinary-tract infections.

CO-TRIMOXAZOLE

Synonym: Sulfamethoxazole plus Trimethoprim; SMZ-TMP.
Therapeutic category: Sulfonamide antibacterial
Pharmacology: Co-trimoxazole is a chemotherapeutic agent exhibiting bactericidal activity against numerous Gram-positive and Gram-negative bacteria. The combination of sulfamethoxazole and trimethoprim (in 5:1 ratio) acts on two levels in the biosynthesis of tetrahydrofolic acid: sulfamethoxazole inhibits the incorporation of PABA into folic acid, whereas trimethoprim blocks the reduction of dihydrofolic acid to tetrahydrofolic acid. This combination may prevent emergence of

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bacterial resistance better than when either agent is used alone. The combination is synergistic against many gram-negative organisms.

Indications: Urinary-tract infections; respiratory-tract infections including bronchitis, pneumonia, infections in cystic fibrosis; melioidosis; listeriosis; brucellosis; granuloma inguinale; otitis media; skin infections; Pneumocystis carinii pneumonia (section 9.3.5).

Contra-indications: Hypersensitivity to sulfonamides or trimethoprim; porphyria.

Precautions: Renal impairment (avoid if severe; Appendix 4); hepatic impairment (avoid if severe; Appendix 5); maintain adequate fluid intake (to avoid crystalluria); avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rash—discontinue immediately; predisposition to folate deficiency, elderly; asthma; G6PD deficiency; pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid in infants under 6 weeks; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, diarrhoea, headache; hypersensitivity reactions including rashes, pruritus, photosensitivity reactions, exfoliative dermatitis, and erythema nodosum; rarely, erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis; systemic lupus erythematosus, myocarditis, serum sickness; crystalluria—resulting in haematuria, oliguria, anuria; blood disorders including granulocytopenia, agranulocytosis, aplastic anaemia, purpura—discontinue immediately; also reported, liver damage, pancreatitis, antibiotic-associated colitis, eosinophilia, cough and shortness of breath, pulmonary infiltrates, aseptic meningitis, depression, convulsions, ataxia, tinnitus, vertigo, dizziness, hallucinations, and electrolyte disturbances; megaloblastic anaemia due to trimethoprim.

Advice to patients: See label 9 in Appendix 6. Take oral medication with a full glass of water on an empty stomach (1 hour before or 2 hours after meals) for best absorpton; report any skin rashes immediately; finish all medication, do not skip doses; avoid aspirin and vitamin C products.

Nursing considerations: •Obtain specimen for C&S tests before first dose; therapy may begin pending test results.

•Give on an empty stomach 1 hr before or 2 hr after meals with a full glass of water to maintain adequate hydration. Encourage patient to increase fluid intake to avoid crystallization in kidneys.

•Observe for signs of superinfection namely fever, sore throat, fatigue.

•Signs of blood dyscrasias include skin rash, sore throat, fever, or mouth sore and should be reported immediately to the physician

•Note that the "DS" or "DF" product means "double strength".

•Monitor patient for allergic reactions.

Dose: *Severe infections due to susceptible organisms (not susceptible to other antibacterials)*, by mouth or by intravenous infusion, ADULT sulfamethoxazole 800 mg with trimethoprim 160 mg every 12 hours, increased to sulfamethoxazole 1.2 g with trimethoprim 240 mg, every 12 hours in more severe infections; by mouth, CHILD 6 weeks–5 months, sulfamethoxazole 100 mg with trimethoprim 20 mg every 12 hours; 6 months–5 years, sulfamethoxazole 200 mg with trimethoprim 40 mg every 12 hours; 6–12 years, sulfamethoxazole 400 mg with trimethoprim 80 mg every 12 hours; by intravenous infusion, CHILD sulfamethoxazole 30 mg/kg daily with trimethoprim 6 mg/kg daily in 2 divided doses.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Sulfamethoxazole plus Trimethoprim** *(WMF 6.2.2.9)*

Tablets, Sulfamethoxazole 100 mg with trimethoprim 20 mg; Sulfamethoxazole 400 mg with trimethoprim 80 mg.

Oral suspension, Sulfamethoxazole 200 mg with trimethoprim 40 mg/5 ml.

Injection (Solution for dilution for infusion), Sulfamethoxazole 80 mg with trimethoprim 16 mg/ml, 5-ml and 10-ml ampoules.

POM **Co-trimoxazole** *(EDL 6.8)*

Tablets, Co-trimoxazole 120 mg, 480 mg.

Suspension, Co-trimoxazole 240 mg per 5 ml.

POM **BACTRIM®** *(Swipha)*

Tablet, Co-trimoxazole 480 mg; white scored tab.

480 mg - 20.

Tablet (Forte) Co-trimoxazole 960 mg.

960 mg - 10; 100.

Suspension, Co-trimoxazole 240 mg per 5 ml; milky white with banana flavour/aroma.

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Pack - 50 ml.

POM **BIOTRIM®** *(Farmex)*
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 50 ml.

POM **CADIPRIM®** *(Interpharma)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 10 x 10's.
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 50 ml; 100 ml.

POM **CHEMOTRIM®** *(Afrab-Chem)*
Tablet, Co-trimoxazole 480 mg; average size (13 mm), golden yellow scored tab. marked 'afrab'.
Pack - 1000.
Suspension, Co-trimoxazole 240 mg per 5 ml; cream, moderately thick.
Pack - 60 ml; 100 ml.

POM **Co-Trimoxazole** *(Doyin)*
Tablet, Co-trimoxazole 480 mg; white tab.
480 mg - 100
Suspension, Co-trimoxazole 240 mg per 5 ml
Pack - 50 ml.

POM **Co-Trimoxazole** *(Neimeth)*
Tablet, Co-trimoxazole 480 mg
480 mg - 500.
Suspension, Co-trimoxazole 240 mg per 5 ml
Pack - 50 ml.

POM **Co-Trimoxazole** *(Novel)*
Tablet, Co-trimoxazole 480 mg; white tab. marked 'Cotrim/480' on one side and 'NOVEL' on the reverse.
480 mg - 1000.

POM **Co-Trimoxazole** *(Ulticare-Lyka)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 10 x 100; 1000.
Suspension, Co-trimoxazole 240 mg per 5 ml
Pack - 50 ml.

POM **Co-Trimoxazole** *(Vitabiotics)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 1000's.

POM **COTRIZOL®** *(Ranbaxy)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 500; 1000
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 50 ml; 100 ml.

POM **EMTRIM®** *(Emzor)*
Tablet, Co-trimoxazole 480 mg; white scored biconvex tab. marked 'EMZOR'.
480 mg - 100; 1000.
Suspension, Co-trimoxazole 240 mg per 5 ml; pink raspberry flavoured suspension
Pack - 50 ml.

POM **EVATRIM®** *(David)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 1000.
Syrup, Co-troxazole 240 mg per 5 ml.
Pack - 50 ml.

POM **FAPTRIMOX®** *(Food & Pharma)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 1000
Tablet (forte), Co-trimoxazole 960 mg.
960 mg - 1000
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 50 ml; 100 ml.

POM **JAWATRIM®** *(Jawa)*
Syrup,Co-trimoxazole 240 mg per 5 ml.
Pack - 60 ml.

POM **JUTRIM®** *(Juhel)*
Tablets, Co-trimoxazole BP 480 mg; white scored biconvex tablet marked 'Jutrim 480' on one side and 'Juhel' on the reverse.
480 mg – 10 x 100's; 1000's.
Paediatric suspension, Co-trimoxazole 240 mg per 5 ml.
Pack – 50 ml; 100 ml.

POM **MEPTRAN-480®** *(Chris-Ejik)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 10; 1000.

POM **MIRASEPT®** *(Mirapharm)*
Tablet, Co-trimoxazole 480 mg.

POM **PARKAPRIM®** *(Pharma–Deko)*
Tablet, Co-trimoxazole 480 mg; white uncoated plain tab. marked 'PARKAPRIM'.
480 mg - 20; 1000.
Suspension, Co–trimoxazole 240 mg per 5 ml; pink coloured well flavoured suspension.
Pack - 50 ml; 2 L.

POM **PRIMPEX®** *(SKG)*
Tablet, Co-trimoxazole 480 mg; white scored tab. marked 'SKG D3A'.
Suspension, Co-trimoxazole 240 mg per 5 ml; syrup flavoured suspension.

POM **R-COTRIM®** *(Strides Vital)*
Tablet, Co-trimoxazole 480 mg.
480 mg – 100's; 1000's.
Tablet (DS), Co-trimoxazole 960 mg.
960 mg – 100's; 1000's.

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POM **RANCOTRIM®** *(Ranbaxy)*
Tablet, Co-trimoxazole 480 mg.
480 mg - 10's; 1000's.
Tablet (forte), Co-trimoxazole 960 mg.
960 mg - 10's; 500's.
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 50 ml; 1000 ml; 2500 ml.

POM **SAMTRIM®** *(Dana)*
Tablet, Co-trimoxazole 480 mg
480 mg - 1000.

POM **SEPOX®** *(Sam)*
Tablet, Co-trimoxazole 480 mg
480 mg - 10 x 10's.

POM **SEPTRIN®** *(GSK)*
Tablet, Co-trimoxazole 480 mg; white tab. coded 'Y2B' and marked with tab. and maker's names.
Susension, Co-trimoxazole 240 mg per 5 ml

POM **SUPRIM®** (*Hovid*)
Tablets, Co-trimoxazole 480 mg, 960 mg.
480 mg - 10 x 10 (blister)
960 mg - 10 x 10 (blister).
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 60 ml; 100 ml.

POM **SYNOSULF®** (*KRSNA*)
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 50 ml.

POM **TAVTRIM®** *(Justeen)*
Tablet, Co-trimoxazole BP 480 mg.
Pack - 10 x 10's.

POM **TECOTRIM®** *(GoldMoore)*
Tablet (480 mg) Sulfamethoxazole BP 400 mg, trimethoprim BP 80 mg.
Pack - 1 x 10's; 2 x 10's; 100 x 10's.
Tablet (960 mg) Sulfamethoxazole BP 800 mg, trimethoprim BP 160 mg.
Pack - 1 x 10's; 2 x 10's; 100 x 10's.

POM **TEVASEPT®** *(Dizpharm)*
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 100 ml.

POM **TIESUL®** (*Panvij Biotec*)
Tablet, Co-trimoxazole 480 mg; off-white, scored tab. marked 'TIESUL' and '480' on one side and plain on the reverse.
480 mg - 10 x 10.

POM **TPRIM-480®** *(Justeen)*
Tablet, Co-trimoxazole BP 480 mg.
Pack - 10 x 10's; 1000's.

POM **ZOTRIM®** *(Fidson)*
Tablet, Co-trimoxazole 480 mg.
Suspension, Co-trimoxazole 240 mg per 5 ml.
Pack - 50 ml.

PHTHALYLSULFATHIAZOLE

Therapeutic category: Antibacterial
Pharmacology: A sulfonamide which is sparingly absorbed after oral administration; its bacteriostatic activity in the bowel is 2-4 times as great as that of succinylsulfathiazole.
Indications: Treatment of acute phase of shigellosis (bacillary dysentery).
Contra-indications: Acute intermittent porphyria, sensitivity to other sulfonamides.
Advice to patients: See labels 9 and 27 in Appendix 6.
Dose: Adult, 1.5 g 3-4 times daily.

POM **Phthalylsulfathiazole** *(EDL 6.8)*
Tablet, Phthalylsulfathiazole 500 mg.

POM **DIASTOP-HS®** *(Afrab-Chem)*
Tablet, Phthalysulfathiazole 500 mg; cream yellowish scored tab. marked 'afrab'.

POM **Phthalysulfathiazole** *(Emzor)*
Tablets, Phthalylsulfathiazole 500 mg.
500 mg - 1000.

POM **Phthalylsulfathiazole** *(Vitabiotics)*
Tablet, Phthalylsulfathiazole 500 mg.
500 mg - 500.

POM **SULPHAZOLE®** *(Sam)*
Tablet, Phthalylsulfathiazole 500 mg
500 mg - 1000's

POM **THALAL®** *(Strides Vital)*
Tablet, Phthalylsulfathiazole 500 mg.
500 mg – 100's.

POM **THALAZOLE®** *(May & Baker)*
Tablet, Phthalylsulfathiazole 500 mg; white scored tab. marked 'THALAZOLE'.
500 mg - 20; 500.

SULFADIAZINE

Sulfadiazine is a complementary antibacterial drug.
Indications: Prevention of recurrences of rheumatic fever; toxoplasmosis (section 9.3.5).
Contra-indications: Hypersensitivity to sulfonamides; porphyria.

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Precautions: Hepatic impairment (avoid if severe; Appendix 5); renal impairment (avoid if severe; Appendix 4); maintain adequate fluid intake (to avoid crystalluria); avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rashes—discontinue immediately; predisposition to folate deficiency; elderly; asthma; G6PD deficiency; pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid in infants under 6 weeks; **interactions**: Appendix 1.
Adverse effects: Nausea, vomiting, diarrhoea, headache; hypersensitivity reactions including rashes, pruritus, photosensitivity reactions, exfoliative dermatitis, and erythema nodosum; rarely, erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis; systemic lupus erythematosus, myocarditis, serum sickness; crystalluria—resulting in haematuria, oliguria, anuria; blood disorders including granulocytopenia, agranulocytosis, aplastic anaemia, purpura—discontinue immediately; also reported, liver damage, pancreatitis, antibiotic-associated colitis, eosinophilia, cough and shortness of breath, pulmonary infiltrates, aseptic meningitis, depression, convulsions, ataxia, tinnitus, vertigo, dizziness, hallucinations, and electrolyte disturbances.
Dose: *Prevention of recurrences of rheumatic fever*, by mouth, ADULT 1 g daily; CHILD 500 mg daily.

POM **Sulfadiazine** *(WMF 6.2.2.9)*
Tablets, Sulfadiazine 500 mg.
Injection (Solution for injection), sulfadiazine (as sodium salt) 250 mg/ml, 4-ml ampoule.

SULFADIMIDINE

Therapeutic category: Antibacterial
Pharmacology: Orally active sulfonamide used for the treatment of respiratory and urinary tract infections.
Indications: Treatment of acute infections caused by pneumococci, streptococci, staphylococci, gonorrhoea; also urinary tract infections due to susceptible organisms, prophylactic agent in meningo-coccal meningitis especially during epidemics.
Contra-indications: Acute intermittent porphyria or sensitivity to other sulfonamides; pregnancy, infants under six weeks
Precautions: Renal dysfunction.
Adverse effects: Nausea and vomiting, mental changes, cyanosis, drug fever, drug rashes, crystalluria.
Advice to patients: See Labels 9 and 27 in Appendix 6. Drink plenty of fluids; take on an empty stomach; avoid prolonged exposure to sunlight or wear protective clothing and sunscreen; notify physician if rash, difficulty in breathing, severe or persistent fever, or sore throat occurs.
Nursing considerations: •See under Cotrimoxazole.
Dose: *Acute infections*, Adult, initially 2 g; then, 1 g 4-6 hourly.
Child (up to 6 yrs), initially 1 g; then, 0.5 g 4-6 hourly.
Infants (6 mths to 1 yr), initially 0.5 g; then, 0.25 g 4-6 hourly.

POM **Sulfadimidine** *(EDL 6.8)*
Tablet, Sulfadimidine 500 mg.
Suspension, Sulfadimidine 500 mg per 5 ml

POM **SAMIDINE®** *(Sam)*
Tablet, Sulfadimidine 500 mg
500 mg - 1000

POM **Sulfadimidine** *(Emzor)*
Tablet, Sulfadimidine 500 mg; white biconvex tab.
500 mg - 1000.

POM **Sulfadimidine** *(Novel)*
Tablet, Sulfadimidine 500 mg; white tab marked 'SULPHADIMIDINE 500' on one side and scored on the reverse.
500 mg - 1000.

POM **Sulfadimidine** *(Rajrab)*
Tablet, Sulfadimidine 500 mg; white scored tab.
500 mg - 1000.

POM **Sulfadimidine** *(Vitabiotics)*
Tablet, Sulfadimidine 500 mg.
500 mg - 500.

SULFATHIAZOLE

Therapeutic category: Antibacterial
Pharmacology: Orally active sulphonamide employed in the treatment of a wide range of acute bacterial infections.
Indications: Treatment of acute infections by pneumococci, meningococci, beta-haemolytic streptococci, *E. coli*; also bacillary dysentery, urinary tract infections; as an adjunct to treatment with penicillin.

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Precautions: Renal dysfunction; maintain a high fluid intake and a slightly alkaline urine to prevent crystal deposition in the urinary tract.
Adverse effects: Nausea, vomiting, mental changes, cyanosis, drug fever, drug rashes, blood dyscrasias, crystal deposition in the urinary tract.
Advice to patients: See labels 9 and 27 in Appendix 6. See also under Sulfadimidine.
Nursing considerations: •See under Cotrimoxazole.
Dose: *Acute infections*, Adult, initially 2 g; then, 1 g 4-6 hourly daily.
Child (up to 6 yrs), initially 1 g; then, 0.5 g 4-6 hourly.
Infants (6 mths-1 yr), initially 0.5 g; then 0.25 g 4-6 hourly.

POM **Sulfathiazole** *(EDL 6.8)*
Tablet, Sulfathiazole 500 mg.

POM **THIAZAMIDE**® *(May & Baker)*
Tablet, Sulfathiazole 500 mg; white scored tab. marked 'M & B 760'.
500 mg - 20, 500.

SULFATHIAZOLE plus SULFADIAZINE plus SULFAMERAZINE

Synonym: Trisulfonamide.
Indications: Acute infections by pneumococci, meningococci, etc.; infections susceptible to sulfonamides like bacillery dysentery, UTI.
Contra-indications: Acute intermittent porphyria; sensitivity to other sulfonamides; infants under 6 months; pregnancy.
Precautions: Renal dysfunction; maintain slightly alkaline urine and high fluid intake.
Adverse effects: See under sulfathiazole.
Advice to patients: See labels 9 and 27 in Appendix 6. See also under Sulfadimidine.
Nursing considerations: •See under Cotrimoxazole.
Dose: Acute infections, Adult, initially 2 g; then, 1 g 4-6 hourly daily.
Child (up to 12 yrs), initially 1 g; then, 0.5 g 4-6 hourly.
Infants (6 mths - 1 yr), initially 0.5 g; then, 0.25 g 4-6 hourly.
See lit. for prophylaxis.

POM **Sulfathiazole plus Sulfadiazine plus Sulfamerazine** *(EDL 6.8)*
Tablets, 185 mg + 185 mg + 130 mg respectively.

POM **NOVA-3-SULFA**® *(SKG)*
Tablets, Sulfathiazole 185 mg, sulfadiazine 185 mg, sulfamerazine 130 mg; white tab. marked 'SKG' on one side and 'NOVA-3-SULFA' on the reverse.
Pack - 20.

POM **SULPHATRIAD**® *(May & Baker)*
Tablets, Sulfathiazole 185 mg, sulfadiazine 185 mg, sulfamerazine 130 mg.
Pack - 20; 500.

TRIMETHOPRIM

Indications: Urinary-tract infections; bronchitis.
Contra-indications: Blood disorders; porphyria.
Precautions: Renal impairment (avoid if severe, Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); predisposition to folate deficiency; elderly; blood counts on long-term therapy (but practical value not proven); neonates (specialist supervision required); **interactions**: Appendix 1.
Adverse effects: Rashes, pruritus; depression of haematopoiesis; gastrointestinal disturbances including nausea and vomiting; rarely exfoliative dermatitis and toxic epidermal necrolysis, photosensitivity and other allergic reactions including angioedema and anaphylaxis; aseptic meningitis.
Dose: *Acute infections*, by mouth, ADULT 200 mg every 12 hours; CHILD 6 weeks–5 months, 25 mg twice daily; 6 months–5 years, 50 mg twice daily; 6–12 years, 100 mg twice daily.
Acute infections, by slow intravenous injection or by intravenous infusion, ADULT 200 mg every 12 hours; CHILD under 12 years, 8 mg/kg daily in 2–3 divided doses
Chronic infections and prophylaxis, by mouth , ADULT 100 mg at night; CHILD 1–2 mg/kg at night.
DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Trimethoprim** *(WMF 6.2.2.9)*
Tablets, Trimethoprim 100 mg, 200 mg.
Injection (Solution for injection), Trimethoprim (as lactate) 20 mg/ml, 5-ml ampoule [not included on WHO Model List].

9.1.2.10 Clindamycin

Clindamycin is a bacteriostatic antibacterial with activity against Gram-positive aerobes and a wide range of anaerobes. However, its use is limited because of adverse effects. Antibiotic-

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associated colitis can occur with a wide range of antibacterials, but occurs most frequently with clindamycin. It may be fatal and is most common in women and the elderly; it can develop during or after treatment with clindamycin. Patients should discontinue treatment immediately if diarrhoea develops. Clindamycin is recommended for the treatment of staphylococcal bone and joint infections and for intra-abdominal sepsis. It is also used for endocarditis prophylaxis when a penicillin is not appropriate.

CLINDAMYCIN

Clindamycin is a complementary drug when penicillin is not appropriate.

Indications: Staphylococcal bone and joint infections; peritonitis; endocarditis prophylaxis.

Contra-indications: Diarrhoeal states; avoid injections containing benzyl alcohol in neonates.

Precautions: Discontinue immediately if diarrhoea or colitis develop; hepatic impairment (Appendix 5); renal impairment (Appendix 4); monitor liver and renal function on prolonged therapy and in neonates and infants; elderly; females; pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid rapid intravenous administration; **interactions**: Appendix 1.

Adverse effects: Diarrhoea (discontinue treatment); nausea, vomiting, abdominal discomfort, antibiotic-associated colitis; rashes, pruritus, urticaria, and rarely anaphylaxis; erythema multiforme, exfoliative and vesiculobullous dermatitis; jaundice and altered liver function tests; neutropenia, eosinophilia, agranulocytosis, and thrombocytopenia; pain, induration, and abscess after intramuscular injection; thrombophlebitis after intravenous injection.

Advice to patients: See Labels 9 and 27 in Appendix 6. Report any severe diarrhoea immediately and do not take antidiarrheal medication; take each oral dose with a full glass of water; finish all medication; do not skip doses.

Nursing considerations: •Obtain specimen for C&S tests before first dose; therapy may begin pending test results.

•Administer oral dosage form with a full glass of water; may give with food to minimize GI irritation.

•Reconstituted oral suspension is stable for 2 weeks at room temperature; it should not be refrigerated, as it will thicken.

•Give around-the-clock in equal intervals to promote less variation in peak and trough serum levels.

•Administer deep IM injection and rotate sites.

•Give IV by infusion only; observe daily for phlebitis and vein irritation during I.V. therapy.

•Discontinue drug and notify physician immediately if persistent diarrhoea and severe abdominal cramps develop; these may be symptoms of pseudomembranous colitis which may end fatally.

•Observe for symptoms of superinfection namely fever, sore throat, fatigue.

Dose: *Osteomyelitis or peritonitis*, by mouth, ADULT 150–300 mg every 6 hours; up to 450 mg every 6 hours in severe infections; CHILD 3–6 mg/kg every 6 hours; by deep intramuscular injection or by intravenous infusion , ADULT 0.6–2.7 g daily in 2–4 divided doses, increased up to 4.8 g daily in life-threatening infections; single doses over 600 mg by intravenous infusion only; single doses by intravenous infusion not to exceed 1.2 g; neonates 15–20 mg/kg daily; CHILD over 1 month, 15–40 mg/kg daily in 3–4 divided doses; severe infections, at least 300 mg daily, regardless of weight.

Endocarditis prophylaxis (for procedures under local or no anaesthetic), by mouth, ADULT 600 mg, 1 hour before procedure.

Endocarditis prophylaxis (for procedures under general anaesthetic), by intravenous infusion, ADULT 300 mg over at least 10 minutes, at induction or 15 minutes before procedure, then 150 mg 6 hours later by mouth or infusion.

PATIENT ADVICE: PATIENTS SHOULD DISCONTINUE IMMEDIATELY AND CONTACT DOCTOR IF DIARRHOEA DEVELOPS; CAPSULES SHOULD BE SWALLOWED WITH A GLASS OF WATER.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Clindamycin** *(WMF 6.2.2.10)*
Capsules, Clindamycin (as HCl) 150 mg.
Injection (Solution for injection), Clindamycin (as phosphate) 150 mg/ml, 2-ml ampoule.

POM **Clindamycin** *(EDL 6.8)*
Capsules, Clindamycin HCl 75 mg, 150 mg.
Suspension, Clindamycin HCl 75 mg per 5 ml.
Injection, Clindamycin phosphate 150 mg per ml; in 2 ml, 4 ml amps.

POM **CLAMYCEF®** *(Korlyns)*
Capsules, Clindamycin 500 mg

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POM **CLIMYCIN**® *(Taylek)*
Capsule, Clindamycin HCl 150 mg
Injection, Clindamycin (as phosphate) 150 mg per ml; in 2 ml amp.

POM **DALACIN C**® *(Pfizer)*
Capsule, Clindamcin HCl 150 mg.
150 mg - 10's; 16's.
Injection, Clindamycin (as phosphate) 150 m per ml; in 2 ml ampoule.

LINCOMYCIN

Therapeutic category: Antibiotic
Indications: Severe infections due to susceptible microorganisms: bone and connective tssue infections, respiratory tract infections, urogenital infections, skin and soft tissue infections.
Contra-indications: Hypersensitivity to lincomycin or clindamycin, moniliasis, severe liver or kidney damage.
Precautions: GI diseases esp. colitis; asthma; history of allergies; newborn, pregnancy; periodic LFT and blood counts - during prolonged therapy.
Adverse effects: See under Clindamycin.
Advice to patients: See labels 9 and 23 in Appendix 6. See also under Clindamycin.
Nursing considerations: •See under Clindamycin.
Dose: By mouth, Adult and children over 14 years, 500 mg 3-4 times daily, depending on the severity of the infection.
Child (over 1month), 30 mg/kg daily in 3-4 divided doses; increased to 60 mg/kg daily in 3-4 divided doses in more serious infections.
By I.M. injection, 600 mg 12-24 hourly.
Child (over 1 month), 10 mg/kg 12-24 hourly.
By I.V. infusion (over 1 hour), 600 mg 2-3 times daily diluted in 250 ml of saline or glucose solution.
Child (over 1 month), 10-20 mg/kg daily in 2-3 divided doses.
Max. daily dose is 8 g
Not recommended for children under 1 month.
Note: Lincomycin should not injected IV as a bolus. Intravenous doses are given on the basis of 1mg of lincocin diluted in not less than 100 ml of appropriate solution and infused over a period of not less than one hour. Severe cardiopulmonary reactions have occurred when this drug has been given at greater than the recommended concentration and rate.

POM **Lincomycin** *(EDL6.8)*
Capsule, Lincomycin 500 mg
Syrup, Lincomycin 250 mg per 5 ml
Injection, Lincomycin (as phosphate) 150 mg per ml; in 2 ml, 4 ml amps.

POM **LINCOCIN**® *(Pfizer)*
Capsule, Lincomycin (as HCl) 500 mg
500 mg – 12's; 100's
Syrup, Lincomycin 250 mg per 5 ml
Pack – 60 ml
Injection, Lincomycin (as HCl) 300 mg per ml; in 2 ml vial.

POM **LINCOLECIN**® *(Pharmabox)*
Capsule (250 mg), Lincomycin (as HCl) 250 mg; dark blue cap and light blue body capsule filled with white powder.
250 mg – 10's; 100's; 500's; 1000's.
Capsule (500 mg), Lincomycin (as HCl) 500 mg; dark blue cap and light blue body capsule filled with white powder.
500 mg – 10's; 100's; 500's; 1000's.

POM **NELOREN**® (*Taylek*)
Capsule, Lincomycin HCl 500 mg.
500 mg - 12; 16; 100.
Injection, Lincomycin HCl 300 mg per ml; in 2 ml amp.
Pack - 10.

9.1.2.11 Vancomycin

Vancomycin is not significantly absorbed from the gastrointestinal tract and must be given intravenously for systemic infections which cannot be treated with other effective, less toxic antimicrobials. It is used to treat serious infections due to Gram-positive cocci including methicillin-resistant staphylococcal infections, brain abscess, staphylococcal meningitis and septicaemia.

VANCOMYCIN

Vancomycin is a complementary antibacterial drug for use only when there is significant resistance to other drugs on the WHO Model List.
Indications: Methicillin-resistant staphylococcal pneumonia; staphylococcal meningitis; endocarditis prophylaxis (with gentamicin).
Precautions: Avoid rapid infusion (risk of anaphylactoid reactions, see Adverse effects); rotate infusion sites; renal impairment (Appendix 4); elderly; history of deafness—avoid; plasma-vancomycin concentration measured after 3 or 4 doses

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(earlier if renal impairment), blood counts, urinalysis, and renal function tests—use only in hospital setting; monitor auditory function and plasma-vancomycin concentrations in elderly or in renal impairment; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Nephrotoxicity including renal failure and interstitial nephritis; ototoxicity (discontinue if tinnitus occurs); blood disorders; nausea, chills, fever, eosinophilia, anaphylaxis, rashes, including exfoliative dermatitis, erythema multiforme (Stevens-Johnson syndrome), toxic epidermal necrolysis, and vasculitis; phlebitis; on rapid infusion, severe hypotension (with shock, cardiac arrest), wheezing, dyspnoea, urticaria, pruritus, flushing of the upper body ('red man' syndrome), pain and muscle spasm of back and chest.

Dose: *Serious staphylococcal infections*, by intravenous infusion, ADULT 500 mg over at least 60 minutes every 6 hours or 1 g over at least 100 minutes every 12 hours; elderly (over 65 years), 500 mg every 12 hours or 1 g once daily; neonate up to 1 week, 15 mg/kg initially, then 10 mg/kg every 12 hours; infant 1–4 weeks, 15 mg/kg initially, then 10 mg/kg every 8 hours; CHILD over 1 month, 10 mg/kg every 6 hours.

Endocarditis prophylaxis (for procedures under general anaesthetic), by intravenous infusion, ADULT 1 g over at least 100 minutes then gentamicin 120 mg at induction or 15 minutes before procedure.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO THE MANUFACTURER'S DIRECTIONS.

NOTE: PLASMA CONCENTRATION MONITORING REQUIRED; PEAK PLASMA CONCENTRATION (MEASURED 2 HOURS AFTER INFUSION) SHOULD NOT EXCEED 30 MG/LITRE; PRE-DOSE (TROUGH) CONCENTRATION SHOULD NOT EXCEED 5–10 MG/LITRE.

POM **Vancomycin** *(WMF 6.2.2.11)*
Infusion (Powder for solution for infusion), vancomycin (as HCl) 250-mg vial.

9.1.3 Antileprosy drugs

Leprosy is a chronic mycobacterial infection due to *Mycobacterium leprae*, which is a slow-growing intracellular bacillus that infiltrates the skin, peripheral nerves, the nasal and other mucosa, and the eyes; it affects people of all ages and both sexes. The incubation period between infection and appearance of leprosy is normally between 2 to 10 years, but may be up to 20 years. It is transmitted from person-to-person when bacilli are shed from the nose; most individuals have natural immunity and symptoms are suppressed. For treatment purposes patients may be classified as having paucibacillary (PB) or multibacillary (MB) leprosy. The 2 forms may be distinguished by skin smears, but facilities are not always available to process them and their reliability is often doubtful. In practice, most leprosy programmes classify and choose a regimen based on number of skin lesions; these are PB leprosy (1–5 skin lesions) and MB leprosy (more than 5 skin lesions).

Medicines used in the treatment of leprosy should always be used in combination; this is essential to prevent the emergence of resistance. **Rifampicin** is now combined with **dapsone** to treat PB leprosy and **rifampicin** and **clofazimine** are now combined with **dapsone** to treat MB leprosy. The WHO Programme for the Elimination of Leprosy currently provides, free of charge, oral multidrug therapy in colour-coded blister packs (MDT blister packs) to improve patients' adherence to treatment. Any patient with a positive skin smear should be treated with the MDT regimen for MB leprosy. The regimen for PB leprosy should never be given to a patient with MB leprosy. If diagnosis classification in a particular patient is not possible the MDT regimen for MB leprosy must be used.

Lepra reactions are episodes of sudden increase in the activity of leprosy and are often accompanied by neuritis; reactions must always be treated promptly to prevent permanent nerve damage and disability. Leprosy multidrug therapy should continue during a lepra reaction without interruption. This reduces the frequency and severity of lepra reactions.

Type 1 lepra reactions, or reversal reactions, are delayed hypersensitivity reactions and may occur in either PB or MB leprosy. If there is no nerve damage, type 1 reactions may be treated with analgesics such as acetylsalicylic acid or paracetamol. If there is nerve involvement

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corticosteroids, such as oral prednisolone should be used in addition to analgesics.

The type 2 lepra reaction, also known as erythema nodosum leprosum (ENL), is an antibody response to dead leprosy bacteria and occurs only in MB leprosy. Therapy for type 2 reactions may include analgesics, such as acetylsalicylic acid or paracetamol, and a corticosteroid, such as oral prednisolone. In patients not responding to a corticosteroid, clofazimine may be used. Severe type 2 lepra reactions should be treated under medical supervision in hospital.

If a patient does not respond to lepra reaction treatment within 6 weeks or seems to become worse, the patient must be sent immediately to the nearest specialist centre. Neuritis may occur during or independently of lepra reactions. It can be successfully treated with a 12-week course of oral prednisolone; if patients do not respond, specialist centre treatment is required.

TREATMENT REGIMENS

The recommended regimen for paucibacillary leprosy in adults (50–70 kg) is rifampicin 600 mg once monthly and dapsone 100 mg daily. Children aged 10–14 years may be given rifampicin 450 mg once monthly and dapsone 50 mg daily. Appropriate dose adjustments are required for younger children. For example, dapsone 25 mg daily and rifampicin 300 mg once a month. Treatment is continued for 6 months for PB leprosy.

The recommended regimen for multibacillary (MB) leprosy in adults (50–70 kg) is rifampicin 600 mg and clofazimine 300 mg, both given once a month together with clofazimine 50 mg and dapsone 100 mg, both daily. Children aged 10–14 years may be given rifampicin 450 mg and clofazimine 150 mg, both once a month together with clofazimine 50 mg every other day and dapsone 50 mg daily. Appropriate dosage adjustments are required for younger children. For example, dapsone 25 mg daily, clofazimine 50 mg twice a week, and clofazimine 100 mg and rifampicin 300 mg once a month. Treatment is continued for 12 months for MB leprosy.

For patients who cannot take rifampicin because of allergy, other diseases, or rifampicin-resistant leprosy, and for patients who refuse to take clofazimine, there are alternative regimens which incorporate ofloxacin and minocycline [not included on WHO Model List].

CLOFAZIMINE

Therapeutic category: Antibiotic; Leprostatic agent.

Indications: Multibacillary (MB) leprosy; type 2 lepra reactions.

Precautions: Pre-existing gastrointestinal symptoms (reduce dose, increase dose interval or discontinue if symptoms develop during treatment); liver and renal impairment; pregnancy and breastfeeding; may discolour soft contact lenses.

Adverse effects: Reversible discoloration of skin, hair, cornea, conjunctiva, tears, sweat, sputum, faeces, and urine; dose-related gastrointestinal symptoms including pain, nausea, vomiting and diarrhoea; severe mucosal and submucosal oedema, with prolonged treatment with high doses—may be severe enough to cause subacute small-bowel obstruction (see also Precautions).

Advice to patients: See Labels 8, 14 and 22 in Appendix 6. Drug may cause a red to brownish-black discolouration of the skin, conjunctiva, tears, sweat, urine, faeces, and nasal secretions; although reversible, may take months to years to disappear after therapy is completed; take with meals; dry skin can be relieved with skin oil or cream.

Nursing considerations: •Advise patient to take the drug with meals.

•If patient complains of colicky or burning abdominal pain or any other GI symptoms, report this to the doctor, who may reduce the dose or increase the interval between doses.

•Use cautiously in GI dysfunction, such as abdominal pain and diarrhoea.

•Warn patient that clofazimine may cause a red to brownish-black discolouration of skin, body fluids, and excrement. Reassure patient that the unsightly skin discolouration is reversible but may not disappear until several months or years after therapy is completed.

•Recommend application of skin oil or cream to help reverse skin dryness or ichthyosis.

Dose: *Multibacillary leprosy (in combination with dapsone and rifampicin, see notes above)*, by mouth, ADULT 50 mg once daily and 300 mg once a month; CHILD 10–14 years 50 mg on alternate days and 150 mg once a month; CHILD under 10 years, see notes above; continue treatment for 12 months.

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Type 2 lepra reaction (erythema nodosum leprosum; see notes above), by mouth, ADULT and CHILD 200–300 mg daily in 2 or 3 divided doses; 4–6 weeks treatment may be required before effect is seen.

POM **Clofazimine** *(WMF 6.2.3)*
Capsules, Clofazimine 50 mg, 100 mg.

POM **Clofazimine** *(EDL 6.9)*
Capsules, Clofazimine 50 mg, 100 mg.

POM **LAMPRENE®** *(Novartis)*
Capsules, Clofazimine 100 mg; brown gelatin cap. marked 'GEIGY' and 'GM'.
100 mg - 100.

DAPSONE

Synonym: Diaminodiphenylsulphone; DSS.
Therapeutic category: Antibiotic; Leprostatic Agent.
Pharmacology: Dapsone is a sulphone bacteriostatic with mechanism of action similar to that of the sulfonamides. It inhibits folic acid biosynthesis in susceptible organisms. See notes above.
Indications: Paucibacillary (PB) and multibacillary (MB) leprosy.
Contra-indications: Hypersensitivity to sulfones; severe anaemia.
Precautions: Anaemia (treat severe anaemia before therapy, and monitor blood counts during treatment); susceptibility to haemolysis including G6PD deficiency (including breastfeeding affected infants); pregnancy (Appendix 2); breastfeeding (Appendix 3); porphyria; **interactions**: Appendix 1.
BLOOD DISORDERS: ON LONG-TERM TREATMENT PATIENTS AND THEIR CARERS SHOULD BE TOLD HOW TO RECOGNIZE BLOOD DISORDERS AND ADVISED TO SEEK IMMEDIATE MEDICAL ATTENTION IF SYMPTOMS SUCH AS FEVER, SORE THROAT, RASH, MOUTH ULCERS, PURPURA, BRUISING OR BLEEDING DEVELOP.
Adverse effects: Haemolysis and methaemoglobinaemia; allergic dermatitis (rarely including toxic epidermal necrolysis and the Stevens-Johnson syndrome); rarely, hepatitis and agranulocytosis; 'dapsone syndrome' resembling mononucleosis—rare hypersensitivity reaction with symptoms including rash, fever, jaundice, and eosinophilia; gastrointestinal irritation; tachycardia, headache, nervousness, insomnia, blurred vision, paraesthesia, reversible peripheral neuropathy, and psychoses reported.
Advice to patients: See Label 8 in Appendix 6.
Nursing considerations: •Frequent blood tests are required during early therapy; dosage may be reduced or treatment discontinued temporarily if low levels of Hb, WBC or RBC are obtained.
•Withhold therapy if rash develops and report to the physician; antihistamines may be prescribed for dapsone-induced allergic dermatitis.
•Persistent sore throat, fever, malaise or fatigue should be reported to the physician.
•Nursing mothers should be advised to report cyanosis in infants as this may indicate high sulphone level.
Dose: *Paucibacillary leprosy (in combination with rifampicin, see notes above)*, by mouth, ADULT 100 mg daily; CHILD under 10 years, see notes above; 10–14 years 50 mg daily; continue treatment for 6 months.
Multibacillary leprosy (in combination with rifampicin and clofazimine, see notes above), ADULT 100 mg daily; CHILD under 10 years, see notes above; 10–14 years 50 mg daily; continue treatment for 12 months.

POM **Dapsone** *(WMF 6.2.3)*
Tablets, Dapsone 25 mg, 50 mg, 100 mg.

POM **Dapsone** *(EDL 6.9)*
Tablets, Dapsone 50 mg, 100 mg.

POM **DAPSOSAM®** *(Sam)*
Tablet, Dapsone 100 mg
100 mg - 500.

RIFAMPICIN

Indications: Paucibacillary leprosy; multibacillary leprosy; tuberculosis (section 9.1.4).
Contra-indications: Hypersensitivity to rifamycins; jaundice.
Precautions: Reduce dose in hepatic impairment (Appendix 5); liver function tests and blood counts required in liver disorders, alcohol dependency, elderly, and on prolonged therapy; renal impairment (if dose above 600 mg daily); pregnancy (Appendix 2); breastfeeding (Appendix 3); porphyria; discolours soft contact lenses; important: advise patients on oral contraceptives to use additional means; **interactions**: Appendix 1.
NOTE: RESUMPTION OF RIFAMPICIN TREATMENT AFTER A LONG INTERVAL MAY CAUSE SERIOUS IMMUNOLOGICAL REACTIONS, RESULTING IN RENAL IMPAIRMENT, HAEMOLYSIS, OR THROMBOCYTOPENIA—DISCONTINUE PERMANENTLY IF SERIOUS ADVERSE EFFECTS OCCUR.

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LIVER DISORDERS: PATIENTS OR THEIR CARERS SHOULD BE TOLD HOW TO RECOGNIZE SIGNS OF LIVER DISORDERS AND ADVISED TO DISCONTINUE TREATMENT AND SEEK IMMEDIATE MEDICAL ATTENTION IF SYMPTOMS SUCH AS PERSISTENT NAUSEA, VOMITING, MALAISE OR JAUNDICE DEVELOP.

Adverse effects: Severe gastrointestinal disturbances including anorexia, nausea, vomiting, and diarrhoea (antibiotic-associated colitis reported); headache, drowsiness; rashes, fever, influenza-like syndrome and respiratory symptoms, collapse, shock, haemolytic anaemia, acute renal failure, and thrombocytopenic purpura—more frequent with intermittent therapy; alterations of liver function—jaundice and potentially fatal hepatitis (dose-related; do not exceed maximum daily dose of 600 mg); also reported, oedema, muscular weakness and myopathy, exfoliative dermatitis, toxic epidermal necrolysis, pemphigoid reactions, leukopenia, eosinophilia and menstrual disturbances; urine, tears, saliva, and sputum coloured orange-red.

Advice to patients: See labels 8, 14 and 22 in Appendix 6. May discolour urine, tears, sweat, or other body fluids to a red-orange colour; take 1 hour before or 2 hours after a meal on an empty stomach; soft contact lenses may be permanently stained; report to physician any severe or persistent flu-like symptoms, nausea, vomiting, dark urine or pale stools, or unusual bleeding or bruising.

Dose: *Paucibacillary leprosy (in combination with dapsone; see notes above)*, by mouth, ADULT 600 mg once a month; CHILD under 10 years, see notes above; 10–14 years 450 mg once a month; continue treatment for 6 months.

Multibacillary leprosy (in combination with dapsone and clofazimine; see notes above), by mouth, ADULT 600 mg once a month under supervision; CHILD under 10 years, see notes above; 10–14 years 450 mg once a month under supervision; continue treatment for 12 months.

PATIENT ADVICE: TAKE DOSE AT LEAST 30 MINUTES BEFORE A MEAL, SINCE ABSORPTION IS REDUCED BY FOOD.

POM **Rifampicin** *(WMF 6.2.3)*
Tablets, Rifampicin 150 mg, 300 mg.
Capsules, Rifampicin 150 mg, 300 mg.

POM **Rifampicin** *(EDL 6.10)*
Tablet or capsule, Rifampicin 150 mg, 300 mg.

See section 9.1.4 for the proprietary preparations of Rifampicin.

9.1.4 Antituberculosis drugs

Tuberculosis is a chronic infectious disease caused primarily by *Mycobacterium tuberculosis* or sometimes *M. bovis*. Infection is usually due to inhalation of infected droplet nuclei with the lung generally being the first organ affected, but the primary infection is usually asymptomatic. Infection and inflammatory responses resolve with the development of acquired immunity. Surviving bacteria may become dormant or in susceptible patients, progress to active primary disease; dormant organisms may produce disease and this often occurs if immune status is altered.

Tuberculosis is the most prevalent infectious disease of adults and causes 26% of avoidable adult deaths in the developing world. More than 80% of tuberculosis cases are pulmonary (PTB). At least 30% of patients who are infected with HIV will also develop active tuberculosis. The increase in resistant strains and poor compliance which may contribute to resistance and treatment failure has led to the development of regimens with directly supervised treatment. Directly observed treatment, short-course (DOTS) therapy which lasts for 6 or 8 months, given under direct observation is one of the most important components of the WHO strategy against tuberculosis. Simplified drug regimens and intermittent therapy have been introduced to improve compliance. WHO does not generally recommend twice weekly regimens. If a patient receiving a twice weekly regimen misses a dose of tablets, the missed dose represents a bigger fraction of the total number of treatment doses than if the patient was receiving a three times weekly or daily dose regimen. Therefore, there is a greater risk of treatment failure with twice weekly regimens. Fixed-dose combination tablets incorporating 2 or more drugs are also used to improve compliance and decrease medication errors; they should be used unless one of the components cannot be given because of resistance or intolerance.

Modern short-course therapy is usually in 2 phases. The initial phase (2 months)

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involves the concurrent use of at least 3 drugs to reduce the bacterial population rapidly and prevent drug-resistant bacteria emerging. The second continuation phase (4–6 months) involves fewer drugs and is used to eliminate any remaining bacteria and prevent recurrence. Direct observation of therapy is considered essential to ensure compliance in the initial phase and also useful in the continuation phase if patients are receiving rifampicin. Five antituberculosis drugs, **isoniazid**, **rifampicin**, **pyrazinamide**, **streptomycin**, (which are bactericidal) and **ethambutol** (which is bacteriostatic) are used in various combinations as part of WHO-recommended treatment regimens; **thioacetazone** is used only if ethambutol cannot be used. In supervised regimens change of drug regimen should be considered only if the patient fails to respond after 5 months of DOTS.

Isoniazid, rifampicin, and pyrazinamide are components of all antituberculosis drug regimens currently recommended by WHO. Unsupervised and alternative regimens as set out in the following tables may be administered as specified.

ADDITIONAL RESERVE ANTITUBERCULOSIS DRUGS (**AMIKACIN, P-AMINOSALICYLIC ACID, CAPREOMYCIN, CIPROFLOXACIN, CYCLOSERINE, ETHIONAMIDE, KANAMYCIN, LEVOFLOXACIN,** AND **OFLOXACIN**) FOR THE TREATMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS SHOULD BE USED IN SPECIALIZED CENTRES ADHERING TO WHO STANDARDS FOR TB CONTROL.

Worldwide, an important predisposing cause of immunosuppression leading to tuberculosis is human immunodeficiency virus (HIV) infection; it increases susceptibility to primary infection and increases the reactivation rate of

Recommended 6-month treatment regimens for tuberculosis[1]

Drug	Initial phase (2 months)	Continuation phase (4 months)
Isoniazid	5 mg/kg daily	5 mg/kg daily
Rifampicin	10 mg/kg daily	10 mg/kg daily
Pyrazinamide	25 mg/kg daily	
together with		
Streptomycin	15 mg/kg daily	
or		
Ethambutol	15 mg/kg daily	
Isoniazid	10 mg/kg 3 times weekly	10 mg/kg 3 times weekly
Rifampicin	10 mg/kg 3 times weekly	10 mg/kg 3 times weekly
Pyrazinamide	35 mg/kg 3 times weekly	
together with		
Streptomycin	15 mg/kg 3 times weekly	
or		
Ethambutol	30 mg/kg 3 times weekly[2]	

Recommended 8-month treatment regimen for tuberculosis[1]

Drug	
Initial phase (2 months)	Continuation phase (6 months)
Isoniazid 5 mg/kg daily	5 mg/kg daily
Rifampicin 10 mg/kg daily	
Pyrazinamide 25 mg/kg daily	

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together with

Ethambutol 15 mg/kg daily[4] 15 mg/kg daily[5]

or

Streptomycin[3] 15 mg/kg daily

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[1]Unless otherwise indicated, doses are suitable for both adults and children
[2]Not suitable for children
[3]Streptomycin always replaces ethambutol in meningeal TB
[4]Not suitable for children under 5 years
[5]Thioacetazone (2.5 mg/kg daily) may be used (only if ethambutol cannot be given) in combination with isoniazid in the continuation phase; risk of severe toxicity, particularly in HIV-infected individuals

TREATMENT REGIMENS BY CATEGORY OF TUBERCULOSIS DIAGNOSIS

Category I: New pulmonary disease (smear-positive or smear-negative with extensive involvement of parenchyma), concomitant severe HIV disease, and new severe extra-pulmonary disease

Initial phase[1] (antibacterials administered daily or 3 times weekly): isoniazid + rifampicin + pyrazinamide + ethambutol (or streptomycin) for 2 months

Continuation phase[1] (antibacterials administered daily or 3 times weekly): isoniazid + rifampicin for 4 months (or isoniazid + ethambutol for 6 months but less effective than isoniazid + rifampicin)

Category II: Previously treated smear-positive pulmonary disease which has relapsed, or failed 2 to respond, or if treatment was interrupted

Initial phase 1 (antibacterials administered daily or 3 times weekly): isoniazid + rifampicin + pyrazinamide + ethambutol + streptomycin for 2 months

then:
isoniazid + rifampicin + pyrazinamide + ethambutol for 1 month

Continuation phase[1] (antibacterials administered daily or 3 times weekly):isoniazid + rifampicin + ethambutol for 5 months

Category III: New smear-negative pulmonary disease (other than in Category I) and less severe extra-pulmonary disease

Initial phase[1] (antibacterials administered daily or 3 times weekly):isoniazid + rifampicin + pyrazinamide + ethambutol3 for 2 months

Continuation phase[1] (antibacterials administered daily or 3 times weekly):isoniazid + rifampicin for 4 months (or isoniazid + ethambutol for 6 months but less effective than isoniazid + rifampicin)

Category IV: Chronic and multi-drug-resistant tuberculosis (MDR-TB) (smear-positive despite supervised re-treatment)[4]

specially designed standardized or individualized regimens recommended

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[1]Drug intake should be directly observed in patients who are smear positive during the initial phase, and always when rifampicin is given
[2]Drug sensitivity testing recommended before prescribing Category II treatment in failure cases; patients with MDR-TB should be prescribed Category IV regimen
[3]Omit ethambutol in initial phase if disease is not complicated by cavitary disease or concomitant HIV disease, and in patients infected with fully susceptible bacilli or young children with primary tuberculosis
[4]Early culture and sensitivity testing recommended for contacts of patients with MDR-TB

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tuberculosis. Preventative antituberculosis therapy of such persons is recommended.

Chemoprophylaxis with isoniazid can prevent the development of clinically apparent disease in persons in close contact with infectious patients, and also prevent the reactivation of previously dormant disease in other persons at high risk particularly those who are immunodeficient.

Where the disease remains highly prevalent routine immunization of infants within the first year of age with BCG vaccine is cost-effective. However, there is no evidence that BCG will protect children older than 15 years of age. Infants born to HIV-positive mothers should be vaccinated during the first year of life, provided they have no clinical signs suggestive of HIV.

The **tuberculin test** has limited diagnostic value. A positive tuberculin test indicates previous exposure to mycobacterial antigens through infection with one of the tubercle bacilli, or BCG vaccination. The tuberculin test does not distinguish between tuberculosis and other mycobacterial infection, between active and quiescent disease, or between acquired infection and seroconversion induced by BCG vaccination.

ETHAMBUTOL

Indications: Tuberculosis, in combination with other drugs (see notes and tables above).

Contra-indications: Optic neuritis; children under 5 years—unable to report symptomatic visual disturbances; severe renal impairment.

Precautions: Visual disturbances—ocular examination recommended before and during treatment (see note below); reduce dose in renal impairment (Appendix 4) and monitor plasma concentration; elderly; pregnancy (not known to be harmful); breastfeeding (Appendix 3).

NOTE: PATIENTS SHOULD REPORT VISUAL DISTURBANCES IMMEDIATELY AND DISCONTINUE TREATMENT; CHILDREN WHO ARE INCAPABLE OF REPORTING SYMPTOMATIC VISUAL CHANGES ACCURATELY SHOULD BE GIVEN ALTERNATIVE THERAPY, AS SHOULD, IF POSSIBLE, ANY PATIENT WHO CANNOT UNDERSTAND WARNINGS ABOUT VISUAL ADVERSE EFFECTS.

Adverse effects: Optic neuritis—reduced visual acuity and red/green colour blindness (early changes usually reversible, prompt withdrawal may prevent blindness); peripheral neuritis—especially in legs; gout; rarely, rash, pruritus, urticaria, thrombocytopenia.

Advice to patients: See Label 8 in Appendix 6. Report any visual changes or rash to physician; may cause stomach upset, take with food; do not take within 2 hours of aluminium-containing antacids.

Nursing considerations: •Obtain specimen for C&S test including sputum before treatment.
•Administer with meals to minimise GI upset; give antiemetic if vomiting occurs. Antacids should not be used within 2 hr of medication.
•Emphasize the need to comply with dosage and appointments to prevent relapse; to avoid alcoholic beverages.
•Advise periodic visual testing before and during therapy; reassure patient that visual disturbances will clear weeks to months after therapy.
•Monitor regularly the serum uric acid and observe patient for symptoms of gout.

Dose: *Tuberculosis (initial phase of combination therapy; see notes and tables above)*, by mouth, ADULT 15 mg/kg daily or 30 mg/kg 3 times a week; CHILD 15 mg/kg daily.

NOTE: 'PEAK' CONCENTRATION (2–2.5 HOURS AFTER DOSE) SHOULD BE 2–6 MG/LITRE (7–22 MICROMOL/LITRE); 'TROUGH' (PRE-DOSE) CONCENTRATION SHOULD BE LESS THAN 1 MG/LITRE (4 MICROMOL/LITRE).

POM **Ethambutol** *(WMF 6.2.4)*
Tablets, Ethambutol HCl 100 mg, 400 mg.

POM **Ethambutol** *(EDL 6.10)*
Tablets, Ethambutol (as HCl) 100-500 mg.

ETHAMBUTOL plus ISONIAZID

Indications: Tuberculosis, in combination with other drugs (see notes and tables above).

Contra-indications: Preparation not suitable for use in children; see Ethambutol Hydrochloride and Isoniazid.

Precautions: See Ethambutol Hydrochloride and Isoniazid.

Adverse effects: See Ethambutol Hydrochloride and Isoniazid.

Dose: *Tuberculosis, continuation phase of 8-month regimen in place of thioacetazone with isoniazid (see notes and tables)*, by mouth, ADULT ethambutol hydrochloride 800 mg and isoniazid 300 mg daily.

POM ***Ethambutol plus Isoniazid*** *(WMF 6.2.4)*
Tablets, Ethambutol HCl 400 mg with

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isoniazid 150 mg.

ISONIAZID

Synonym: Isonicotinic acid hydrazide; INH. Isoniazid

Indications: Tuberculosis treatment, in combination with other drugs (see notes and tables above); tuberculosis prophylaxis.

Contra-indications: Drug-induced hepatic disease.

Precautions: Hepatic impairment (monitor hepatic function; Appendix 5); malnutrition, chronic alcohol dependence, chronic renal failure (Appendix 4), diabetes mellitus, and HIV infection—prophylactic pyridoxine 10 mg daily required because risk of peripheral neuritis; epilepsy; slow acetylator status (increased risk of adverse effects); history of psychosis; pregnancy (not known to be harmful); breastfeeding (Appendix 3); porphyria; **interactions**: Appendix 1.

LIVER DISORDERS: PATIENTS OR THEIR CARERS SHOULD BE TOLD HOW TO RECOGNIZE SIGNS OF LIVER DISORDER, AND ADVISED TO DISCONTINUE TREATMENT AND SEEK IMMEDIATE MEDICAL ATTENTION IF SYMPTOMS SUCH AS NAUSEA, VOMITING, MALAISE OR JAUNDICE DEVELOP.

Adverse effects: Gastrointestinal disorders including nausea and vomiting, diarrhoea and pain, also constipation, dry mouth; hypersensitivity reactions including fever, rashes, joint pain, erythema multiforme, purpura usually during first weeks of treatment; peripheral neuropathy; blood disorders including agranulocytosis, haemolytic anaemia, aplastic anaemia; optic neuritis, toxic psychoses, and convulsions; hepatitis (especially over age of 35 years and regular users of alcohol)—withdraw treatment; also reported, systemic lupus erythematosus-like syndrome, pellagra, hyperreflexia, difficulty with micturition, hyperglycaemia and gynaecomastia.

Advice to patients: See labels 8 and 22 in Appendix 6. Report any prodromal symptoms of hepatitis (fatigue, weakness, nausea, vomiting, dark urine, or yellowing of eyes) or any burning, tingling, or numbness in the extremities.

Nursing considerations: •Obtain specimen for C&S test including sputum before treatment.

•Advise patient to take with food if GI irritation occurs; better absorbed on an empty stomach.

•Advise against use with alcohol as it may exacerbate isoniazid-induced hepatitis.

•Pyridoxine may be given to prevent peripheral neuropathy, especially in malnourished patients.

•Emphasize the need to comply with dosage and appointments to prevent relapse.

•Monitor hepatic function and notify doctor immediately if symptoms of hepatic impairment occur namely fatigue, loss of appetite, nausea, dark urine, or yellowing of eyes.

Dose: *Tuberculosis, treatment (combination therapy; see also notes and tables)*, by mouth, ADULT and CHILD 5 mg/kg (4–6 mg/kg) daily (maximum, 300 mg daily), or 10 mg/kg 3 times weekly.

Tuberculosis, treatment in critically ill patients unable to take oral therapy (combination therapy), by intramuscular injection, ADULT 200–300 mg as single daily dose; CHILD 10–20 mg/kg daily.

Tuberculosis, prophylaxis, by mouth, ADULT 300 mg daily for at least 6 months; CHILD 5 mg/kg daily for at least 6 months.

PATIENT ADVICE: ISONIAZID SHOULD BE TAKEN ON AN EMPTY STOMACH; IF TAKEN WITH FOOD TO REDUCE GASTROINTESTINAL IRRITATION, ORAL ABSORPTION AND BIOAVAILABILITY MAY BE IMPAIRED.

POM **Isoniazid** *(WMF 6.2.4)*
Tablets, Isoniazid 100 mg, 300 mg.
Injection (Solution for injection), Isoniazid 25 mg/ml, 2-ml ampoule [not included on WHO Model List].

POM **Isonaizid** *(EDL 6.10)*
Tablets, Isonaizid 100-300 mg

POM **Isoniazid** *(BCN)*
Tablets, Isoniazid 100 mg, 200 mg.
100 mg - 1000.
200 mg - 1000

POM **Isoniazid** *(Rajrab)*
Tablet, Isoniazid 100mg; white scored tab.
100mg - 1000.

ISONIAZID plus THIOACETAZONE

Thioacetazone with isoniazid is a complementary drug combination.

Indications: Tuberculosis, in combination with other drugs (see notes and tables above).

Contra-indications: See Isoniazid; hepatic impairment; renal impairment; HIV infection—thioacetazone associated with high incidence of serious, sometimes fatal cutaneous hypersensitivity reactions, including exfoliative dermatitis.

Precautions: See Isoniazid; determine

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efficacy and toxicity of thioacetazone - geographical differences; hypersensitivity reactions - withdraw treatment; **interactions**: Appendix 1.

Adverse effects: See Isoniazid; thioacetazone causes the following—nausea, vomiting, diarrhoea; hypersensitivity reactions including conjunctivitis, vertigo, rashes; fatal exfoliative dermatitis, acute hepatic failure reported; also, agranulocytosis, thrombocytopenia and aplastic anaemia.

Dose: *Tuberculosis, continuation phase of 8-month regimen (see notes and tables above)*, by mouth, ADULT and CHILD thioacetazone 2.5 mg/kg daily and isoniazid 5 mg/kg daily.

POM **Isoniazid plus Thioacetazone** *(WMF 6.2.4)*
Tablets, Thioacetazone 50 mg with isoniazid 100 mg; thioacetazone 150 mg with isoniazid 300 mg.

POM **Isonaizid plus Thioacetazone** *(EDL 6.10)*
Tablets, Isoniazid 100 mg, thioacetazone 50 mg; isoniazid 300 mg, thioacetazone 150 mg.

POM **INAZONE-450**® *(Vitabiotics)*
Tablet, Isoniazid 300 mg, thioacetazone 150 mg. Pack - 500's.

PYRAZINAMIDE

Synonym: Pyrazinoic acid amide.

Indications: Tuberculosis, in combination with other drugs (see notes and tables above).

Contra-indications: Severe hepatic impairment; porphyria.

Precautions: Hepatic impairment (monitor hepatic function; Appendix 5); renal impairment; diabetes mellitus (monitor blood glucose—may change suddenly); gout; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

LIVER DISORDERS: PATIENTS OR THEIR CARERS SHOULD BE TOLD HOW TO RECOGNIZE SIGNS OF LIVER DISORDER, AND ADVISED TO DISCONTINUE TREATMENT AND SEEK IMMEDIATE MEDICAL ATTENTION IF SYMPTOMS SUCH AS PERSISTENT NAUSEA, VOMITING, MALAISE OR JAUNDICE DEVELOP.

Adverse effects: Hepatotoxicity including fever, anorexia, hepatomegaly, splenomegaly, jaundice, liver failure; nausea, vomiting; arthralgia; gout; sideroblastic anaemia; rash, photosensitivity.

Advice to patients: See label 8 in Appendix 6.

Nursing considerations: •Obtain specimen for C&S test including sputum before treatment.
•Administer with meals to minimise GI upset.
•Emphasize the need to comply with dosage and appointments to prevent relapse; to avoid alcoholic beverages.
•Dosage may be reduced in renal insufficiency as the drug is virtually excreted in urine.
•Monitor hepatic function and blood uric acid before and during therapy.
•Notify physician immediately if signs of gout and of hepatic impairment occur namely fever, loss of appetite, malaise, nausea, vomiting, darkened urine, pale stools.

Dose: *Tuberculosis (initial phase of combination therapy; see notes and tables above)*, by mouth, ADULT and CHILD 25 mg/kg daily or 35 mg/kg 3 times weekly.

POM **Pyrazinamide** *(WMF 6.2.4)*
Tablets, Pyrazinamide 400 mg, 500 mg [500-mg strength not included on WHO Model List].

POM **Pyrazinamide** *(EDL 6.10)*
Tablet, Pyrazinamide 500 mg.

POM **PYRAZIN**® *(Hovid)*
Tablet, Pyrazinamide 500 mg.
500 mg - 1000.

POM **ZINAMIDE**® *(Bolax/BPP)*
Tablet, Pyrazinamide 500 mg; white scored tab. marked 'MSD 504'.
500 mg - 100.

RIFAMPICIN

Synonym: Rifampin.

Therapeutic category: Antibiotic; Antituberculous agent.

Indications: Tuberculosis, in combination with other drugs (see notes and tables above); leprosy (section 9.1.3).

Contra-indications: Hypersensitivity to rifamycins; jaundice.

Precautions: Reduce dose in hepatic impairment (Appendix 5); liver function tests and blood counts required in liver disorders, alcohol dependency, elderly, and on prolonged therapy; renal impairment (if dose above 600 mg daily); pregnancy (Appendix 2); breastfeeding (Appendix 3); porphyria; discolours soft contact lenses; important: advise patients on oral contraceptives to use additional means; **interactions**: Appendix 1.

NOTE: RESUMPTION OF RIFAMPICIN TREATMENT AFTER A LONG INTERVAL MAY CAUSE SERIOUS IMMUNOLOGICAL

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REACTIONS, RESULTING IN RENAL IMPAIRMENT, HAEMOLYSIS, OR THROMBOCYTOPENIA—DISCONTINUE PERMANENTLY IF SERIOUS ADVERSE EFFECTS OCCUR

LIVER DISORDERS: PATIENTS OR THEIR CARERS SHOULD BE TOLD HOW TO RECOGNIZE SIGNS OF LIVER DISORDERS AND ADVISED TO DISCONTINUE TREATMENT AND SEEK IMMEDIATE MEDICAL ATTENTION IF SYMPTOMS SUCH AS PERSISTENT NAUSEA, VOMITING, MALAISE OR JAUNDICE DEVELOP.

Adverse effects: Severe GI disturbances including anorexia, nausea, vomiting, and diarrhoea (antibiotic-associated colitis reported); headache, drowsiness; rashes, fever, influenza-like syndrome and respiratory symptoms, collapse, shock, haemolytic anaemia, acute renal failure, and thrombocytopenic purpura—more frequent with intermittent therapy; alterations of liver function—jaundice and potentially fatal hepatitis (dose related; do not exceed maximum dose of 600 mg daily); oedema, muscular weakness and myopathy, exfoliative dermatitis, toxic epidermal necrolysis, pemphigoid reactions, leukopenia, eosinophilia and menstrual disturbances reported; urine, tears, saliva, and sputum coloured orange-red.

Advice to patients: See labels 8, 14 and 22 in Appendix 6. May discolour urine, tears, sweat, or other body fluids to a red-orange colour; take 1 hour before or 2 hours after a meal on an empty stomach; soft contact lenses may be permanently stained; report to physician any severe or persistent flu-like symptoms, nausea, vomiting, dark urine or pale stools, or unusual bleeding or bruising.

Nursing considerations: •Obtain specimen for C&S test including sputum before treatment.

•Give on an empty stomach (i.e., 1 hour prior to or 2 hours after meals) to increase total absorption; it may, however, be given with meals if GI irritation occurs; give antiemetic if vomiting occurs.

•Advise against use with alcohol as it may increase risk of hepatotoxicity.

•Monitor hepatic function and serum uric acid regularly.

•Observe for signs of hepatic impairment namely fever, loss of appetite, fatigue, malaise, jaundice, dark urine, liver tenderness, and report to the physician.

•Warn patient about possible discolouration of the urine, tears, sweat, or other body fluids to a red-orange colour; soft contact lenses may be permanently stained.

•The newborns of rifampicin-treated mothers may suffer haemorrhage.

Dose: *Tuberculosis (combination therapy; see notes and tables above)*, by mouth, ADULT and CHILD 10 mg/kg daily or 3 times weekly (maximum dose, 600 mg daily).

PATIENT ADVICE: TAKE DOSE AT LEAST 30 MINUTES BEFORE A MEAL, AS ABSORPTION IS REDUCED WHEN TAKEN WITH FOOD.

POM **Rifampicin** *(WMF 6.2.4)*
Capsules, Rifampicin 150 mg, 300 mg.

POM **Rifampicin** *(EDL 6.10)*
Tablet or capsule, Rifampicin 150 mg, 300 mg.

POM **RECIN®** *(Strides Vital)*
Capsule, Rifampicin 300 mg.
300 mg – 10 x 10's.

POM **RIFACAP®** *(Hovid)*
Capsule, Rifampicin 300 mg
300 mg - 10 x 10 (blister)

POM **RIFACIN®** *(Fill Pharma)*
Capsule, Rifampicin BP 300 mg

POM **Rifampicin** *(Mopson)*
Syrup, Rifampicin 150 mg per 5 ml; dry powder for reconstitution.
Pack - 60 ml.

POM **RIFAN®** *(Titan)*
Capsule, Rifampicin 300 mg.
300 mg - 10 x 10 (blister).

POM **RIFANEX®** *(Titan)*
Capsule, Rifampicin 300 mg, INH 150 mg.
Pack - 10 x 10 (blister).

POM **RIFASAM®** *(Sam)*
Capsule, Rifampicin 300 mg.
300 mg - 100; 10 x 10 (blister).

POM **RIMACTANE®** *(Novartis)*
Capsules, Rifampicin 150 mg (red cap. coded 'JZ150'), 300 mg (red/brown cap. coded 'CS 300'). Both marked 'CIBA'.
150 mg - 100
300 mg - 100

RIFAMPICIN plus ISONIAZID

Indications: Tuberculosis (see notes and tables above).

Contra-indications: See under Rifampicin and Isoniazid.

Precautions: Combined preparation usually not suitable for use in children; see under Rifampicin and Isoniazid.

Adverse effects: See under Rifampicin and Isoniazid.

Dose: *Tuberculosis, 6-month regimen (combination therapy; see notes and tables)*, by mouth, ADULT 10 mg/kg

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(rifampicin) and 5 mg/kg (isoniazid) daily.

Tuberculosis, 6-month regimen (combination therapy; see notes and tables), by mouth, ADULT 10 mg/kg (rifampicin) and 10 mg/kg (isoniazid) 3 times a week.

POM **Rifampicin plus Isoniazid** *(WMF 6.2.4)*

Tablets, Rifampicin 60 mg with isoniazid 30 mg; Rifampicin 150 mg with isoniazid 75 mg; Rifampicin 300 mg with isoniazid 150 mg; Rifampicin 60 mg with isoniazid 60 mg; Rifampicin 150 mg with isoniazid 150 mg.

POM **Rifampicin plus Isoniazid** *(EDL 6.10)*

Tablets, Rifampicin 150 mg, isoniazid 100 mg; rifampicin 300 mg, isoniazid 150 mg.

POM **RIMACTAZID-300®** *(Novartis)*

Tablets, Rifampicin 300 mg, isoniazid 150 mg; coated tab.

Pack - 40.

Dose: Adult (50 kg or more), 2 tabs once daily i.e., 600 mg rifampicin + 300 mg INH.

Total duration 9 months

For 2 months: 2 tabs Rimactazid® 300 + ethambutol 1.2 g, or streptomycin 1 g daily.

For 7 months: 2 tabs Rimactazid® 300 daily.

Total duration 6 months

For 2 months: 2 tabs Rimactazid® 300 + pyrazinamide 1.5-2.5 g + ethambutol 1.2 g, or streptomycin 1 g daily.

For 4 months: 2 tabs Rimactazid® 300 daily.

RIFAMPICIN plus ISONIAZID plus PYRAZINAMIDE

Indications: Tuberculosis, in combination with other drugs (see notes and tables above).

Contra-indications: Combined preparation not suitable for use in children; see Rifampicin, Isoniazid, and Pyrazinamide.

Precautions: See Rifampicin, Isoniazid, and Pyrazinamide.

Adverse effects: See Rifampicin, Isoniazid, and Pyrazinamide.

Dose: *Tuberculosis, initial phase of 6-month treatment regimens (see notes and tables above)*, by mouth, ADULT rifampicin 10 mg/kg, isoniazid 5 mg/kg, and pyrazinamide 25 mg/kg daily or rifampicin 10 mg/kg, isoniazid 10 mg/kg, and pyrazinamide 35 mg/kg 3 times a week.

POM **Rifampicin plus Isoniazid plus Pyrazinamide** *(WMF 6.2.4)*

Tablets, Rifampicin 60 mg, isoniazid 30 mg, and pyrazinamide 150 mg; Rifampicin 150 mg, isoniazid 75 mg, and pyrazinamide 400 mg; Rifampicin 150 mg, isoniazid 150 mg, and pyrazinamide 500 mg.

RIFAMPICIN plus ISONIAZID plus PYRAZINAMIDE plus ETHAMBUTOL

Indications: Tuberculosis (see notes and tables above).

Contra-indications: Combined preparation not suitable for use in children; see Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol HCl.

Precautions: See Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol HCl.

Adverse effects: See Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol HCl.

Dose: *Tuberculosis, induction phase of 6-month regimen (see notes and tables above)*, by mouth, ADULT rifampicin 10 mg/kg, isoniazid 5 mg/kg, pyrazinamide 25 mg/kg, and ethambutol HCl 15 mg/kg daily.

POM **Rifampicin plus Isoniazid plus Pyrazinamide plus Ethambutol** *(WMF 6.2.4)*

Tablets, Rifampicin 150 mg, isoniazid 75 mg, pyrazinamide 400 mg, and ethambutol HCl 275 mg.

STREPTOMYCIN

Indications: Tuberculosis, in combination with other drugs (see notes and tables above).

Contra-indications: Hearing disorders; myasthenia gravis; pregnancy (Appendix 2).

Precautions: Children—painful injection, avoid use if possible; renal impairment (Appendix 4), infants, and elderly (dosage adjustment and monitor renal, auditory, and vestibular function, and plasma streptomycin concentrations); **interactions**: Appendix 1.

Adverse effects: Vestibular and auditory damage, nephrotoxicity; hypersensitivity reactions—withdraw treatment;

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paraesthesia of mouth; rarely, hypomagnesaemia on prolonged therapy; antibiotic-associated colitis; also, nausea, vomiting, rash; rarely, haemolytic anaemia, aplastic anaemia, agranulocytosis, thrombocytopenia; pain and abscess at injection site.

Dose: *Tuberculosis (initial phase of combination therapy; see notes and tables above)*, by deep intramuscular injection, ADULT and CHILD 15 mg/kg daily or 3 times a week (patients over 60 years or those weighing less than 50 kg may not tolerate doses above 500–750 mg daily).

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

NOTE: ONE HOUR (PEAK) CONCENTRATION SHOULD BE 15–40 MG/LITRE; PRE-DOSE (TROUGH) CONCENTRATION SHOULD BE LESS THAN 5 MG/LITRE (LESS THAN 1 MG/LITRE IN RENAL IMPAIRMENT OR THOSE OVER 50 YEARS).

POM **Streptomycin** *(WMF 6.2.4)*
Injection (Powder for solution for injection), streptomycin (as sulfate) 1-g vial.

BCG VACCINE

BCG vaccine should comply with the recommendations published in the report of the WHO Expert Committee on Biological Standardization, WHO Technical Report Series, No. 745, 1987 and Amendment 1987, WHO Technical Report Series, No. 771, 1988.

Indications: For active immunization against tuberculosis; see also section 17.1.1.1.

Contra-indications: See section 17.1.1; generalized oedema; hypogammaglobulinaemia and immunodeficiency due to antimetabolites, irradiation, corticosteroids; HIV positive—except asymptomatic children in areas of high tuberculosis risk; malignant disease; antimycobacterial treatment.

Precautions: See section 17.1.1; pregnancy (Appendix 2); eczema, scabies—vaccine site must be lesion-free; **interactions**: Appendix 1.

Adverse effects: Lymphadenitis and keloid formation; osteitis and localized necrotic ulceration; rarely, disseminated BCG infection in immunodeficient patients; rarely, anaphylaxis.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization against tuberculosis, by intradermal injection, infants up to 3 months, 0.05 ml; ADULT and CHILD over 3 months 0.1 ml.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **BCG Vaccine** *(WMF 6.2.4)*
Injection (Powder for solution for injection), Live bacteria of a strain derived from the bacillus of Calmette and Guérin.

TUBERCULIN PURIFIED PROTEIN DERIVATIVE

All tuberculins should comply with the WHO Requirements for Tuberculins (revised 1985). WHO Expert Committee on Biological Standardization Thirty-sixth report (WHO Technical Report Series, No. 745, 1987, Annexe 1).

Synonym: Tuberculin PPD

Indications: Test for hypersensitivity to tuberculoprotein.

Contra-indications: Should not be used within 3 weeks of receiving a live viral vaccine.

Precautions: Elderly; malnutrition, viral or bacterial infections (including HIV and severe tuberculosis), malignant disease, corticosteroid or immunosuppressant therapy—diminished sensitivity to tuberculin; avoid contact with open cuts, abraded or diseased skin, eyes or mouth.

Adverse effects: Occasionally nausea, headache, malaise, rash; immediate local reactions (more common in atopic patients); rarely, vesicular or ulcerating local reactions, regional adenopathy and fever.

Dose: NOTE: NATIONAL RECOMMENDATIONS MAY VARY.

Test for hypersensitivity to tuberculoprotein, by intradermal injection, ADULT and CHILD 5 or 10 units (1 unit may be used in hypersensitive patients or if tuberculosis is suspected).

ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Tuberculin purified protein derivative** *(WMF 6.2.4)*
Injection, Tuberculin purified protein derivative 10 units/ml, 100 units/ml.

9.2 Systemic antifungal drugs

Fungal infections can be superficial or systemic. Superficial infections affect only the skin, hair, nails or mucous membranes whereas systemic fungal infections affect the body as a whole.

Systemic fungal infections are sometimes

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caused by inhalation, ingestion or inoculation of primary pathogens, and sometimes by opportunistic invasion of commensals in patients with lowered host resistance. They are increasing in prevalence not only because of the pandemic of HIV infection, but also because of the rise in illicit intravenous drug use in many countries, and greater use of broad spectrum antibiotics and invasive medical procedures. In immunodeficient patients systemic fungal infections are often disseminated.

Amphotericin B is a lipophilic polyene antibiotic; it is fungistatic against a broad spectrum of pathogenic fungi, including *Candida* spp., *Aspergillus* spp., *Cryptococcus neoformans* , *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Coccidioides immitis*, *Paracoccidioides brasiliensis*, *Mucor*, *Absidia* and *Phicopes* spp.; it is active against algal *Prototheca* spp. and against the *Leishmania protozoa*. It is used for the empirical treatment of serious fungal infections and is used in conjunction with flucytosine to treat cryptococcal meningitis and systemic candidosis.

Amphotericin B has to be administered parenterally as there is little or no absorption from the gastrointestinal tract; amphotericin B is liable to cause nephrotoxicity. Duration of therapy varies with the initial severity of the infection and the clinical response of the patient. In some infections a satisfactory response is only obtained after several months of continuous treatment. Intrathecal infusion has been used successfully in patients with meningeal coccidioidomycosis.

Fluconazole, an orally active synthetic imidazole derivative, possesses fungistatic activity against dermatophytes, yeasts and other pathogenic fungi. It is widely used in the treatment of serious gastrointestinal and systemic mycoses as well as in the management of superficial infections. Fluconazole is also used to prevent fungal infections in immunocompromised patients.

Flucytosine is a synthetic fluorinated pyrimidine with a narrow spectrum of antifungal activity, particularly against *Cryptococcus* and *Candida* spp. In susceptible fungi, it is converted to fluorouracil by cytosine deaminase. Flucytosine is myelosuppressive and plasma concentrations above 75 micrograms/ml are associated with myelotoxicity.

Griseofulvin is a fungistatic antibiotic derived from *Penicillium griseofulvum* with selective activity against the dermatophytes causing ringworm, *Microsporum canis*, *Trichophyton rubrum* and *T. verrucosum*. It has no activity against pityriasis versicolor or candida infections. Griseofulvin is deposited selectively in keratin precursor cells of skin, hair and nails where it disrupts the mitotic apparatus of fungal cells thus preventing fungal invasion of newly-formed cells. It is unsuitable for prophylactic use. Close attention should be given to hygiene and to possible reservoirs of reinfection in clothing, footware and bedding.

Nystatin, a polyene antifungal antibiotic derived from *Streptomyces noursei*, is effective against infections caused by a wide range of yeasts and yeast-like fungi. It is poorly absorbed from the gastrointestinal tract and it is not absorbed from the skin or mucous membranes when applied topically. It is used for the prophylaxis and treatment of candidosis.

Potassium iodide aqueous oral solution is a clear liquid with a characteristic, strong salty taste. It is effective against sporotrichosis and subcutaneous phycomycosis, which are fungal infections caused by *Sporothrix schenckii* and *Basidiobolus haptosporus* respectively. In subcutaneous sporotrichosis, amphotericin B is often effective in patients unable to tolerate iodides. Itraconazole, by mouth has been tried as an alternative to potassium iodide in both cutaneous and extracutaneous sporotrichosis. In phycomycosis, fluconazole may be effective.

AMPHOTERICIN B

Amphotericin B is a complementary antifungal drug.

Indications: Life-threatening fungal infections including histoplasmosis, coccidioidomycosis, paracoccidioidomycosis, blastomycosis, aspergillosis, cryptococcosis, mucormycosis, sporotrichosis, and candidosis; leishmaniasis (section 9.3.3)

Precautions: Close medical supervision throughout treatment and initial test dose required (see note, below); renal impairment (Appendix 4); hepatic and renal function tests; blood counts and plasma

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electrolyte monitoring; corticosteroids (avoid, except to control reactions); pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid rapid infusion (risk of arrhythmias); **interactions**: Appendix 1.

ANAPHYLAXIS: ANAPHYLAXIS OCCURS RARELY WITH INTRAVENOUS AMPHOTERICIN B AND A TEST DOSE IS ADVISABLE BEFORE THE FIRST INFUSION. THE PATIENT SHOULD BE OBSERVED FOR ABOUT 30 MINUTES AFTER THE TEST DOSE.

Adverse effects: Fever, headache, anorexia, weight loss, nausea and vomiting, malaise, diarrhoea, muscle and joint pain, dyspepsia, and epigastric pain; renal function disturbances including hypokalaemia, hypomagnesaemia and renal toxicity; blood disorders; cardiovascular toxicity (including arrhythmias); neurological disorders (including peripheral neuropathy); abnormal liver function (discontinue treatment); rash; anaphylactoid reactions (see above); pain and thrombophlebitis at injection site.

Advice to patients: Report any cramping, muscle weakness, or pain at or near injection site.

Nursing considerations: •Obtain specimen for C&S test including sputum before treatment.

•Give a test dose and monitor patient's pulse, respiration, temperature, B.P. for about 30 minutes prior to the amphotericin B infusion; avoid rapid injection which may cause circulation collapse (usually 4- to 6-hourly infusion required).

•Reconstitute the dry form with 10 ml of sterile water only.

•Do not use if solution contains precipitate.

•Give antipyretic, antihistamine or antiemetic as premedication to prevent adverse effects fever, chills, headache as needed.

•Monitor for signs of hypokalaemia (muscle weakness, cramping, drowsiness, anorexia, etc.).

Dose: *Systemic fungal infections*, by intravenous infusion, ADULT and CHILD initial test dose of 1 mg over 20–30 minutes, then 250 micrograms/kg daily, gradually increased up to 1 mg/kg daily or in severe infection, up to 1.5 mg/kg daily or on alternate days.

NOTE: PROLONGED TREATMENT USUALLY NECESSARY; IF INTERRUPTED FOR LONGER THAN 7 DAYS, RECOMMENCE AT 250 MICROGRAMS/KG DAILY AND INCREASE GRADUALLY. RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Amphotericin B** *(WMF 6.3)*

Injection (Powder for solution for injection), amphotericin B 50-mg vial.

POM **Amphotericin B** *(EDL 6.11)*

Injection, Amphotericin B 50 mg; in vial.

FLUCONAZOLE

Fluconazole is a representative azole antifungal. Various drugs can serve as alternatives.

Indications: Systemic mycoses including histoplasmosis, non-meningeal coccidioidomycosis, paracoccidioidomycosis and blastomycosis; treatment and, in AIDS and other immunosuppressed patients, prophylaxis of cryptococcal meningitis; oesophageal and oropharyngeal candidosis, vaginal candidosis and systemic candidosis.

Precautions: Renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); monitor liver function—discontinue if signs or symptoms of hepatic disease (risk of hepatic necrosis; Appendix 5); **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, abdominal pain; flatulence, diarrhoea; headache, taste disturbance, hepatic disorders, dizziness, seizures, alopecia, pruritus; rash (withdraw treatment); angioedema, anaphylaxis, bullous lesions, toxic epidermal necrolysis and erythema multiforme (Stevens-Johnson syndrome) reported (skin reactions more common in AIDS); hyperlipidaemia, leukopenia, thrombocytopenia, hypokalaemia.

Advice to patients: See Label 9 in Appendix 6. May take with food; complete full course of therapy; contact physician or pharmacist if side effects develop.

Nursing considerations: •Oral bioavailability of fluconazloe is greater than 90% and is unaffected by gastric pH; dosage is the same for oral or I.V use.

•Administer with food to reduce GI upset; shake oral suspension before each use.

•I.V. fluconazole may be administered by continous infusion at a rate not exceeding 200 mg/hour; do not connect in series with other infusions to prervent air embolism; do not add any other drugs to the solution.

•Advise patient that prolonged treatment may be needed to control infection and prevent relapse, even if symptoms abate in first few days of therapy.

•Dosage should be adjusted in renal failure as the drug is excreted unchanged by the kidneys.

Dose: *Systemic mycoses*, by mouth or by intravenous infusion, ADULT 200 mg daily for at least 6 months; CHILD over 2 years 3–6 mg/kg daily for at least 6 months.

Cryptococcal meningitis (following amphotericin B induction therapy), by mouth or by intravenous infusion, ADULT 800 mg daily for 2 days, then

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400 mg daily for 8 weeks; CHILD 6–12 mg/kg daily (every 72 hours in neonates up to 2 weeks old, every 48 hours in neonates 2–4 weeks old).
Prevention of relapse of cryptococcal meningitis in AIDS patients after completion of primary therapy, by mouth or by intravenous infusion, ADULT 100–200 mg daily.
Systemic candidosis (in patients unable to tolerate amphotericin B), by mouth or by intravenous infusion , ADULT 400 mg as initial dose, then 200 mg daily for at least 4 weeks; CHILD 6–12 mg/kg daily (every 72 hours in neonates up to 2 weeks old, and every 48 hours in neonates 2–4 weeks old).
Oesophageal and oropharyngeal candidosis, by mouth or by intravenous infusion, ADULT 200 mg as an initial dose, then 100 mg daily until symptoms resolved; up to 400 mg daily in very resistant infections; CHILD 3–6 mg/kg on the first day, then 3 mg/kg daily (every 72 hours in neonates up to 2 weeks old, every 48 hours in neonates 2–4 weeks old).
Vaginal candidosis, by mouth, ADULT 150 mg as a single dose.

POM **Fluconazole** *(WMF 6.3)*
Capsules, Fluconazole 50 mg.
Oral suspension (Powder for oral suspension), Fluconazole 50 mg/5 ml.
Infusion (Solution for infusion), Fluconazole 2 mg/ml, 25-ml bottle, 100-ml bottle.

POM **DIFLUCAN®** *(Pfizer)*
Capsule, Fluconazole 50 mg.
50 mg - 3; 30.
Suspension, Fluconazole 50 mg per 5 ml; powder for oral suspension. To be reconstituted with 24 ml of water.

POM **FLUZON®** *(Interpharma)*
Tablets, Fluconazole 100 mg, 150 mg.
100 mg - 5 x 4's
150 mg - 10 x 2's.

FLUCYTOSINE

Flucytosine is a complementary drug.
Indications: Adjunct to amphotericin B (or fluconazole) in cryptococcal meningitis; adjunct to amphotericin B in systemic candidosis.
Precautions: Elderly; renal impairment (Appendix 4); also use with amphotericin B (both nephrotoxic); liver- and kidney function tests and blood counts required (weekly in renal impairment or in blood disorders); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Rash, nausea, vomiting and diarrhoea; alterations in liver function tests; less frequently, confusion, hallucinations, convulsions, headache, sedation, vertigo; blood disorders including leukopenia, potentially fatal thrombocytopenia and aplastic anaemia.
Dose: *Systemic candidosis and cryptococcosis*, by intravenous infusion (over 20–40 minutes), ADULT and CHILD 200 mg/kg daily in 4 divided doses, for usually no more than 7 days (at least 4 months in cryptococcal meningitis); extremely sensitive organisms, 100–150 mg/kg daily in 4 divided doses.
Systemic candidosis, initial treatment or after intravenous therapy, by mouth, ADULT and CHILD 50–150 mg/kg daily in 4 divided doses.
NOTE: FOR PLASMA CONCENTRATION MONITORING BLOOD SHOULD BE TAKEN SHORTLY BEFORE STARTING NEXT INFUSION (OR BEFORE NEXT DOSE BY MOUTH); PLASMA CONCENTRATION FOR OPTIMUM RESPONSE 25–50 MG/LITRE—SHOULD NOT BE ALLOWED TO EXCEED 80 MG/LITRE.

POM **Flucytosine** *(WMF 6.3)*
Capsules, Flucytosine 250 mg.
Infusion (Solution for infusion), Flucytosine 10 mg/ml, 250-ml infusion.

GRISEOFULVIN

Indications: Fungal infections of the skin, scalp, hair and nails where topical treatment has failed or is inappropriate.
Contra-indications: Severe liver disease (Appendix 5); pregnancy (avoid pregnancy during and for 1 month after treatment; men should not father children within 6 months of treatment; Appendix 2); porphyria; systemic lupus erythematosus and related disorders.
Precautions: Pre-existing hepatic insufficiency (closely monitor hepatic function throughout treatment); blood disorders (monitor blood count weekly during first month of treatment); breastfeeding; **interactions**: Appendix 1.
SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

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Adverse effects: Headache, nausea, vomiting, diarrhoea, rashes, dizziness, fatigue reported; dry mouth and angular stomatitis; leukopenia, agranulocytosis; proteinuria reported; photosensitivity; lupus erythematosus, toxic epidermal necrolysis, erythema multiforme; serum sickness, angioedema; peripheral neuropathy; confusion and impaired coordination.

Advice to patients: See Labels 9 and 21 in Appendix 6. Take with fatty meal for better absorption; avoid exposure to sunlight; if patient gets headache, it usually goes away with continued therapy; may cause dizziness, drowsiness, and impair judgement; do not drive or perform other hazardous activities; effect of alcohol enhanced by the drug; do not take if pregnant; if you become pregnant, discontinue immediately.

Nursing considerations: •Advise patient that prolonged treatment may be needed to control infection and prevent relapse, even if symptoms abate in first few days of therapy.

•Most effectively absorbed and causes least GI distress when given after high-fat meal.

•Tell patient to keep skin clean and dry and to avoid intense sunlight.

•Advise patient to avoid alcoholic beverages.

Dose: *Superficial fungal infections*, by mouth , ADULT 0.5–1 g (but not less than 10 mg/kg) daily with food in single or divided doses; CHILD 10 mg/kg daily with food in single or divided doses.

NOTE: DURATION OF TREATMENT DEPENDS ON THE INFECTION AND THICKNESS OF KERATIN AT SITE OF INFECTION; AT LEAST 4 WEEKS FOR SKIN AND HAIR, AT LEAST 6 WEEKS FOR SCALP RINGWORM AND IN SEVERE INFECTION, UP TO 3 MONTHS; 6 MONTHS FOR FINGERNAILS AND 12 MONTHS OR MORE FOR TOENAILS.

POM **Griseofulvin** *(WMF 6.3)*
Tablets, Griseofulvin 125 mg, 250 mg.
Capsules, Griseofulvin 250 mg.

POM **Griseofulvin** *(EDL 6.11)*
Tablet, Griseofulvin 125 mg, 500 mg.
Suspension, Griseofulvin 125 mg per 5 ml.

POM **GENEVIN®** *(Geneith)*
Tablet, Griseofulvin 500 mg.
500 mg – 10's (in blister).

POM **GRIFULVIN®** *(Dizpharm)*
Tablet, Griseofulvin 125 mg.
125 mg - 100.

POM **GRISACTIN®** *(Wyeth/Delpitano)*
Tablet, Griseofulvin 500 mg.
500 mg - 60
Capsules, Griseofulvin 125 mg, 250 mg.
125 mg - 100
250 mg - 100; 500.

POM **GRISAM®** *(Sam)*
Tablets, Griseofulvin 125 mg, 500 mg
125 mg - 1000
500 mg - 20; 250

POM **Griseofulvin** *(Hovid)*
Tablets, Griseofulvin 125 mg, 500 mg; f-c tabs.
125 mg - 1000
500 mg - 20; 500.

POM **GRISOVIN®** *(GSK)*
Tablets, Griseofulvin 125 mg, 500 mg; white f-c biconvex tabs. marked 'GLAXO' and 'GRISOVIN 125' and 'GRISOVIN 500' respectively.
125 mg - 20; 1000.
500 mg - 20; 250.

POM **KEZZ GRISEOFULVIN®** *(Kezz)*
Tablet, Griseofulvin BP 500 mg; f-c tab.
500 mg – 20's (in blister).

POM **RECGRISO®** *(GoldMoore)*
Tablet, Griseofulvin BP 500 mg.
Pack - 20's.

POM **RYSOVIN-500®** *(Beta Drugs)*
Tablet, Griseofulvin BP 500 mg.
500 mg – 20's (in blister).

POM **VITAFULWIN®** *(Strides Vital)*
Tablet, Griseofulvin 500 mg; white scored tab. marked 'GRISEO 500'.
500 mg - 20's.

ITRACONAZOLE

Therapeutic category: Antifungal agent, systemic.

Pharmacology: Itraconazole is a triazole derivative active against infections with dermatophytes, yeast, Aspergillus spp and various other yeasts and fungi. Oral bioavailability is maximal when it is given immediately after a full meal. It is extensively metabolized by the liver and should be avoided in patients with a history of liver disease.

Indications: Vulvovaginal candidosis, pityriasis versicolor, dermatophytoses, fungal keratitis, oral candidosis; may also be used in systemic fungal infections (including aspergillosis, candidiasis, and cryptococcosis) where other antifungal drugs are inappropriate or in-

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effective.

Contra-indications: Pregnancy; hypersensitivity to any component.

Precautions: Patients with history of liver disease; breast-feeding; renal impairment (bioavailability may be reduced); children; elderly.

Interactions: •Avoid co-administration with astemizole, terfenadine, cisapride, rifampicin, antacids, H_2 antagonists such as cimetidine.

Adverse effects: Nausea, abdominal pain, headache, dyspepsia, constipation, (diarrhoea and vomiting with oral liquid), dizziness, fatigue; hypersensitivity reactions such as rash, pruritus, urticaria and angio-oedema; decreased libido, impotence; abnormal hepatic function.

Advice to patients: See labels 9, 21 and 25 in Appendix 6. Take with food; report any signs and symptoms that may suggest liver dysfunction so that appropriate laboratory testing can be done; such signs and symptoms may include unusual fatigue, anorexia, nausea and/or vomiting, jaundice, dark urine or pale stool.

Nursing considerations: •Administer capsule whole after full meal to ensure absorption.

•Advise patient that prolonged treatment may be needed to control infection and prevent relapse, even if symptoms abate in first few days of therapy.

•*See also under Ketoconazole*.

Dose: By mouth, *Vulvovaginal candidosis*, 200 mg morning and evening for 1 day; *Oral candidosis*, 100 mg daily for 15 days; *Pityriasis versicolor*, 200 mg daily for 7 days; *Tinea corporis and tinea cruris*, 100 mg daily for 15 days (or 200 mg twice daily for 7 days); *Tinea pedis and tinea manuum*, 100 mg daily for 30 days (or 200 mg twice daily for 7 days); *Onychomycosis*, 200 mg daily for 3 months (or a course of 200 mg twice daily for 7 days, subsequent courses repeated after 21-day interval; finger nails 2 courses, toenails 3 courses). *Histoplasmosis*, 200 mg 1-2 times daily. *Systemic fungal infections where other antifungal drugs are inappropriate or in effective*, 200 mg once daily (candidiasis 100-200 mg once daily); increased in invasive or disseminated disease and cryptococcal meningitis to 200 mg twice daily.

Not recommended for the child and elderly.

POM **ITRANOX**® *(Alpha)*

Tablet, Itraconazole 100 mg; white or almost white oblong film coated tablets.

100 mg - 10

POM **SPORANOX**® (*Janssen-Cilag)*

Capsule, Itraconazole 100 mg; pellets in a blue/pink cap.

100 mg - 4; 15 (in blisters).

KETOCONAZOLE

Therapeutic category: Antifungal agent.

Pharmacology: Ketoconazole is an imidazole-dioxolane antimycotic which acts by inhibiting purine transport and DNA, RNA, and protein synthesis; it increases cell wall permeability, making the fungus more susceptible to osmotic pressure. It is effective orally and has a broad-spectrum of activity against dermatophytes, yeasts and other pathogenic fungi. Much larger doses may be needed to treat fungal meningitis.

Indications: Fungal infections of the skin, hair, nails; yeast infection of the mouth such as oral thrush,; vaginal candidosis; systemic mycotic infections; prophylactic against mycotic infections in patients with reduced host defences e.g. cancer patients.

Contra-indications: Hypersensitivity to the drug; acute or chronic liver disease.

Precautions: Monitor liver enzyme levels for patients with history of liver disease; acute porphyria, pregnancy.

Interactions: •Avoid co-administration with alcohol or hepatotoxic drugs such as terfenadine, cisapride, astemizole, cyclosporine, isoniazid or rifampin.

•Antacids, anticholinergics, antispasmodics, histamine H_2-receptor antagonists or omeprazole may decrease the absorption and hence the antifungal effect of Ketoconazole (give about 2-hour interval).

Adverse effects: Occasionally nausea and vomiting; idiosyncratic liver reaction (discontinue if occur).

Advice to patients: See Labels 5, 9 and 21 in Appendix 6. Avoid taking antacids at the same time as ketoconazole; may take with food; may cause drowsiness, impair judgement or coordination; notify physician of unusual fatigue, anorexia, vomiting, dark urine, or pale stools.

Nursing considerations: •Administer 2 hours prior to antacids or other drugs that increase gastric pH to prevent decreased absorption due to the high pH of gastric contents (it requires acidity for dissolution and absorption).

•Give with acidic products such as fruit juice to aid dissolution and absorption of ketoconazole.

•Advise patient to take oral suspension with straw, to avoid contact with the teeth and to drink a glass of water immediately after; nausea may be minimised if drug is divided into 2 doses;

•Advise patient to avoid driving or other hazardous

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activities if dizziness occurs.
•Teach patient symptoms of liver dysfunction viz unusual fatigue, jaundice, dark urine or pale stools, anorexia, vomiting and to notify physician if they occur.

Dose: By mouth, Adult, *Vaginal candidosis*, 200-400 mg once daily with meals for 5 days.
Pityriasis versicolor, 200 mg once daily with meals for 5 -10 days.
Skin, GI and systemic infections, 200-400 mg once daily with meals usually for 14 days or at least one week after the symptoms have cleared and cultures become negative
Child (upto 15 kg), 20 mg 3 times daily; 15-30 kg, 100 mg once daily; above 30 kg, 200 mg once daily.

POM **Ketoconazole** *(EDL 6.11)*
Tablet, Ketoconazole 200 mg.
Suspension, Ketoconazole 100 mg per 5 ml.

POM **FUNGRAL®** *(Medreich)*
Tablet, Ketoconazole USP 200 mg.

POM **KETACON®** *(Strides Vital)*
Tablet, Ketoconazole 200 mg.
200 mg – 2 x 10's.

POM **Ketoconazole** *(Hovid)*
Tablet, Ketoconazole 200 mg; white scored tab. marked 'H/D'.
200 mg - 10 x 10.

POM **KW Ketoconazole** *(Korlyns)*
Tablet, Ketoconazole 200 mg; white round tablet.
200 mg – 100's.

POM **NIZORAL®** *(Janssen-Cilag)*
Tablet, ketoconazole 200 mg; white scored tab. marked 'JANSSEN' and 'K over 200'.
200 mg - 10, 30.
Suspension, Ketoconazole 100 mg per 5 ml
Pack - 100 ml.

MICONAZOLE

Therapeutic category: Antifungal Agent.
Pharmacology: Miconazole is a synthetic imidazole derivative which acts by inhibiting purine transport and DNA, RNA, and protein synthesis; it increases cell wall permeability, making the fungus more susceptible to osmotic pressure. It has high fungicidal activity against dermatophytes, yeasts and dimorphic fungi as well as bactericidal activity against Gram-positive bacilli and cocci.
Indications: Oral and intestinal candidiasis.
Precautions: Pregnancy.
Adverse effects: Nausea, diarrhoea.
Advice to patients: See labels 9 and 21 in Appendix 6.
Nursing considerations: •May give with meal to lessen GI distress; antiemetic may be needed to prevent nausea and vomiting.
•Encourage good personal hygiene, hand-washing and nail care.
•Inform patient that adequate therapeutic response may take weeks or months.
•*See also under Ketoconazole*.

Dose: By mouth, Adult, 250 mg 4 times daily. Allow to slowly melt in the mouth before swallowing.
Continue treatment for up to 2 days after symptoms have cleared.

POM **Miconazole** *(EDL 6.11)*
Tablet, Miconazole 250 mg.

NYSTATIN

Therapeutic category: Oral nonabsorbed antifungal agent.
Indications: Oral, oesophageal, intestinal, vaginal, and cutaneous candidosis.
Precautions: Pregnancy and breastfeeding (Appendices 2 and 3).
Adverse effects: Nausea, vomiting, diarrhoea at high doses; oral irritation and sensitization; rash and rarely, erythema multiforme (Stevens-Johnson syndrome).
Advice to patients: See label 9 in Appendix 6.
The oral suspension should be swished about the mouth and retained in the mouth for as long as possible (several minutes) before swallowing. For neonates and infants, paint nystatin suspension into recesses of the mouth.
Nursing considerations: •Nystatin is quite safe when used orally, vaginally or topically, but advise patient to report redness, swelling, or irritation.
•Vaginal tablets can be used by pregnant women up to 6 weeks before term to treat maternal infection that may cause thrush in newborns.
•Continue therapy during menstruation.
•Instruct patient to wash applicator thoroughly after each use.
•Explain to the patient that the following factors can predispose to vaginal infection: Use of antibiotics, oral contraceptives, and corticosteroids; diabetes; reinfection by sexual patner; and tight-fitting panty hose.
•For treatment of oral candidiasis (thrush): Be sure the mouth is clean of food debris before administering drug, then tell patient to hold suspension in mouth for several minutes before swallowing. When treating infants, swab medication on oral mucosa. Insrtuct patient on good oral hygiene techniques. Inform patient overuse of mouthwash may alter flora and promote infection

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•Advise patient to continue the medication for the prescribed duration even if symptoms abate.
•Instruct patient on careful hygiene for affected areas
•Not effective against systemic infections

Dose: *Oral candidosis*, by mouth, ADULT and CHILD over 1 month, 100 000 units after food 4 times daily.
Intestinal and oesophageal candidosis, by mouth, ADULT 500 000 units 4 times daily; CHILD over 1 month 100 000 units 4 times daily; continue for 48 hours after clinical cure.
Vaginal candidosis, vaginal administration, ADULT insert 1–2 pessaries at night for at least 2 weeks.

POM **Nystatin** *(WMF 6.3)*
Tablets, Nystatin 100 000 units, 500 000 units.
Oral suspension, Nystatin 100 000 units/ml [not included on WHO Model List].
Lozenge, Nystatin 100 000 units.
Pessaries, Nystatin 100 000 units.

POM **Nystatin** *(EDL 6.11)*
Tablet, Nystatin 500,000 units
Suspension, Nystatin 100,000 units per ml.
Pessary, **See under Section 11.2**

POTASSIUM IODIDE

Potassium iodide is a complementary drug.

Indications: Sporotrichosis; subcutaneous phycomycosis; thyrotoxicosis (section 10.2).

Contra-indications: Hypersensitivity to iodides; pregnancy (Appendix 2); breastfeeding (Appendix 3); acute bronchitis or active tuberculosis.

Precautions: Addison disease; cardiac disease; hyperthyroidism; myotonia congenita; renal impairment.

Adverse effects: Goitre, hypothyroidism, hyperthyroidism; iodism characterized by metallic taste, increased salivation, coryza and irritation and swelling of the eyes (resulting from prolonged administration); also gastrointestinal disturbances and diarrhoea; pulmonary oedema, bronchitis; depression, insomnia, impotence, headache reported.

Dose: *Sporotrichosis and subcutaneous phycomycosis*, by mouth, ADULT initially 1 ml 3 times daily, increased by 1 ml daily, depending on tolerance, to 10 ml daily; continue treatment for at least 4 weeks after resolution or stabilization of lesions.

NOTE: IF SIGNS OF IODISM OCCUR, SUSPEND TREATMENT TEMPORARILY AND RESTART AFTER A FEW DAYS AT LOWER DOSAGE.

POM **Potassium iodide** *(WMF 6.3)*
Oral solution, Potassium iodide 1 g/ml (saturated solution).

TERBINAFINE

Therapeutic category: Broad spectrum antifungal agent

Pharmacology: Terbinafine is an allylamine which has a broad spectrum of antifungal activity. It acts by interfering specifically with fungal sterol biosynthesis at an early step resulting in a deficiency in ergosterol, intracellular accumulation of squalene and fungal cell death. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity against yeasts is fungicidal or fungistatic, depending on the species. When given orally, the drug concentrates in skin and nails at levels associated with fungicidal activity.

Indications: Treatment of ringworm (tinea corporis, tinae cruris and tinea pedis) and yeast infections of the skin caused by the genus candida where oral therapy is considered appropriate owing to the site, severity or extent of the infection; onychomycosis (fungal infection of the nail) caused by dermotophyte fungi. Oral terbinafine is not effective in pityriasis versicolor; the topical form is recommended.

Precautions: Severe liver dysfunction or impaired renal function (reduce dose) ; pregnancy, breast feeding.

Interactions: Rifampicin, cimetidine

Adverse effects: GI symptoms such as fullness, mild abdominal pain; skin reactions such as rash, urticaria.

Advice to patients: See label 9 in Appendix 6.

Nursing considerations: •Teach patient symptoms of liver dysfunction viz unusual fatigue, jaundice, dark urine or pale stools, anorexia, vomiting and to notify physician if they occur.

Dose: By mouth, Adult, 125 mg twice a day or 250 mg once a day; duration of treatment depends on the indication and severity *Tinea pedis*: 2-6 weeks
Tinea corporis, cruris: 2-4 weeks
Cutaneous candidiasis: 2-4 weeks
Onychomycosis: 6 weeks - 3 months
Child: not yet recommemded.

POM **LAMISIL®** *(Novartis)*

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Tablets, Terbinafine (as HCl) 125 mg, 250 mg; off-white, scored tabs.

9.3 Antiprotozoal drugs

9.3.1 Antimalarial drugs
9.3.2 Antiamoebic, antigiardial and antitrichomonal drugs
9.3.3 Antileishmanial drugs
9.3.4 Antitrypanosomal drugs
9.3.5 Antipneumocystosis and antitoxoplasmosis drugs

9.3.1 Antimalarial drugs

Human malaria, which is transmitted by anopheline mosquitoes (and rarely by congenital transmission, transfusion of infected blood or use of contaminated syringes among drug addicts), is caused by four species of plasmodial parasites. *Plasmodium vivax* is the most extensively distributed and causes much debilitating disease. *P. falciparum* is also widespread, and causes the most severe infections which are responsible for nearly all malaria-related deaths. *P. ovale* is mainly confined to Africa and is less prevalent, while *P. malariae*, which causes the least severe but most persistent infections, also occurs widely.

Certain tissue forms of *P. vivax* and *P. ovale* which persist in the liver for many months and even years are responsible for the relapses characteristic of malaria. Such latent forms are not generated by *P. falciparum* or *P. malariae*. Recrudescence of these infections results from persistent blood forms in inadequately treated or untreated patients.

Treatment of malaria

Blood schizontocides, which suppress malaria by destroying the asexual blood forms of the parasites, are the mainstay of the treatment of acute malaria and some are used for prophylaxis. They include the 4-aminoquinolines (**amodiaquine** and **chloroquine**), the related arylaminoalcohols (**mefloquine** and **quinine**), and **artemisinin** and its derivatives (**artemether** and **artesunate**). Blood schizontocides are not active against intrahepatic forms and therefore they do not eliminate infections by *P. vivax* and *P. ovale*.

Some antimetabolites act synergistically when given in combination. For example, **pyrimethamine** in combination with a sulfonamide (**sulfadoxine**) or sulfone and some antibiotics (for example **doxycycline**) are blood schizontocides. Because they act more slowly, these substances are of little value when used alone. The tetracyclines are used primarily as adjuncts to quinine where multiple-drug-resistant *P. falciparum* is prevalent.

Chloroquine, a rapidly acting schizontocide, is well tolerated, safe and inexpensive. It should be used to treat malaria wherever the parasites remain susceptible. *P. malariae* and *P. ovale* remain fully sensitive to chloroquine. However, chloroquine-resistant strains of *P. falciparum* are widespread in south-east Asia, parts of the Indian subcontinent, South America, Africa and Oceania; strains of *P. vivax* in Papua New Guinea and Indonesia are also resistant to chloroquine.

A 3-day course of chloroquine by mouth is sufficient to eliminate susceptible *P. falciparum* infections because effective plasma-chloroquine concentration is sustained for several weeks.

If subsequent relapse occurs in *P. ovale* and *P. vivax* infections **primaquine** should be administered, after a second course of chloroquine, to eliminate the intrahepatic infection.

Amodiaquine is an alternative to chloroquine for the treatment of uncomplicated *P. falciparum* infection; but cross-resistance with chloroquine exists in some areas. It should preferably be used as part of combination therapy with other antimalarials, for example artesunate. Hepatitis and blood disorders were reported when amodiaquine was used for prophylaxis of malaria; patients should be told how to recognise the symptoms of these conditions and advised to seek medical help if they occur.

The combination of **sulfadoxine with pyrimethamine** is recommended for the treatment of malaria only in areas of high chloroquine resistance. A single dose of sulfadoxine with pyrimethamine is usually sufficient to eliminate infection; quinine should also be given for 3 days in patients in whom quinine may accelerate reduction of parasitaemia and in those at risk of fulminating disease. However, resistance to these combinations is now widespread, particularly in south-east Asia and South America and it occurs at low prevalence in east and central Africa. Because

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sulfonamides are associated with a risk of haemolysis and methaemoglobinaemia in the newborn, quinine is preferred to treat chloroquine-resistant malaria during pregnancy (see note on quinine).

Mefloquine remains effective except in certain areas of resistance in Thailand, Myanmar and Cambodia. No parenteral preparations are currently available, and it is thus suitable only for patients who can take drugs by mouth. It is generally well tolerated, although, some adverse effects have been reported (see notes). However, because of the danger of the emergence of mefloquine-resistant strains of *P. falciparum* and because of its potential toxicity, it should be used only following either microscopic or careful clinical diagnosis of *P. falciparum* infections that are known or strongly suspected to be resistant to chloroquine or sulfadoxine with pyrimethamine.

Quinine, given orally, should be reserved for *P. falciparum* infections likely to be unresponsive to other drugs. Resistance to quinine was, until recently, rare, but the prevalence of resistant strains is now increasing in parts of south-east Asia and South America. Doxycycline, which is an effective oral schizontocide, should be given in combination with quinine except in pregnant women and children under 8 years.

In multi-drug resistant malaria, preparations of **artemisinin** or its derivatives (**artemether** or **artesunate**) offer the only prospect of cure. They should not be used in the first trimester of pregnancy. For the treatment of multiresistant falciparum malaria oral **artesunate** may be an effective antimalarial. It should always be given in combination with mefloquine. Parenteral artemether or artesunate, whose use is restricted, are effective alternatives to quinine for the treatment of severe falciparum malaria and are preferred in areas where decreased efficacy of quinine has been documented. To ensure radical cure following parenteral treatment with artemether or oral treatment with artesunate, a full therapeutic dose of mefloquine should be given. A fixed-dose oral formulation of **artemether with lumefantrine** has recently become available and is recommended for the treatment of uncomplicated falciparum malaria in areas with significant resistance. The combination is not for use in pregnancy or breastfeeding.

Prophylaxis against malaria

No drug regimen gives assured protection to everybody, and indiscriminate use of antimalarials can increase the risk of inducing resistance.

Chloroquine, which is usually well tolerated at the required dosage, is preferred where *P. falciparum* remains fully sensitive. The combination of proguanil with chloroquine may overcome mild chloroquine resistance. Chloroquine must be started 1 week before exposure, and be continued in pregnant women until after delivery and for at least 4 weeks after the last risk of exposure in the case of non-immune individuals. This is sufficient to ensure elimination of *P. falciparum* and *P. malariae*, but not of *P. vivax* and *P. ovale*, whose residual hepatic forms survive.

Mefloquine may be used for prophylaxis in areas of high risk or where multiple-drug resistance has been reported. Where possible prophylaxis should be started 2–3 weeks before travel to enable any adverse reactions to be identified before exposure (over three-quarters of adverse reactions occur by the third dose) and should be continued for 4 weeks after last exposure. Mefloquine may be used for prophylaxis during the second and third trimesters. It should be used in early pregnancy only if alternative drugs are either not available or unlikely to be effective and when it is impracticable for the woman to leave the endemic area.

Proguanil, a predominantly tissue schizontocide with little blood schizontocidal activity, is a causal prophylactic agent since it is active against pre-erythrocytic intrahepatic forms, particularly of *P. falciparum*. The latent persistent liver forms of *P. ovale* and *P. vivax* are unresponsive. However, there is evidence that it may be effective against *P. vivax* only immediately after the initial infection. *P. falciparum* resistance to proguanil or related compounds may occur in malaria endemic areas and particularly where it has been employed in mass prophylaxis. Proguanil is used for prophylaxis with chloroquine in areas where there is resistance to chloroquine but a low risk of infection as it may give some protection against *P. falciparum* and

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may alleviate symptoms if an attack occurs. Proguanil and chloroquine may also be used prophylactically in areas of high risk or multi-drug resistance as a second choice where mefloquine is not appropriate.

There is no evidence that proguanil is harmful in prophylactic doses during pregnancy. Because of the vulnerablility of pregnant women to falciparum malaria, it should be used at full prophylactic dosage wherever the disease is prevalent and likely to be responsive to proguanil, if chloroquine is not available or with chloroquine, if the latter alone is unlikely to be effective.

AMODIAQUINE

Amodiaquine is a restricted drug used for the treatment of malaria.

Indications: Treatment of uncomplicated malaria caused by *P. falciparum.*

Contra-indications: Hepatic impairment (Appendix 5); blood disorders, retinopathy.

Precautions: Pregnancy (Appendix 2) and breastfeeding (Appendix 3); G6PD deficiency; avoid concurrent therapy with hepatotoxic drugs; **interactions**: (Appendix 1).

PATIENT ADVICE: PATIENTS AND THEIR CARERS SHOULD BE TOLD HOW TO RECOGNIZE THE SIGNS OF BLOOD DISORDERS AND ADVISED TO SEEK MEDICAL ATTENTION AS SOON AS POSSIBLE IF SYMPTOMS SUCH AS FEVER, SORE THROAT, RASH, MOUTH ULCERS, PURPURA, BRUISING OR BLEEDING DEVELOP. THEY SHOULD ALSO BE TOLD HOW TO RECOGNIZE SIGNS OF HEPATITIS AND ADVISED TO SEEK MEDICAL ATTENTION IF SYMPTOMS SUCH AS ANOREXIA, ABNORMAL WEIGHT LOSS, ASTHENIA, ABDOMINAL PAINS, FEVER, NAUSEA OR VOMITING DEVELOP.

Adverse effects: Blood disorders including leukopenia and agranulocytosis, hepatitis, gastrointestinal disturbances, visual disturbances (retinopathy associated with long-term, high-dose therapy); rarely rash, pruritus, skin pigmentation, neuromyopathy.

Dose: NOTE: ALL DOSES ARE IN TERMS OF THE BASE.

Treatment of uncomplicated falciparum malaria, by mouth ADULT and CHILD over 20 kg, initially 7.5 mg/kg twice daily for 1 day then 5 mg/kg twice daily for 2 days; total dose, 35 mg/kg over 3 days.

POM **Amodiaquine** *(WMF 6.4.3)*
Tablets, Amodiaquine base (as HCl) 153 mg, 200 mg.

POM **AMOQUIN**® *(Pharma-Deko)*
Tablet, Amodiaquine HCl 200 mg; yellow f-c tab. scored on one side and marked 'AMOQUIN' on the other.
200 mg - 3; 1000.
Syrup, Amodiaquine HCl 50 mg per 5 ml; smooth mustard yellow suspension with a fruity peppermint taste.
Pack - 60 ml.

POM **CAMOQUIN**® *(Pfizer)*
Tablet, Amodiaquine (as HCl) 200 mg; yellow scored tablet.
200 mg – 25 x 3's (in blister).
Suspension, Amodiaquine (as HCl) 50 mg per 5 ml.
Pack – 60 ml.

Amodiaquine + Artesunate combination kit
POM **LARIMAL**® *(IPCA)*
Tablets, Amodiaquine base 153.1 mg, yellow tablet + Artesunate 50 mg, white tablet; in a combination kit containing co-packaged blister packs of Amodiaquine tablets and Artesunate tablets.
Adult Pack - 10 x 1 x 12 + 12 (in blister).
Junior Pack - 10 x 1 x 6 + 6 (in blister).
Child Pack - 10 x 1 x 3 + 3 (in blister).

Dose: Adult, by mouth, 2 Amodiaquine tablets and 2 Artesunate tablets twice daily for 3 days.
Child (above 6 months and 5 kg b. wt.), by mouth, 10 mg/kg b.wt of Amodiaquine and 4 mg/kg b.wt of Artesunate for 3 days.

ARTEMETHER

Artemether is a complementary antimalarial drug for restricted use in the treatment of malaria.

Indications: Treatment of severe *P. falciparum* malaria in areas where evidence that quinine is ineffective.

Contra-indications: First trimester of pregnancy.

Precautions: SKILLED TASKS: DIZZINESS MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Headache, nausea, vomiting, abdominal pain, diarrhoea; dizziness, tinnitus, neutropenia, elevated liver enzyme values; cardiotoxicity (after high doses); neurotoxicity—in animal studies.

Dose: *Treatment of severe P. falciparum malaria (in areas of quinine resistance)*, by intramuscular injection, ADULT and CHILD over 6 months, loading dose of 3.2 mg/kg, then 1.6 mg/kg daily until patient can

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tolerate oral medication or to maximum of 7 days; this is followed by a single dose of mefloquine 15 mg/kg (or occasionally, if necessary 25 mg/kg) to effect a radical cure.

ADMINISTRATION: SINCE SMALL VOLUMES ARE REQUIRED FOR CHILDREN, A 1-ML SYRINGE SHOULD BE USED TO ENSURE CORRECT DOSAGE.

See also under the proprietary preparations below.

Note: For I.M. use only; administer aseptically in the upper-outer quadrant of the buttock. Do mix with other drugs in the same syringe.

Storage conditions: Artemether injection should be protected from light and stored at room temperature. If stored for long periods in the cold, precipitation may occur which may clear on storage at room temperature. If precipitate does not clear, the contents of the ampoules should be discarded. Do not store below room temperature.

The suspension should be stored at a room temperature in their original containers and protected from light and moisture. Under this conditions the oral suspension have a shelf life of 2 years.

POM **Artemether** *(WMF 6.4.3)*

Oily injection (Solution for injection), Artemether 80 mg/ml, 1-ml ampoule.

POM **GVITHER®** *(Greenlife)*

Injection, Artemether 80 mg per ml; sterile and colourless solution in 1 ml colourless glass amp. with disposable 2 ml syringe & needle.

Oral Suspension, Artemether 15 mg per 5 ml. Pack - 100 ml.

Dose: By mouth, Child (1 month - 6 months), 10 ml on the first day, then 5 ml once a day for the next 4 days; 7 months - 3 years, 20 ml on the first day, then 10 ml once a day for the next 4 days; 4-8 years, 30 ml on the first day, then 15 ml once a day for the next 4 days; 9-12 years, 40 ml on the first day, then 20 ml once a day for the next 4 days.

POM **LARITHER®** *(IPCA)*

Capsule, Artemether 40 mg.
40 mg - 6's.

Injection (40 mg), Artemether 40 mg per ml. Pack - 1 ml x 6's.

Injection (80 mg), Artemether 80 mg per ml. Pack - 1 ml x 6's.

POM **PALUTHER®** *(May and Baker)*

Injection, Artemether 80 mg per ml; arachis oil based solution in 1 ml colourless glass amp. Pack - 1 ml x 6.

Dose: By intramuscular injection only, Adult, 80 mg 2 times a day on the first day, then 80 mg once a day for the next 4 days; alternatively, 80 mg 2 times a day for 3 days; not exceeding a total dose of 480 mg.

Child: by i.m. injection only, 1.6 mg/kg 2 times a day on the first day, then 1.6 mg/kg once a day for the next 4 days; alternatively, 1.6 mg/kg 2 times a day for 3 days; not exceeding a total dose of 9.6 mg/kg.

ARTEMETHER plus LUMEFANTRINE

Indications: Treatment of acute uncomplicated malaria due to *Plasmodium falciparum* or mixed infections including *P. falciparum* in areas with significant drug resistance.

Contra-indications: Pregnancy (Appendix 2); breastfeeding (Appendix 3); history of arrhythmias, of clinically relevant bradycardia, and of congestive heart failure accompanied by reduced left ventricular ejection fraction; family history of sudden death or of congenital prolongation of QTc interval (also see Precautions).

Precautions: Electrolyte disturbances, concomitant administration of drugs that prolong QT interval; monitor patients unable to take food (greater risk of recrudescence); severe renal impairment (Appendix 4) or hepatic impairment (Appendix 5); **interactions**: Appendix 1.

SKILLED TASKS: DIZZINESS MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Abdominal pain, anorexia, diarrhoea, nausea and vomiting; headache, dizziness, sleep disorders; palpitations; arthralgia, myalgia; cough; asthenia, fatigue; pruritus, rash.

Dose: *Treatment of uncomplicated falciparum malaria*, by mouth, ADULT and CHILD over 12 years and body weight over 35 kg, initially 4 tablets followed by 5 further doses of 4 tablets each at 8, 24, 36, 48 and 60 hours (total 24 tablets over 60 hours); CHILD body weight 10–14 kg, initially 1 tablet followed by 5 further doses of 1 tablet each at 8, 24, 36, 48 and 60 hours (total 6 tablets over 60 hours); body weight 15–24 kg, initially 2 tablets followed by 5 further doses of 2 tablets each at 8, 24, 36, 48 and 60 hours (total 12 tablets over 60

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hours); body weight 25–34 kg, initially 3 tablets followed by 5 further doses of 3 tablets each at 8, 24, 36, 48 and 60 hours (total 18 tablets over 60 hours).

PATIENT ADVICE: TAKE TABLETS WITH FOOD; REPEAT DOSE IF VOMITING OCCURS WITHIN 1 HOUR OF ADMINISTRATION.

POM **Artemether plus Lumefantrine** *(WMF 6.4.3)*
Tablets, Artemether 20 mg with lumefantrine 120 mg.

ARTESUNATE

Artesunate is a complementary antimalarial drug for restricted use in the treatment of malaria.

Indications: Treatment of uncomplicated *P. falciparum* malaria in areas of multiple-drug resistance.

Contra-indications: First trimester of pregnancy.

Precautions: Risk of recurrence if used alone in non-immune patients.

SKILLED TASKS: DIZZINESS MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Headache, nausea, vomiting, abdominal pain, diarrhoea, dizziness, tinnitus, neutropenia, elevated liver enzyme values; ECG abnormalities, including prolongation of QT interval; temporary suppression of reticulocyte response and induction of blackwater fever, reported; neurotoxicity—in animal studies.

Dose: *Treatment of uncomplicated malaria (in areas of multiple-drug resistance)*, by mouth, ADULT and CHILD over 6 months, 4 mg/kg daily for 3 days; a single dose of mefloquine 15 mg/kg (or occasionally 25 mg/kg, if necessary) is given on day 2 or 3 to effect a radical cure; if artesunate used alone, 4 mg/kg on day 1, then 2 mg/kg daily for 6 days.

See also under the proprietary preparations below.

POM **Artesunate** *(WMF 6.4.3)*
Tablets, Artesunate 50 mg.

POM **ARSUMAX®** *(Sanofi)*
Tablet, Artesunate 50 mg; white scored tab.
50 mg – 12.

Dose: By mouth, Adult, 100 mg twice daily on day one; followed by 50 mg twice daily for the next 4 consecutive days. Child, 2 mg/kg b. wt. twice daily on day one; followed by 1 mg/kg b. wt. twice daily for the next 4 consecutive days.

Note: The drug should be taken in the morning and evening regularly for 5 consecutive days. It can be taken with or without meals.

POM **GSUNATE®** *(Greenlife)*
Tablet, Artesunate 100 mg; coated tab.

Dose: By mouth, Adult, 100 mg twice daily on day one; followed by 100 mg once daily for the next 4 consecutive days. Child: 2 mg/kg b. wt. twice daily on day one; followed by 1 mg/kg b. wt. twice daily for the next 4 consecutive days.

POM **ARTHLON-50®** *(GoldMoore)*
Tablet, Artesunate 50 mg; uncoated tab.
Pack - 12's.

POM **PLASMOTRIM®** *(Oculus)*
Lactabs, Artesunate 50 mg, 200 mg.
50 mg - 12.
200 mg - 6.
Rectocaps, Artesunate 50 mg, 200 mg.
50 mg - 6; 12.
200 mg - 6.

Indications: Lactab: Treatment of non-complicated *P. falciparum* malaria including multidrug-resistant strains.
Rectocaps: Treatment of non-complicated and cerebral *P. falciparum* malaria especially in unconscious patients.
Plasmotrim is not recommended for the prophylaxis of malaria.

Dose: Adults, *Non-complicated malaria*:
Day 1: 200 mg b.i.d.
Days 2 to 5: 200 mg/day in once daily doses.
Total artesunate dose 1200 mg. This dosage scheme has been shown to avoid relapses during a 28 days observation period.
Child, Adjust dose according to the b.wt. using the 50 mg formulation as follows:
Day 1: 5 mg/kg twice daily
Days 2 to 5: 5 mg/kg/day in once daily doses
Clinical experience in children is limited and different dosage regimens are still under evaluation.

ARTESUNATE plus MEFLOQUINE

Therapeutic category: Antimalarial.

Indications: Treatment of acute uncomplicated malaria infection caused by *Plasmodium falciparum* acquired in areas with high trans-

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mission of the disease (e.g. Africa).

Contra-indications: Hypersensitivity to artesunate or mefloquine, to their chemically related compounds like other artesunate derivatives, quinine or quinidine or any other ingredient of the tablets. Due to limited data, use in patients (especially children) who have less than 30kg body weight is not recommended. Not appropriate for prophylactic use against malaria infections.

Precautions: Avoid use of halofantrine concomitantly with mefloquine-containing antimalarial drugs or shortly afterwards because of the danger of a heart attack.

Ability to drive or operate machinery may be impaired, because feelings of dizziness or disturbed sense of balance may occasionally occur during the period of use and up to three weeks after the last dose.

Pregnancy and lactation: Not recommended for use during pregnancy or lactation. Women of childbearing age should take contraceptive measures while on treatment and for the next 3 months thereafter.

Adverse effects: Common side effects include: abdominal pain, nausea, vomiting, diarrhoea or loss of appetite, dizziness, headache, trouble in sleeping, fatigue and general weakness. Rarely, rash and itching of the skin may also occur.

Advice to patients: Patient should be advised to complete the full course of therapy even if he starts feeling better.

Dose: A full treatment course comprises 3 identical daily doses of two tablets, one artesunate 200 mg tablet and one mefloquine 250 mg tablet. The daily dose must be taken at the same time (simultaneously) with out chewing them, with a large amount of liquid such as drinking water and if possible with a meal. For patients have difficulties swallowing, the tablets can be crushed and dissolved in some water.

The first dose of 2 tablets should be taken at the time of initial diagnosis of your malaria infection (Day 1), followed by a second dose of 2 tablets 24 hours thereafter (Day 2) and a third (last) dose of 2 tablets 48 hours after the initial dose (Day 3)

POM **ARTEQUIN®-600/750** *(Oculus)*

Tablet, Artesunate 200 mg, Mefloquine base 250 mg (in the form of 275 mg Mefloquine HCl); available in pack of 3 Lactab (tablets) each containing 200 mg artesunate (total 600 mg) and 3 lactab each containing 250 mg mefloquine base (total 750 mg).

Pack - 6 Lactab.

CHLOROQUINE

Indications: Treatment of acute malaria caused by *P. malariae* and susceptible *P. falciparum* ; *P. vivax* and *P. ovale* (followed by primaquine to eliminate intrahepatic forms); prophylaxis of malaria for pregnant women and non-immune individuals at risk; rheumatic disorders (section 2.1.2).

Precautions: If patient continues to deteriorate after chloroquine—suspect resistance and administer quinine intravenously as emergency measure; hepatic impairment; renal impairment (Appendix 4); pregnancy (but in malaria, benefit considered to outweigh risk; Appendix 2); breastfeeding (Appendix 3); may exacerbate psoriasis; neurological disorders (avoid for prophylaxis if history of epilepsy); may aggravate myasthenia gravis; severe gastrointestinal disorders; G6PD deficiency; avoid concurrent therapy with hepatotoxic drugs; **interactions**: Appendix 1.

Adverse effects: Headache, gastrointestinal disturbances; also convulsions; visual disturbances (retinopathy associated with long-term, high dose therapy or inappropriate self-medication); depigmentation or loss of hair; rashes; pruritus—may become intolerable; bone-marrow suppression; hypersensitivity reactions such as urticaria and angioedema; atrioventricular block (may be result of inappropriate self-medication); porphyria and psoriasis in susceptible individuals.

Advice to patients: See Label 5 in Appendix 6. May take with meals; report any visual disturbances or difficulty in hearing or ringing in the ears; tablets are bitter tasting; may cause diarrhoea, loss of appetite, nausea, stomach pain; notify physician if these become severe.

Nursing considerations: •Administer oral dose before or after meals as prescribed; advise patient to take at the same time each day to maintain blood level. •Aspirate to avoid injecting drug into the blood system, prior to I.M. therapy (I.V. dose causes hypotension, asystole, heart block); rotate inj sites. •Avoid use in retinal or visual field changes or porphyria; children are extremely susceptible to toxicity.

Dose: NOTE: ALL DOSES ARE IN TERMS OF THE BASE

Treatment of malaria, by mouth, ADULT and CHILD 10 mg/kg followed by 5 mg/kg 6–8 hours later; then 5

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mg/kg daily on next 2 days (or 10 mg/kg for 2 days, followed by 5 mg/kg daily on day 3); total dose, 25 mg/kg over 3 days.

PATIENT ADVICE: ORAL CHLOROQUINE SHOULD BE TAKEN AFTER MEALS TO MINIMIZE NAUSEA AND VOMITING; IF PART OR ALL A DOSE IS VOMITED, THE SAME AMOUNT MUST BE IMMEDIATELY READMINISTERED.

Treatment of malaria (in patients unable to take chloroquine by mouth, but quinine preferred in falciparum malaria), by very slow intravenous infusion (over at least 8 hours), ADULT and CHILD 10 mg/kg as an initial dose, then 2 further infusions of 5 mg/kg at 8-hour intervals (as soon as patient is able to take chloroquine by mouth, discontinue infusions and complete the course with oral preparations total dose, 25 mg/kg over 3 days); by intramuscular or by subcutaneous injection (when intravenous infusion facilities not available) ADULT and CHILD 2.5 mg/kg every 4 hours or 3.5 mg/kg every 6 hours (until total dose of 25 mg/kg administered)

Prophylaxis of malaria, by mouth, ADULT 300 mg once a week; CHILD 5 mg/kg once a week.

PATIENT ADVICE: WARN TRAVELLERS ABOUT IMPORTANCE OF AVOIDING MOSQUITO BITES, IMPORTANCE OF TAKING PROPHYLAXIS REGULARLY, AND IMPORTANCE OF IMMEDIATE VISIT TO DOCTOR IF ILL WITHIN 1 YEAR AND ESPECIALLY WITHIN 3 MONTHS OF RETURN.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. AVOID RAPID PARENTERAL ADMINISTRATION (RISK OF TOXIC PLASMA CONCENTRATIONS AND FATAL CARDIOVASCULAR COLLAPSE).

Note: **Parenteral Chloroquine** - If a patient is unable to take chloroquine by mouth, e.g. due to vomiting, adequate hydration should first be ensured e.g. by admitting the patient and giving intravenous fluids or food and drink. The blood pressure should be checked. Reducing fever before parenteral therapy with chloroquine helps to minimise the risk of hypotension by minimising the peripheral vasodilation caused by fever. Chloroquine hydrochloride should be given I.M. or, in the case of shock, I.V. every 6 to 8 hours up to a maximum 900 mg base per day. Usually after 2 injections, the patient should feel better and therapy can be continued by the use of tablets or syrup to complete the 10 mg base/kg/2nd day and 5 mg/kg/3rd day.

OTC **Chloroquine** *(WMF 6.4.3)*

Tablets, Chloroquine base (as phosphate or sulfate) 100 mg, 150 mg.
Oral syrup, Chloroquine base (as phosphate or sulfate) 50 mg/5 ml.
Injection (Solution for injection), Chloroquine base (as phosphate or sulfate) 40 mg/ml, 5-ml ampoule.

OTC **Chloroquine** *(EDL 6.6)*
Tablet or Capsule, Chloroquine 150 mg base (as phosphate or sulphate).
Syrup, Chloroquine 50 mg base per 5 ml
Injection, Chloroquine 40 mg base per ml; in 5 ml amp.

POM **AFRIM®** (*Panvij Biotec*)
Tablet, Chroloquine phosphate 250 mg; white, scored tab. marked 'CQ' and '250' on one side and plain on the reverse.
250 mg - 10 x 10; 50 x 10; 1000.

OTC **ASSIQUINE®** *(Dizpharm)*
Syrup, Chloroquine phosphate 80 mg per 5 ml
Pack - 60 ml.

OTC **AVLOCLOR®** *(Reals)*
Tablet, Chloroquine phosphate 250 mg; white biconvex scored tab. marked 'ICI'.
250 mg - 10's
Syrup, Chloroquine phosphate 125 mg per 5 ml
Pack - 60 ml.

OTC **CAPQUIN®** *(Evans)*
Capsule, Chloroquine phosphate 250 mg; yellow cap. marked 'CG' and 'FEV'.
250 mg - 10

OTC **Chloroquine** *(Emzor)*
Tablet, Chloroquine phosphate 250 mg; white plain biconvex tab.
250 mg - 1000.
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml; 2 L.

OTC **Chloroquine** *(Evans)*
Tablet, Chloroquine phosphate 250 mg; yellow plain tab.
250 mg - 10; 1000.
Syrup, Chloroquine phosphate 80 mg per 5 ml; clear colourless sweentened syrup.
Pack - 60 ml.

OTC **Chloroquine** *(Fill Pharma)*
Tablet, Chloroquine phosphate 250 mg.
250 mg - 1000's.

OTC **Chloroquine** *(Juhel)*
Tablet, Chloroquine phosphate 250 mg.

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250 mg - 1000's.
Syrup, Chloroquine phosphate BP 80 mg per 5 ml.
Pack – 60 ml.

OTC **Chloroquine** *(Neimeth)*
Tablet (Double-strenght), Chloroquine phosphate 500 mg (equiv. to 300 mg Chloroquine base).
500 mg - 5's.
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

OTC **Chloroquine** *(Novel)*
Tablet, Chloroquine phosphate 250 mg; white shallow concave tab. marked 'CQ 250' on one side and 'NOVEL' on the reverse.
250 mg - 1000.

OTC **Chloroquine** *(Strides Vital)*
Tablet, Chloroquine phosphate 250 mg; white tab. marked 'CQ/250'.
250 mg - 1 x 10's; 1000's.

POM **CLOTIN®** *(Beta Drugs)*
Injection, Chloroquine phosphate BP 128.8 mg per 2 ml equiv. to 80 mg chloroquine base; clear sterile solution in 2-ml ampoule.
Pack – 2-ml x 10's; 2-ml x 50's
Injection, Chloroquine phosphate BP 250 mg per 5 ml equiv. to 155 mg chloroquine base; clear sterile solution in 5-ml ampoule.
Pack – 5-ml x 5's; 5-ml x 100's
Injection, Chloroquine phosphate BP 322 mg per 5 ml equiv. to 200 mg chloroquine base; clear sterile solution in 5-ml ampoule.
Pack – 5-ml x 5's; 5-ml x 100's.

POM **CQP-500®** *(GoldMoore)*
Tablet, Chloroquine phosphate BP 500 mg; f-c tab.
Pack - 5's.

OTC **DONAQUINE®** *(Doyin)*
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

OTC **EMZOQUINE®** *(Emzor)*
Tablet , Chloroquine phosphate 250 mg.
250 mg - 10; 1000.
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml; 2 L.
Capsule (forte), Chloroquine phosphate 500 mg (equiv. to 300mg Chloroquine base); yellow/green cap.
500 mg - 5; 100; 250.
Dose: *Treatment of malaria*, by mouth, Adult:
Day 1:- 2 capsules as single dose;
Day 2:- 2 capsules as single dose;
Day 3:- 1 capsule.
Prophylaxis, Adult, One capsule to be taken each week on exactly the same day.

OTC **FAPCHLOR®** *(Food & Pharma)*
Tablet, Chloroquine phosphate 250 mg.
250 mg - 10 x 10; 1000.
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

OTC **FASTAQUINE®** *(NGC)*
Caplet, Chloroquine phosphate 250 mg; white, oblong-shaped, scored tab.
250 mg -10; 10 x 10.
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

OTC **FEVAQUINE®** *(David)*
Tablet, Chloroquine phosphate 250 mg.
250 mg - 10; 100
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

OTC **FEVOKINE®** *(GSK)*
Tablet, Chloroquine phosphate 250 mg; white biconvex tab. marked 'F'.
250 mg - 10; 1000.

OTC **KIDIQUINE®** *(BCN)*
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 110 ml.

OTC **KLOQUIN®** *(Ranbaxy)*
Tablet, Chloroquine phosphate 250 mg.
250 mg - 10; 1000.
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml; 2 L.

OTC **L-QUINE®** *(Leady)*
Syrup, Chloroquine phosphate 80 mg per 5 ml.

OTC **LARIAGO®** *(IPCA)*
Tablet, Chloroquine phosphate BP 250 mg.
250 mg - 1000's.

OTC **MALADRIN®** *(P.Z.)*
Tablet, Chloroquine phosphate 250 mg.
Syrup, Chloroquine phosphate 80 mg per 5 ml.

OTC **MALAQUINE®** *(Farmex-Meyer)*
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

OTC **MATHEWQUINE®** *(Daily Need)*
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

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OTC **MAXIQUINE**® *(Vitabiotics)*
Syrup, Chloroquine phosphate 81 mg, Promethazine HCl 3 mg, Paracetamol 100 mg per 5 ml
Pack - 60 ml.

OTC **MIRAQUINE**® *(Mirapharm)*
Tablet, Chloroquine phosphate 250 mg.
250 mg - 1000.
Syrup, Chloroquine phosphate 80 mg per 5 ml

OTC **MOKO CHLOROQUINE**® *(New Healthway)*
Syrup, Chloroquine phosphate 80 mg per 5 ml
Pack - 60 ml.

OTC **NASMOQUIN**® *(NASDMU)*
Tablet, Chloroquine phosphate 250 mg; white tab. marked "NASMOQUIN" on one side and "NASDMU" on the reverse.
250 mg - 1000.

OTC **NIVAQUINE**® *(May & Baker)*
Tablet, Chloroquine sulphate 200 mg; white scored tab. marked 'NIVAQUINE 200'.
200 mg - 10.
Tasteless tablet, Chloroquine sulphate 200 mg; yellow f-c tab. marked 'NIVAQUINE 200'.
200 mg - 10.
Tablet (minor), Chloroquine sulphate 68 mg (equiv. to 50 mg chloroquine base); white tab. marked 'NIVAQUINE'.
68 mg - 10
Syrup, Chloroquine sulphate 68 mg per 5 ml.
60 ml; 100 ml.
Capsule (forte), Chloroquine sulphate 400 mg (equiv. to 300 mg Chloroquine base); lemon green cap. marked 'NIVAQUINE 400MG'
400 mg - 5; 400
Dose: *Treatment of malaria*, by mouth, Adult,
Day 1: 2 capsules as single dose;
Day 2: 2 capsules as single dose;
Day 3: 1 capsule.
Suspension (forte), Chloroquine sulphate 136 mg per 5 ml; in 30 ml amber coloured bottle.

POM **NORMAQUINE**® *(Geneith)*
Tablet, Chloroquine phosphate 250 mg.
250 mg – 10's (in blister); 1000's
Injection, Chloroquine phosphate 322 mg per 5 ml.

OTC **NOROLON**® *(GSK)*
Tablet, Chloroquine phosphate 250 mg; white biconvex tab. marked 'NOROLON'.
250 mg - 10.

OTC **NOVALOR**® *(SKG)*
Caplet, Chloroquine phosphate 250 mg; caplet marked 'CQ 250' on one side and 'SKG' on the reverse.
250 mg - 500; 1000.
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

OTC **PENTACLOR**® *(Morison)*
Syrup, Chloroquine phosphate 80 mg per 5 ml; pale brown vanilla flavoured Syrup
Pack - 60 ml.

OTC **QUIMAL**® *(Dana)*
Tablet, Chloroquine phosphate BP 250 mg.
250 mg - 1000's.

OTC **ROBAQUINE**® *(Swipha)*
Caplet (forte), Chloroquine phosphate 500 mg (equiv. to 300 mg Chloroquine base).
500 mg - 5.
Dose: Adult, 600 mg base on 2 consecutive days followed by 300 mg on the 3rd day.

OTC **SAMQUINE**® *(Sam)*
Caplet, Chloroquine phosphate 250 mg
250 mg - 1000.

POM **SILAQUINE**® *(GoldMoore)*
Tablet, Chloroquine phosphate 128.8 mg per 2 ml (equiv. to 80 mg Chloroquine base).
Pack - 10's; 50's.

POM **TAVQUINE**® *(Justeen)*
Injection, Chloroquine phosphate 322 mg per 5 ml.
Pack – 1 x 100's.

OTC **ULTIQUINE**® *(Ulticare-Lyka)*
Syrup, Chloroquine phosphate 80 mg per 5 ml.
Pack - 60 ml.

CHLORPROGUANIL plus DAPSONE

Indications: A combination of two antimalarial compounds, chlorproguanil hydrochloride and dapsone, in a fixed ratio of 2:2.5; for treatment of acute uncomplicated *Plasmodium falciparum* infections, including those strains resistant to other anti-malarial drugs, espcially to chloroquine and sulfadoxine/pyrimethamine.
Contra-indications: Hypersensitivity to biguanides (e.g. proguanil, chlorproguanil) or sulfonamides or sulfones or any of the excipients in the tablets.
Precautions: History of G6PD deficiency, methaemoglobin reductase deficiency, haemoglobin M or E, porphyria (increased susceptibility to the haemolytic effects

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associated with dapsone); History of intravenous haemolysis, pre-existing severe anaemia, or cardiac or pulmonary disease (risk of haemolytic anaemia associated with dapsone); Discontinue immediately if signs of haemolysis (anaemia, dark coloured urine) or methaemoglobinaemia (cyanosis) develop during administration; Severe renal or hepatic impairment; Children under 3 months of age; not recommended for prophylaxis; pregnancy and lactation.

Interactions: Co-administration other folate antagonists or agents associated with myelosupression (e.g. trimethoprim, co-trimoxazole, methotrexate, zidovudine) may result in increased impairment of folic acid metabolism, leading to haematological side effects.

Adverse effects: *Blood and lymphatic system disorders*: Anaemia, methaemoglobinaemia; *Immune system disorders*: Hypersensitivity reactions; *Metabolism and nutrition disorders*: Anorexia; *Nervous system disorders*: Dysgeusia, dizziness and headache; *Respiratory, thoracic and mediastinal disorders*: Cough; *GI disorders*: Vomiting,, nausea, abdominal pain, diarrhoea, mouth ulceration and tongue ulceration; *Hepatobiliary disorders*: Jaundice, increases in liver transaminases; *Skin and subcutaneous tissue disorders*: Pruritus, face oedema, rash (including papular and maculopapular rash); *General disorders and administration site condition*: Asthenia and fatigue.

Other adverse reactions associated with component drugs chlorproguanil or dapsone may also occur.

Advice to patients: Tablets may be swallowed whole, chewed or crushed; with a small amount of fluid and without regard to meals. Dosing should be repeated if vomiting occurs within 30 minutes of taking any dose.

Dose: By mouth, 2 mg chlorproguanil: 2.5 mg dapsone/kg body-weight daily for 3 days as follows:

Child (15/18.75 mg tablet): 5-7.9 kg, 1 tablet; 8-11.9 kg, 1½ tablet; 12-15.9 kg, 2 tablets.

Adult (80/100 mg tablet): 16-20.9 kg, ½ tablet; 21-39.9 kg, 1 tablet; 40-59.9 kg, 1½ tablet; above 60 kg, 2 tablets.

Above dosages should be taken once daily for 3 days.

Use in eldery: No dosage adjustment necessary unless there is severe renal or hepatic impairment.

POM **LAPDAP**® *(GSK)*

Tablet (15/18.75 mg), Chlorproguanil 15 mg, dapsone 18.75 mg; white tab.

Tablet (80/100 mg), Chlorproguanil 80 mg, dapsone 100 mg; pink tab.

DIHYDROARTEMISININ

Pharmacology: Dihydroartemisinin belongs to the sesquiterpene lactone group of antimalarials; effective against *P. falciparum, P. vivax, P. malariae* and *P. ovale.* It is a blood schizonticide and acts on the erythrocytic stages of the parasite which are directly responsible for the clinical symptoms of the disease. It elicits its action on the plasmodium parasite through inhibition of protein synthesis via DNA replication. It is rapidly absorbed after oral administration (2.2mg/kg) and rectal insertion (8mg/kg); Tmax in the serum are 1.33hrs and 4.4hrs respectively. It is rapidly excreted from the body; the elimination half-life is 1.57hrs for the tablet and 4.8hrs for the suppository. About 0.15% of the drug is excreted unchanged in the urine. Excretion is via glomerular filtration and tubular secretion.

Indications: All forms of malaria including simple malaria, cerebral malaria, chloroquine-resistant malaria, severe malaria, and multi-drug resistant malaria caused by *P. falciparum;* other forms of malaria caused by *P. vivax, P. malariae* and *P. ovale.*

Precautions: Pregnancy (first trimester); use in pregnancy during the second and third trimesters has been proven to be safe but the benefit should be seen to outweigh the risk before administration.

Adverse effects: Transient slight lowering of reticulocyte count which normalizes during or after completion of therapy; dizziness, nausea, headache and abdominal pain may occur within the first 2 days of treatment and may be due to malaria itself.

Dose: By mouth, Adult, 120 mg start; then 60 mg on subsequent days for 6 days.

CHILD (under 1 year), 20 mg start, then 10 mg on subsequent days for 6 days; 1-6 years, 40 mg start, then 20 mg on subsequent days for 6 days; 7-12 years, 80 mg start, then 40 mg on subsequent days for 6 days.

By rectum, Adult(11 years & above), 160 mg start, then 80 mg on subsequent days for 6 days.

CHILD (under 2 years), 40 mg start, then 20 mg on subsequent days for 6 days; 3-10 years, 80 mg start, then 40 mg on subsequent days for 6 days.

Note: Add freshly boiled and cooled water to

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marked level. Shake well before use. The suspending liquid can be stored for 14 days in refrigerator, and 7 days in room temperature.

POM **ALAXIN®** *(Greenlife)*
Tablet, Dihydroartemisinin 60 mg; white coated tab.
60 mg - 8.
Oral Suspension, Dihydroartemisinin 10 mg per 5 ml; white powder for reconstitution.
Pack - 80 ml.

POM **COTECXIN®** *(Churchbells)*
Tablet, Dihydroartemisinin 60 mg.
60 mg - 8.
Powder (for reconstitution), Dihydroartemisinin 10 mg, 20 mg, 40 mg; pleasantly flavoured powder.
10 mg - 8 (for 3 - 11 months).
20 mg - 8 (for 1 - 6 years).
40 mg - 8 (for 7 - 12 years).
Suppository, Dihydroartemisinin 20 mg, 40 mg, 80 mg.
20 mg - 8 (for 3 months - 2 years).
40 mg - 8 (for 3 - 10 years).
80 mg - 8 (for 11 years and above).

DOXYCYCLINE

Doxycycline is a complementary drug for the treatment of malaria.

Indications: Supplement to quinine in treatment of multiple-drug resistant *P. falciparum* malaria (where quinine resistance, in cases of hypersensitivity to sulfonamides); short-term prophylaxis of multiple-drug resistant P. falciparum malaria; bacterial infections (section 9.1.2.3).

Contra-indications: Pregnancy (Appendix 2); children under 8 years; porphyria; systemic lupus erythematosus.

Precautions: Avoid exposure to sunlight or sunlamps—photosensitivity reported; renal impairment (Appendix 4); hepatic impairment (Appendix 5); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances; anorexia; erythema (discontinue treatment); photosensitivity; hypersensitivity reactions; headache and visual disturbances; hepatotoxicity, blood disorders, pancreatitis and antibiotic-associated colitis reported; staining of growing teeth and occasional dental hypoplasia.

Dose: *Supplement to malaria treatment (see notes above)*, by mouth, ADULT and CHILD over 8 years, 100 mg twice daily for 7–10 days.
Short-term prophylaxis of malaria, by mouth, ADULT 100 mg daily for up to 8 weeks; CHILD over 8 years, 1.5 mg/kg daily for up to 8 weeks; doxycycline should be started on the day before exposure and continued for 4 weeks after last risk of exposure.

PATIENT ADVICE. CAPSULES SHOULD BE SWALLOWED WHOLE WITH PLENTY OF FLUID WHILE SITTING OR STANDING TO PREVENT OESOPHAGEAL IRRITATION. MAY BE GIVEN WITH FOOD OR MILK, TO COUNTER GASTRIC IRRITATION.

POM **Doxycycline** *(WMF 6.4.3)*
Capsules, Doxycycline (as HCl) 100 mg.
Dispersible tablets, Doxycycline (as monohydrate) 100 mg.

HALOFANTRINE

Therapeutic category: Antimalarial

Pharmacology: Halofantrine is a phenanthrenemethanol antimalarial which is schizonticidal with a high degree of activity against the asexual erythrocytic stage of malaria parasites. It is devoid of significant activity against exoerythrocytic or gametocyte stages of malaria parasites. It is used for the treatment of single or mixed infections of *Plasmodium falciparum* or *Plasmodium vivax*. It has been shown to be effective against *P. falciparum* in areas where chloroquine or multi-drug resistant strains are common. Limited data indicates favourable results with *P. Ovale* and *P. Malariae*. It should not be used as either a casual or suppressive prophylactic.

Indications: All forms of acute malaria including chloroquine-resistant malaria.

Contra-indications: Pregnancy and breast feeding (avoid during treatment); cardiac disorders.

Interactions: •Avoid co-administration with other drugs which may induce arrhythmias viz chloroquine, mefloquine, quinine, TCAs, antipsychotics, certain antiarrhythmics, and antihistamines such as astemizole.

Adverse effects: Abdominal pain, diarrhoea, pruritus and skin rash.

Advice to patients: See Label 23 in Appendix 6. Food, especially high fat food, enhances absorption of halofantrine and may increase the incidence of adverse effects.

Dose: Adult and children above 40 kg, 2 tabs (500 mg) six hourly x 3 doses.
Children (< 40 kg), 8 mg/kg six hourly x 3 doses, according to the following scheme: 10-12 kg, 5 ml suspension 6

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hourly x 3 doses; 13-18 kg, 7.5 ml suspension 6 hourly x 3 doses; 19-25 kg, 10 ml suspension 6 hourly x 3 doses; 26-31 kg, 1 tab (250 mg) 6 hourly x 3 doses; 32-40 kg, 1½ tab. (375 mg) 6 hourly x 3 doses.

Note: A second course of therapy may be given to patients with no previous exposure to malaria (i.e travellers from non-endemic areas) or minimal exposure (i.e young children) one week after the first course.

POM **Halofantrine** *(EDL 6.6)*
Tablets: Halofantrine HCl 250 mg
Syrup, Halofantrine HCl 100 mg per 5 ml

POM **HALFAN®** *(GSK)*
Tablets, Halofantrine HCl 250 mg; white, scored, capsule-shaped tab.
250 mg - 6.
Suspension, Halofantrine HCl 100 mg per 5 ml; white suspension.
Pack - 30 ml.

MEFLOQUINE

Mefloquine is a complementary drug for the treatment of malaria.

Indications: Treatment of uncomplicated malaria due to multiple-resistant *P. falciparum*; treatment of severe and complicated malaria, after quinine; adjunct to treatment with artemisinin and derivatives; prophylaxis of malaria for travellers to areas where high risk of multiple-resistant *P. falciparum*.

Contra-indications: History of neuropsychiatric disorders including depression or convulsions; hypersensitivity to quinine.

Precautions: Pregnancy (use only if other antimalarials inappropriate; Appendix 2), avoid pregnancy during and for 3 months after use; cardiac conduction disorders; avoid for prophylaxis in severe hepatic impairment (Appendix 5) and in epilepsy; breastfeeding (Appendix 3); not recommended for infants under 3 months (5 kg); **interactions**: Appendix 1

Note: Patients should be informed about adverse effects associated with mefloquine and if they occur advised to seek medical advice on alternative antimalarials.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING; EFFECTS MAY PERSIST FOR UP TO 3 WEEKS.

Adverse effects: nausea, vomiting, diarrhoea, abdominal pain, anorexia, headache, dizziness (can be severe), loss of balance, somnolence, insomnia and abnormal dreams; neurological and psychiatric disturbances including sensory and motor neuropathies, tremor, ataxia, visual disturbances, tinnitus, vestibular disorders; convulsions, anxiety, depression, confusion, hallucinations, panic attacks, emotional instability, aggression, agitation and psychoses; circulatory disorders, tachycardia, bradycardia, cardiac conduction disorders; muscle weakness, myalgia, arthralgia; rash, urticaria, pruritus, alopecia; disturbances in liver function tests, leukopenia, leucocytosis, thrombocytopenia; rarely, Stevens-Johnson syndrome, atrioventricular block and encephalopathy.

Advice to patients: See Labels 21, 25 and 27 in Appendix 6.

Nursing considerations: •Tell patient not to take the drug on an empty stomach and always to take it with a full glass of water.
•Avoid coadministration with quinine or quinidine. There should be at least 12 hours between the commencement of mefloquine therapy and last dose of quinine or quinidine.
•Advise patient to exercise caution when performing hazardous activities that require alertness and good coordination because dizziness, disturbed sense of balance, and neuropsychiatric reactions have been reported.
•Periodic eye examinations are recommended for patients on long-term therapy.
•Induce vomiting and seek medical advice immediately if overdose is suspected as it can cause cardiotoxicity.
•Patients on mefloquine prophylaxis should discontinue the drug if they notice signs of unexplained anxiety, depression, confusion, or restlessness. These may be signs of impending toxicity.

Dose: NOTE: ALL DOSES ARE IN TERMS OF THE BASE.

Treatment of malaria, by mouth, ADULT and CHILD 15 mg/kg (up to maximum of 1 g) as a single dose (increased to 25 mg/kg in areas of resistance).

Prophylaxis of malaria, by mouth, ADULT 250 mg once a week; CHILD over 15 kg, 5 mg/kg once a week; prophylaxis should start 1–3 weeks before departure and continue for 4 weeks after last exposure, see notes above.

PATIENT ADVICE: WARN TRAVELLERS ABOUT THE IMPORTANCE OF AVOIDING MOSQUITO BITES, IMPORTANCE OF TAKING PROPHYLAXIS REGULARLY, AND IMPORTANCE OF IMMEDIATE VISIT TO DOCTOR IF ILL WITHIN 1 YEAR AND ESPECIALLY WITHIN 3 MONTHS OF POTENTIAL EXPOSURE.

POM **Mefoquine** *(WMF 6.4.3)*

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Tablets, Mefloquine (as HCl) 250 mg.

POM **LARIAM**® *(Swipha)*
Tablet, Mefloquine 250 mg.
250 mg - 4; 50.

PRIMAQUINE

Indications: Elimination of intrahepatic forms of *P. vivax* and *P. ovale* (after standard chloroquine therapy); elimination of gametocytes of *P. falciparum* (after routine therapy with a blood schizontocide)
Contra-indications: Pregnancy (treatment with primaquine should be delayed until after delivery; Appendix 2); breastfeeding (Appendix 3); conditions that predispose to granulocytopenia (including active rheumatoid arthritis and lupus erythematosus).
Precautions: Monitor blood count; if methaemoglobinaemia or haemolysis occurs, withdraw treatment and consult physician; G6PD deficiency (exclude before radical treatment for *P. vivax* and *P. ovale*, but not before single dose gametocytocidal treatment).
Adverse effects: Anorexia, nausea and vomiting, abdominal pain; acute haemolytic anaemia (frequently in G6PD deficiency); rarely, methaemoglobinaemia, haemoglobinuria, agranulocytosis, granulocytopenia and leukopenia.
Dose: NOTE: ALL DOSES ARE IN TERMS OF THE BASE.
Radical treatment of P. vivax and P. ovale malaria (after standard chloroquine therapy), by mouth, ADULT 250 micrograms/kg daily (or 15 mg daily) for 14 days; CHILD 250 micrograms/kg daily for 14 days; in G6PD deficiency, ADULT 750 micrograms/kg once a week for 8 weeks; CHILD 500–750 micrograms/kg once a week for 8 weeks.
Gametocytocidal treatment of P. falciparum (after routine blood schizontocide therapy), by mouth, ADULT and CHILD 500–750 micrograms/kg as a single dose.

POM **Primaquine** *(WMF 6.4.3)*
Tablets, Primaquine (as phosphate) 7.5 mg, 15 mg.

PROGUANIL

Indications: With chloroquine, prophylaxis of malaria in areas of low resistance.
Contra-indications: Use in areas of known resistance to either proguanil or pyrimethamine.
Precautions: Renal impairment (Appendix 4); pregnancy (folate supplements required, Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Mild gastric intolerance, diarrhoea; occasional mouth ulcers and stomatitis; skin reactions and hair loss reported; rarely hypersensitivity reactions such as urticaria and angioedema.
Advice to patients: See label 21 in Appendix 6.
Dose: *Prophylaxis of malaria*, by mouth,
ADULT 200 mg daily, after food;
CHILD under 1 year, 25 mg daily;
CHILD 1–4 years, 50 mg daily;
CHILD 5–8 years, 100 mg daily;
CHILD 9–14 years, 150 mg daily.
PATIENT ADVICE: WARN TRAVELLERS ABOUT THE IMPORTANCE OF AVOIDING MOSQUITO BITES, IMPORTANCE OF TAKING PROPHYLAXIS REGULARLY, AND IMPORTANCE OF IMMEDIATE VISIT TO DOCTOR IF ILL WITHIN 1 YEAR AND ESPECIALLY WITHIN 3 MONTHS OF RETURN.
Note: The daily dose is best taken with water, after food, at the same time each day. For a young child, the dose may be administered crushed and mixed with milk, honey or jam. Non-immune subjects entering a malarious region are advised to begin treatment with proguanil at least 24 hours before arrival. The daily dose of proguanil should be continued throughout exposure to risk and for four weeks after leaving the area.

POM **Proguanil** *(WMF 6.4.3)*
Tablets, Proguanil HCl 100 mg.

POM **Proguanil** *(EDL 6.6)*
Tablet, Proguanil 100 mg (as HCl)

POM **PALUDRINE**® *(Reals)*
Tablet, Proguanil HCl 100 mg; white scored tab. marked 'P/P' and 'ICI'.

PYRIMETHAMINE

Therapeutic category: Antimalaria
Indications: Malaria prophylaxis.
Precautions: Hepatic or renal disorder; folate deficiency due either to innate disease or malnutrition. Give folate supplements in pregnancy.
Interactions: •Co-trimoxazole, lorazepam, methotrexate, cytosine, arabinoside, trimethoprim.
Adverse effects: Occasionally rashes, insomnia, macrocytic anaemia.
Advice to patients: Take with meals to

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minimise vomiting; discontinue at first sign of skin rash; notify physician if persistent fever, sore throat, bleeding or bruising occurs.

Dose: By mouth, Adult and children over 10 years, 25 mg weekly.
Child (under 5 years), 6.25 mg weekly; 5-10 years, 12.5 mg weekly.

OTC **Pyrimethamine** *(EDL 6.6)*
Tablet, Primethamine 12.5 mg, 25 mg.

QUININE

Indications: Multiple-drug resistant *P. falciparum* malaria.

Contra-indications: Haemoglobinuria; optic neuritis; tinnitus.

Precautions: Atrial fibrillation, conduction defects, heart block; monitor for signs of cardiac toxicity and blood glucose levels (with intravenous use); pregnancy (but appropriate for treatment of malaria, Appendix 2); renal impairment (Appendix 4); G6PD deficiency; may aggravate myasthenia gravis; **interactions**: Appendix 1.

Adverse effects: Cinchonism (tinnitus, headache, blurred vision, temporary blindness, altered auditory acuity, nausea, diarrhoea, hot and flushed skin, rashes, confusion); hypersensitivity reactions including angioedema; rarely haemorrhage and asthma; hypoglycaemia (especially after parenteral administration); renal damage (culminating in acute renal failure and anuria); blood disorders; cardiovascular, gastrointestinal and CNS effects; very toxic in overdosage—immediate medical attention required.

Advice to patients: Swallow dose whole to avoid bitter taste and irritation to gastric mucosa; avoid use of aluminium-containing antacids because of drug absorption problems; may cause night blindness. Patients should notify their physician if rash, fever, unusual bleeding or bruising, ringing in the ears, visual disturbances, or syncope occur.

Nursing considerations: •Administer before or after meals at the same time to minimise GI distress and maintain drug level; do not crush tablets as drug is irritating to gastric mucosa.
•Give slowly by I.V. infusion over at least 1 hour.
•Observe closely for cinchonism viz nausea, blurred vision, tinnitus, headache, difficulty in focusing.
•Teach patient to avoid OTC preparations (unless on prescription) and tonic water.

Dose: NOTE: QUININE (ANHYDROUS BASE) 100 MG ≡ QUININE BISULFATE 169 MG ≡ QUININE DIHYDROCHLORIDE 122 MG ≡ QUININE SULFATE 121 MG.

QUININE BISULFATE 300 MG TABLETS PROVIDE LESS QUININE THAN 300 MG OF THE SULFATE OR DIHYDROCHLORIDE.

Treatment of multiple-drug resistant P. falciparum malaria, by mouth, ADULT 600 mg (quinine sulfate) every 8 hours for 3, 7, or 10 days; CHILD 10 mg/kg (quinine sulfate) every 8 hours for 3, 7, or 10 days; duration of treatment depends on local susceptibility of *P. falciparum* and whether or not additional antimalarials also used.

PATIENT ADVICE: IF ALL OR PART OF A DOSE IS VOMITED WITHIN ONE HOUR, THE SAME AMOUNT MUST BE READMINISTERED IMMEDIATELY.

Treatment of multiple-drug resistant P. falciparum malaria (in patients unable to take quinine by mouth), by slow intravenous infusion (over 4 hours), ADULT 20 mg/kg (quinine dihydrochloride) followed by 10 mg/kg (quinine dihydrochloride) every 8 hours; CHILD 20 mg/kg (quinine dihydrochloride) followed by 10 mg/kg (quinine dihydrochloride) every 12 hours; initial dose should be halved in patients who have received quinine, quinidine or mefloquine during the previous 12–24 hours.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS; INTRAVENOUS INJECTION OF QUININE IS SO HAZARDOUS THAT IT HAS BEEN SUPERSEDED BY INFUSION; WHERE FACILITIES FOR INTRAVENOUS INFUSION ARE UNAVAILABLE, AN APPROPRIATE DILUTION MAY BE ADMINISTERED BY INTRAMUSCULAR INJECTION.

See also under the proprietary preparations below.

POM **Quinine** *(WMF 6.4.3)*
Tablets, Quinine sulfate 300 mg; quinine bisulfate 300 mg
Injection (Solution for dilution for infusion), Quinine dihydrochloride 300 mg/ml; in 2-ml ampoule.

POM **Quinin** *(EDL 6.6)*
Tablet, Quinine (as bisulphate or sulfate) 300 mg.
Injection, Quinine (as dihydrochloride) 300 mg per ml; in 2 ml amp.

POM **MALAGOLD®** *(Medreich)*
Tablet, Quinine sulfate 300mg (equiv. to Quinine 248 mg); white s-c tab.

POM **Moko Liquid Quinine** *(New Healthway)*
Solution, Quinine (as HCl) 100 mg per 5 ml.

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Pack - 200 ml.

POM **Q-300**® *(Strides Vital)*
Tablet, Quinine sulfate 300 mg.
300 mg – 3 x 10's.

POM **QUINIMAX**® *(Sanofi)*
Tablets, Quinine 125 mg, 500 mg; scored f-c tabs.
125 mg - 18
500 mg - 9.
Dose: By mouth, Adult, 500 mg every 8 hours.
Child (15 kg), 125 mg every 8 hours.
Child (30 kg), 250 mg every 8 hours
Note: The duration of treatment is 5-7 days.
Injection, Quinine 125 mg per ml; solution for injection in 1 ml, 2 ml and 4 ml amber glass amps.
Pack - 3; 25.
Dose: By I.V. infusion or slow deep I.M. injection, 8 mg/kg 2-3 times daily; not exceeding 25 mg/kg daily.

SULFADOXINE plus PYRIMETHAMINE

Sulfadoxine with pyrimethamine are complementary drugs for the treatment of malaria.

Indications: Treatment of malaria due to susceptible *P. falciparum* in areas of high chloroquine resistance and in patients who have not responded to chloroquine; additionally quinine may be given for 3 days (see notes above).

Contra-indications: Hypersensitivity to sulfonamides or pyrimethamine; severe hepatic or renal impairment (except where no alternative treatment available).

Precautions: Avoid in blood disorders—unless specialist supervision; discontinue immediately if blood disorder occurs; rash, sore throat, mouth ulcers, or shortness of breath—withdraw treatment; G6PD deficiency; predisposition to folate deficiency; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Rashes, pruritus, slight hair loss; rarely erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis; gastrointestinal disturbances including nausea, vomiting, stomatitis; rarely, hepatitis, leukopenia, thrombocytopenia, megaloblastic anaemia and purpura—withdraw treatment; fatigue, headache, fever, polyneuritis, also reported; pulmonary infiltrates such as eosinophilic or allergic alveolitis—if symptoms of cough or shortness of breath—withdraw treatment.

Advice to patients: Drink plenty of fluids; avoid prolonged exposure to the sun; notify physician if rash, sore throat, pallor, shortness of breath, or glossitis occurs.

Dose: *Treatment of malaria due to susceptible P. falciparum (see notes above)*, by mouth, ADULT sulfadoxine 1.5 g with pyrimethamine 75 mg (3 tablets) as a single dose; CHILD 5–10 kg, half tablet; 11–20 kg, 1 tablet; 21–30 kg, 1½ tablets; 31–45 kg, 2 tablets, as a single dose.

POM **Sulfadoxine plus Pyrimethamine** *(WMF 6.4.3)*
Tablets, Sulfadoxine 500 mg with pyrimethamine 25 mg.

POM **Sulfadoxine plus Pyrimethamine** *(EDL 6.6)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg.
Syrup, Sulfadoxine 500 mg, pyrimethamine 25 mg per 5 ml.
Injection, Sulfadoxine 500 mg, pyrimethamine 25 mg per 2.5 ml; in 2.5 ml amp.

POM **ANTIMAL**® *(Neimeth)*
Syrup, Sulfadoxine 500 mg, pyrimethamine 25 g per 5 ml.
Pack - 15 ml.

POM **FANSIDAR**® *(Swipha)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg; white doubly scored tab. marked with maker's name and symbol.
525 mg - 3's; 500's.
Syrup, Sulfadoxine 500 mg, pyrimethamine 25 mg per 5 ml.
Pack - 10 ml.
Injection, Sulfadoxine 500 mg, pyrimethamine 25 mg; clear colourless solution in transparent 2.5 ml amp.
Pack - 2.5 ml x 15's.

POM **GOMAXINE**® *(GoldMoore)*
Tablet, Sulfadoxine BP 500 mg, pyrimethamine BP 25 mg.
Pack - 3's.

POM **LARIDOX**® *(IPCA)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg.
525 mg - 3's; 500's.
Syrup, Sulfadoxine 500 mg, pyrimethamine 25 mg per 5 ml.

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Pack - 10 ml.
Injection, Sulfadoxine 500 mg, pyrimethamine 25 mg; in 2.5 ml amp.
Pack - 2.5 ml x 5's.

POM **MALAKARE**® *(Ulticare-Lyka)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg
525 mg - 3; 500.

POM **MALCIDAL**® *(Juhel)*
Tablet, Sulfadoxine BP 500 mg, pyrimethamine BP 25 mg.
525 mg – 50 x 3's; 500's.

POM **MALDOX**® *(Emzor)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg
525 mg - 3 x 50.

POM **MALOXINE**® *(St. Michael)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg.
525 mg - 3 x 50.
Injection, Sulfadoxine 500 mg, pyrimethamine 25 mg; in 2.5 ml amp.
Pack - 2.5 ml x 2 amps.

POM **MALPAN**® (*Panvij Biotec*)
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg; off-white scored tab.
525 mg - 50 x 3.

POM **MALWIN**® *(Fidson)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg
525 mg - 3.

POM **NOVAXINE**® *(SKG)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg.
525 mg - 3.

POM **PRIMALAR**® *(Sam)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg.
525 mg - 3; 250.

POM **PYRAMIN**® *(Dana)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg
525 mg - 20 x 6's.

POM **RIDMAL**® *(Diamond Remedies)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg
525 mg - 3 x 50; 10 x 50.

POM **VITADAR**® *(Strides Vital)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg; scored tab. marked with the company's logo.
525 mg - 3's.

With Paracetamol
POM **FANSIDAR COMBI**® *(Swipha)*
Tablets, 3 round tablets of Fansidar® and 12 oblong tablets of Paracetamol in one blister pack.
Dose: Start with 3 tablets of Fansidar® and 2 tablets of Paracetamol; then 2 tablets of Paracetamol 3 times daily.

SULFADOXINE plus PYRIMETHAMINE plus MEFLOQUINE

Indications: Treatment of *P. falciparum* malaria resistant to other antimalarial agents. When treating *P. vivax* malaria, subsequent prophylaxis of recurrence with an 8-aminoquinoline (e.g. primaquine) may be necessary.
Contra-indications: Hypersensitivity to sulfonamides; neonates in the first weeks of life.
Precautions: Early pregnancy (use only when absolutely necessary).
Interactions: •Quinine, avoid co-administration. In severe cases, however, initial treatment with quinine I.V. for 1-2 days followed by Fansimef® may be necessary. The interval between the last dose of quinine and treatment with Fansimef® should not be less than 12 hours to avoid potentiation of side-effects of quinine and mefloquine.
Adverse effects: Dizziness, nausea, vomiting, gastric discomfort, skin reactions.
Dose: Adult, *non-immune subjects*, a single dose of 3 tabs.
Partially immune subjects, 60 kg or less, a single dose of 2 tabs; more than 60 kg, a single dose of 3 tabs.
Child *(whether immune or not)*, depending on age, a single dose of ½-2 tabs as follows:
5-10 kg (approx. < 2 years), ½ tab.;
10-20 kg (approx. 2-5 years), 1 tab.;
20-30 kg (approx. 5-10 years), 1½ tabs;
30-45 kg (approx. 10-14 years), 2 tabs.
The tablets should be swallowed whole with a good deal of fluid after eating.

POM **FANSIMEF**® *(Swipha)*
Tablet, Sulfadoxine 500 mg, pyrimethamine 25 mg, mefloquine 250 mg.
Pack - 2; 100.

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POM **MALAFLOQ**® *(Medreich)*
Tablet, Sulfadoxine BP 500 mg, pyrimethamine BP 25 mg, mefloquine (as HCl) 250 mg.
Pack - 2's.

SULFAMETHOPYRAZINE plus PYRIMETHAMINE

Therapeutic category: Antimalarial
Pharmacology: The combination has antiplasmodial activity and is effective in malaria caused by *P. falciparum, P. vivax, P. malariae* and *P. ovale*. It provides a double attack at different points of the same metabolic pathway of the pathogen. While sulfamethopyrazine antagonises the plasmodial enzyme dihydro-pteroate synthetase, thus preventing the synthesis of dihydropteroate, an intermediate in the formation of dihydrofolate, pyrimethamine antagonises the enzyme dihydrofolic - reductase, which converts dihydrofolic acid to tetrahydrofolic acid.
Indications: Therapy and prophylaxis of malaria caused by *P. falciparum, P. ovale, P. malariae and P. vivax.*
Contra-indications: Marked liver damage, renal insufficiency, blood dyscrasias, infants during the first two weeks of life, pregnancy (during the last 2 weeks).
Precautions: Pregnancy, infants, patients predisposed to folic acid deficiency; reduce dose in renal disorders; regular blood controls during long therapy.
Adverse effects: Seldomly nausea, vomiting and cutaneous erythema; blood dyscrasias.
Dose: By mouth, Adult, 2-3 tabs as a single dose according to body-wt.
Child: 25 mg/kg body-wt approx. as a single dose.
Prohylaxis: Adult, 1 tab. weekly
Child, 12.5 mg/kg body-wt. weekly.

POM **METAKELFIN**® *(Pharmacia)*
Tablet, Sulfamethopyrazine 500 mg, pyrimethamine 25 mg.
525 mg - 2 x 250 (in strips); 100.

POM **METALENE**® *(Korlyns)*
Tablet, Sulfamethopyrazine 500 mg, Pyrimethamine 25 mg.
Pack – 5 x 6's
Dose: *Antimalarial therapy*: Adults (50-70 kg), 2 tablets; over 70 kg 3 tablets.
Child (5-9 years): ½-1 tablet; 10-14 years, 1-2 tablets.
For adults or children over 14 years (over 40 kg of body weight), 2 tablets.
Child under 5 years: 24 mg/kg of body weight (with reference to sulfamethopyrazine) in one single dose.
Antimalarial prophylaxis: Administer weekly half therapeutic dose, according to above stated age classes.
Note: Prophylaxis must be started just on arrival to malaria zone and continued for 4 weeks after leaving it.
Overdosage and Treatment: *Symptoms*: vomiting, visual and mental disorders, petechiae, purpura and jaundice. Treatment is symptomatic. Gastric lavage (if carried out in time) and forced diuresis can be useful. Alkalinization of urine by administration of alkalizing solutions may favour the excretion of sulfamethopyrazine. Hypersensitivity reactions are treated with corticosteroids. In order to neutralize the effects of pyrimethamine on hemopoiesis 3-6 mg of Leucovorin calcium may be administered by intramuscular route over 5-7 days.

9.3.2 Antiamoebic, antigiardial and antitrichomonal drugs

AMOEBIASIS

Amoebic dysentery is caused by *Entamoeba histolytica*. It is transmitted by the faeco-oral route and infection is usually caused by ingestion of cysts from contaminated food and drink. Asymptomatic carriers are common in endemic areas. In non-endemic areas, symptomless carriers should be treated with a luminal amoebicide which will reduce the risk of transmission and protect the patient from invasive amoebiasis. **Diloxanide furoate** is most widely used, but other compounds, including **clefamide**, **etofamide**, and **teclozan**, are also effective. Treatment with diloxanide furoate is regarded as successful if stools are free of *E. histolytica* for one month. Several specimens should be examined in evaluating response to treatment.

Symptomatic (invasive) amoebiasis may be classified as intestinal or extra-intestinal. Intestinal amoebiasis is either amoebic dysentery or non-dysenteric amoebic colitis. Extra-intestinal amoebiasis most commonly involves the liver, but may involve the skin, genito-urinary tract, lung and brain. Invasive amoebiasis is more likely in malnutrition, immunosuppression and pregnancy. Amoebic dysentery may take a fulminating

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course in late pregnancy and the puerperium; treatment with **metronidazole** may be life saving. In less severe infection, metronidazole should, if possible, be avoided in the first trimester. All patients with invasive amoebiasis require treatment with a systemically active compound such as **metronidazole**, **ornidazole** and **tinidazole** followed by a luminal amoebicide in order to eliminate any surviving organisms in the colon. Combined preparations are useful.

In severe cases of amoebic dysentery, tetracycline given in combination with a systemic amoebicide lessens the risk of superinfection, intestinal perforation and peritonitis. Hepatic abscesses should be lanced by needle aspiration.

GIARDIASIS

Giardiasis is caused by *Giardia intestinalis* and is acquired by oral ingestion of *Giardia* cysts. Giardiasis can be treated with **tinidazole** in a single dose or with another 5-nitroimidazole such as **metronidazole**; both are highly effective and should be offered when practicable to all infected patients. Family and institutional contacts should also be treated. Larger epidemics are difficult to eradicate because of the high proportion of symptomless carriers and because excreted cysts can survive for long periods outside the human host.

TRICHOMONIASIS

Trichomoniasis is an infection of the genito-urinary tract caused by *Trichomonas vaginalis* and transmission is usually sexual. In women it causes vaginitis although some are asymptomatic. It is usually asymptomatic in men but may cause urethritis. Patients and their sexual partners should be treated with *metronidazole* or other nitroimidazole.

DILOXANIDE FUROATE

Indications: Amoebiasis (asymptomatic carriers in non-endemic areas; eradication of residual luminal amoebae after treatment of invasive disease with other drugs).

Precautions: Pregnancy (defer treatment until after first trimester, Appendix 2); breastfeeding (Appendix 3).

Adverse effects: Flatulence; occasionally, vomiting, pruritus and urticaria.

Dose: *Amoebiasis (see above)*, by mouth, ADULT 500 mg 3 times daily for 10 days; CHILD over 25 kg, 20 mg/kg daily in 3 divided doses for 10 days; course may be repeated if necessary.

POM **Diloxanide furoate** *(WMF 6.41)*
Tablets, Diloxanide furoate 500 mg.

METRONIDAZOLE

Metronidazole is a representative antibacterial and antiprotozoal agent. Various drugs can serve as alternatives.

Therapeutic category: Amoebicide; Antiprotozoal.

Indications: Invasive amoebiasis and giardiasis; trichomoniasis; tissue nematode infections (section 9.4.1.3); bacterial infections (section 9.1.2.6); Helicobacter pylori eradication (section 4.1).

Contra-indications: Chronic alcohol dependence.

Precautions: Disulfiram-like reaction with alcohol; hepatic impairment and hepatic encephalopathy (Appendix 5); pregnancy (Appendix 2; see also notes above); breastfeeding (Appendix 3); clinical and laboratory monitoring in courses lasting longer than 10 days; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, unpleasant metallic taste, furred tongue and gastrointestinal disturbances; rarely headache, drowsiness, dizziness, ataxia, darkening of urine, erythema multiforme, pruritus, urticaria, angioedema, and anaphylaxis; abnormal liver function tests, hepatitis, jaundice, thrombocytopenia, aplastic anaemia, myalgia, arthralgia; peripheral neuropathy, epileptiform seizures, leukopenia, on prolonged or high dosage regimens.

Advice to patients: See Labels 4, 9, 21, 25 and 27 for tablets and labels 4, 9, and 23 for oral suspension in Appendix 6. Urine may be discoloured to a dark or reddish-brown; do not take alcohol for at least 24 hours after the last dose; avoid alcohol or alcohol-containing topical products during therapy; may cause metallic taste; may be taken with food to minimise stomach upset; notify physician if numbness or tingling in extremities occurs.

Nursing considerations: •Administer after meals to minimise GI distress and its metallic taste.

•The I.V form should be administered by slow infusion only. Don't give by I.V push.

•Advise patient's partner to use condom for coitus, if receiving treatment for trichomoniasis, to prevent cross transmission.

•Emphasize good personal hygiene after bowel motion viz handwashing and care of perineum.

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•If indicated during pregnancy for trichomoniasis, the 7-day regimen is preferred to the 2-g single dose regimen.
•Use cautiously in patients with a history of blood dyscrasia or CNS disorder, and in patients with retinal or visual field changes.
•Use with caution in hepatic disease or alcoholism and in conjunction with known hepatotoxic drugs.

Dose: *Invasive amoebiasis*, by mouth, ADULT and CHILD 30 mg/kg daily in 3 divided doses for 8–10 days; subsequent course of luminal amoebicide (see notes above).
Invasive amoebiasis (if oral administration not possible), by intravenous infusion, ADULT and CHILD 30 mg/kg daily in 3 divided doses (until patient able to complete course with oral drugs); subsequent course of luminal amoebicide (see notes above).
Giardiasis, by mouth, ADULT 2 g once daily for 3 days; CHILD 15 mg/kg daily in divided doses for 5–10 days.
Urogenital trichomoniasis, by mouth, ADULT 2 g as a single dose or 400–500 mg twice daily for 7 days; sexual partners should be treated concomitantly.

NOTE: IN AMOEBIASIS AND GIARDIASIS, VARIOUS DOSAGE REGIMENS ARE USED AND DEFINITIVE RECOMMENDATIONS SHOULD BE BASED ON LOCAL EXPERIENCE.

PATIENT ADVICE: METRONIDAZOLE TABLETS SHOULD BE SWALLOWED WHOLE WITH WATER, DURING OR AFTER A MEAL; METRONIDAZOLE SUSPENSION SHOULD BE TAKEN ONE HOUR BEFORE A MEAL.

POM **Metronidazole** *(WMF 6.4.1)*
Tablets, Metronidazole 200 mg, 250 mg, 400 mg, 500 mg.
Oral suspension, Metronidazole (as benzoate) 200 mg/5 ml.
Intravenous infusion (Solution for infusion), Metronidazole 5 mg/ml, 100-ml bag.

POM **Metronidazole** *(EDL 6.1)*
Tablet, Metronidazole 200 mg.
Suspension, Metronidazole (as benzoate) 200 mg per 5 ml.

POM **AMBIGYL**® *(Ranbaxy)*
Tablet, Metronidazole 200 mg.
200 mg - 1000.
Suspension, Metronidazole benzoyloxylate 200 mg per 5 ml.
Pack - 60 ml.

POM **AMEBANIL**® *(Dana)*
Tablet, Metronidazole 200 mg.
200 mg - 1000's.

POM **AMIBAGYL**® *(Afrab-chem)*
Tablet, Metronidazole 200 mg; off white scored tab. marked afrab.
200 mg - 1000.
Suspension, Metronidazole 200 mg per 5 ml.
Pack - 60 ml; 100 ml.

POM **CAREGYL**® *(Ulticare-Lyka)*
Tablet, Metronidazole 200 mg; white scored tab. marked "m/200".
200 mg - 10 x 10; 1000.

POM **EMGYL**® *(Emzor)*
Tablet, Metronidazole 200 mg; white biconvex tab.
200 mg - 1000.
Suspension, Metronidazole (as benzoate) 200 mg per 5 ml.
Pack - 60 ml.

POM **ENGIZOLE**® *(NGC)*
Tablet, Metronidazole 200 mg.
Suspension, Metronidazole (as benzoate) 200 mg per 5 ml.

POM **ENTAZIL**® *(KRSNA)*
Suspension, Metronidazole (as benzoate) 200 mg per 5 ml.
Pack - 60 ml.

POM **FAPOGYL**® *(Food & Pharma)*
Tablet, Metronidazole 200 mg.
200 mg -1000.
Suspension, Metronidazole 200 mg per 5 ml.
Pack - 60 ml.

POM **FEVAGYL**® *(David)*
Tablet, Metronidazole 200 mg.
200 mg - 1000
Suspension, Metronidazole 200 mg per 5 ml
Pack - 60 ml

POM **FLAGYL**® *(May & Baker)*
Tablet, Metronidazole 200 mg; white scored tab. marked 'FLAGYL 200'.
200 mg - 21; 250.
Suspension, Metronidazole (as benzoate) 200 mg per 5 ml; clear and colourless solution.
Pack - 100 ml; 500 ml.
Infusion, Metronidazole 0.5%; in 100 ml.

POM **JUGYL**® *(Juhel)*
Tablet, Metronidazole 200 mg; white scored biconvex tablet.
200 mg – 10 x 10's; 10 x 100's; 1000's.

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Paediatric suspension, Metronidazole (as benzoate) 200 mg per 5 ml.
Pack – 60 ml.

POM **METRIN**® *(Titan)*
Tablet, Metronidazole 200 mg.
200 mg - 1000.

POM **METROCIDE**® *(Farmex-Meyer)*
Suspension, Metronidazole 200 mg.
Pack - 60 ml.

POM **METROMAX**® *(GoldMoore)*
Tablet, Metronidazole BP 200 mg.
Pack - 1 x 10's; 1 x 1000's.

POM **Metronidazole** *(Dana)*
Infusion, Metronidazole 500 mg per 100 ml of water for injection.
Pack - 40's x 100 ml.

POM **Metronidazole** *(Dizpharm)*
Tablet, Metronidazole 200 mg.
200 mg - 1000.

POM **Metronidazole** *(Doyin)*
Tablet, Metronidazole 200 mg
200 mg - 100.
Suspension, Metronidazole 200 mg per 5 ml.
Pack - 60 ml.

POM **Metronidazole** *(Novel)*
Tablet, Metronidazole 200 mg; yellow tab. marked 'METRO/200' on one side and 'NOVEL' on the reverse.
200 mg - 1000.

POM **METROSAM**® *(Sam)*
Tablet, Metronidazole 200 mg; yellow scored tab.
200 mg - 1000
Infusion (i.v.), Metronidazole 0.5%; in 100 ml.

POM **METROZOL**® *(Vitabiotics)*
Tablet, Metronidazole 200 mg.
200 mg - 1000's.

POM **MIRAFYL**® *(Mirapharm)*
Tablet, Metronidazole 200 mg.
200 mg - 1000.

POM **MONILE**®*(Chris-Ejik)*
Tablet, Metronidazole 200 mg.
200 mg - 10, 1000.

POM **NIZOLE**® *(Hovid)*
Tablet, Metronidazole 200 mg.
200 mg - 10; 100.

POM **TAVZOLE**® *(Justeen)*
Tablet, Metronidazole BP 200 mg.
Pack - 10 x 10's.

POM **ULTRAGYL**® *(Strides Vital)*
Tablet, Metronidazole 200 mg; yellow tab. marked 'MTZ/200' on one side and doubly scored on the reverse.
200 mg - 10 x 10's; 1000's.

POM **UNIGYL**® *(Unique)*
Infusion, Metronidazole 500 mg per 100 ml of water for injection.
Pack - 100 ml.

SECNIDAZOLE

Therapeutic category: Antimicrobial agent of nitro-imidazole group
Indications: Trichomonas vaginalis, urethritis and vaginitis, intestinal amoebiasis; hepatic amoebiasis.
Contra-indications: Hypersensitivity to imidazole derivatives; first three months of pregnancy; breast-feeding.
Precautions: Disulfiram-like reaction with alcohol.
Interactions: Alcohol, oral anticoagulants
Adverse effects: Metallic taste in the mouth, gastralgia, nausea, abdominal pain, vomiting, stomatitis; rarely, vertigo, moderate neurological troubles.
Advice to patients: See labels 4,9,21,25 and 27 in Appendix 6.
Nursing considerations: •*See under Metronidazole*.
Dose: *Trichomonas vaginalis infections*, by mouth, 2 g (4 tabs) as a single dose.
Intestinal amoebiasis (acute, asymptomatic), by mouth, Adult, 2 g (4 tabs) as a single dose.
Child: 30 mg/kg b.wt. as a single dose.
Hepatic amoebiasis, by mouth, Adult, 1.5 g (3 tabs) once daily or in divided doses for 5 days.
Child: 30 mg/kg b.wt. once daily or in divided doses for 5 days.
Note: To be administered with meals to avoid GI symptoms and metallic taste in the mouth.

POM **FLAGENTYL**® *(May & Baker)*
Tablet, Secnidazole 500 mg; yellowish white scored f-c tab.
500 mg - 4

TINIDAZOLE

Therapeutic category: Antimicrobial agent.
Pharmacology: As for Metronidazole but has

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longer duration of action.
Indications: As for metronidazole.
Contra-indications, Precautions, etc: See under Metronidazole.
Advice to patients: See labels 4, 9, 21 and 25 in Appendix 6.
Dose: *Anaerobic infections*, by mouth, 2 g initially as a single dose, followed by 1 g daily or 500 mg twice daily, usually for 5-6 days.
Non-specific vaginitis, trichomoniasis, giardiasis, and acute ulcerative gingivitis, by mouth, 2 g as a single dose.
Intestinal amoebiasis, by mouth, 2 g daily for 3 days.
See lit. for details and use in children.

POM **Tinidazole** *(EDL 6.1)*
Tablet, Tinidazole 500 mg.

POM **FASIGYN**® *(Pfizer)*
Tablet, Tinidazole 500 mg; white f-c tab. 500 mg - 4; 100.

9.3.3 Antileishmanial drugs

Leishmaniasis is caused by the parasitic protozoa *Leishmania*. It can be categorized as visceral, cutaneous or mucocutaneous. It may be a self-limiting localized skin lesion but may range from this to disseminated progressive disease. In endemic areas there is usually a reservoir of disease in a mammalian host and the usual vectors are sandflies.

VISCERAL LEISHMANIASIS
Visceral leishmaniasis (kala-azar) is caused by *Leishmania donovani* and *L. infantum* (Old World) and by *L. chagasi* (New World), and it is usually responsive initially to the **pentavalent antimony compounds**, **meglumine antimoniate** or **sodium stibogluconate**. Both dosage and duration of treatment need to be adjusted according to the clinical response. Patients are considered to be clinically cured when no parasites are detected in splenic or bone marrow aspirates. However, biopsies should be repeated after 3 and 12 months since relapse is frequent. Antimonials combined with **allopurinol**, **pentamidine isetionate** and **amphotericin B** have been used with success in patients in relapse who have become unresponsive to antimonials alone.

CUTANEOUS LEISHMANIASIS
Cutaneous leishmaniasis comprises two conditions. The Old World variety is caused by *L. tropica*, *L. major*, *L. infantum* and *L. aethiopica*. The New World variety is caused by *L. amazonensis*, *L. mexicana*, *L. peruviana*, *L. guyanensis*, *L. panamensis* and *L. braziliensis*. These conditions are characterized by a cell-mediated reaction of varying intensity at the site of inoculation. The New World variety tends to be more severe and slower to heal. Infections caused by *L. major*, *L. mexicana*, *L. tropica* and *L. peruviana*, are responsive to intralesional injections of antimonial compounds. Mild lesions can often be left to heal spontaneously. However, it is preferable to treat *L. tropica* infections with a view to reducing transmission since humans seem to be the only host. When the lesion is inflamed or ulcerated or when obstruction of lymphatic drainage or destruction of cartilage creates a risk of serious disfigurement or disability, antimonials should be administered systemically as well as locally. Infections due to *L. braziliensis* and the less common *L. panamensis* should be treated with antimonials because of the risk of mucosal involvement. *L. aethiopica* is less responsive at conventional doses and the sores should be left to heal spontaneously if there is no evidence of diffuse cutaneous involvement. *L. guyanensis* infections should be treated with pentamidine.

MUCOCUTANEOUS LEISHMANIASIS
Mucocutaneous leishmaniasis is caused by *L. braziliensis* and *L. panamensis*. In this form of the disease the primary lesions do not heal and spread to the mucosa may occur. It usually responds to antimonials and, when relapses occur, more extended courses of treatment are often successful. Patients who still fail to respond should receive **amphotericin B** or **pentamidine isetionate**, although neither treatment is highly satisfactory. Because of resistance to antimonials, *L. aethiopica* infections should be treated with pentamidine from the outset until complete healing occurs.
Emergency use of corticosteroids may be needed to control pharyngeal or tracheal oedema produced by severe inflammation resulting from antigens liberated from dead parasites during the early phase of treatment.

Antibiotics may also be needed to treat

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secondary infections, and plastic surgery offers the only means of ameliorating disfiguring scars.

DIFFUSE CUTANEOUS LEISHMANIASIS
Diffuse cutaneous leishmaniasis usually occurs following infection with *L. amazonensis*, *L. aethiopica* or *L. mexicana* and is usually treated with **antimonial compounds**, but relapses must be expected and repeated courses of **pentamidine isetionate** may be needed until clinical immunity is established.

PENTAVALENT ANTIMONY COMPOUNDS

Meglumine antimoniate is a representative pentavalent antimony compound used to treat leishmaniasis; sodium stibogluconate can serve as an alternative.

Indications: Leishmaniasis (see notes above).

Contra-indications: Severe kidney disorders; breastfeeding.

Precautions: Provide protein-rich diet throughout treatment and, if possible, correct iron and other nutritional deficiencies; renal and hepatic impairment (Appendices 4 and 5); monitor cardiac, renal and hepatic function—reduce dose or withdraw treatment if abnormalities occur; pregnancy—in potentially fatal visceral leishmaniasis, treat without delay; intravenous injections must be given slowly over 5 minutes (to reduce risk of local thrombosis) and stopped if coughing or substernal pain; mucocutaneous disease (see below); treat intercurrent infection (for example pneumonia).

MUCOCUTANEOUS DISEASE: SUCCESSFUL TREATMENT OF MUCOCUTANEOUS LEISHMANIASIS MAY INDUCE SEVERE INFLAMMATION AROUND LESIONS (MAY BE LIFE-THREATENING IF PHARYNGEAL OR TRACHEAL INVOLVEMENT)—MAY REQUIRE CORTICOSTEROIDS.

Adverse effects: Anorexia, nausea, vomiting, abdominal pain, ECG changes (possibly requiring dose reduction or withdrawal), headache, lethargy, myalgia; raised liver enzymes; renal function impairment; coughing and substernal pain (see Precautions); rarely anaphylaxis, fever, sweating, flushing, vertigo, bleeding from nose or gum, jaundice, rash; pain and thrombosis on intravenous administration; pain on intramuscular injection.

Dose: NOTE: DOSES ARE EXPRESSED IN TERMS OF PENTAVALENT ANTIMONY.

Visceral leishmaniasis, by intramuscular injection, ADULT and CHILD 20 mg/kg daily for a minimum of 20 days; if relapse, retreat immediately with same daily dosage.

Cutaneous leishmaniasis (except L. aethiopica, L. braziliensis, L. amazonensis), by intralesional injection, ADULT and CHILD 1–3 ml into base of lesion; if no apparent response, may be repeated once or twice at intervals of 1–2 days; by intramuscular injection, ADULT and CHILD 10–20 mg/kg daily until a few days after clinical cure and negative slit-skin smear; relapse is unusual.

Cutaneous leishmaniasis (L. braziliensis), by intramuscular injection, ADULT and CHILD 20 mg/kg daily, until lesion has healed and for at least 4 weeks; relapse may occur due to inadequate dosage or interrupted treatment; relapse after full course of treatment requires treatment with pentamidine (see below).

Mucocutaneous leishmaniasis (L. braziliensis), by intramuscular injection, ADULT and CHILD 20 mg/kg daily until slit-skin smears are negative and for at least 4 weeks; if inadequate response, 10–15 mg/kg every 12 hours for same period; if relapse, retreat for at least twice as long; if unresponsive to treatment, treat with pentamidine or amphotericin B (see below).

Diffuse cutaneous leishmaniasis (L. amazonensis), by intramuscular injection, ADULT and CHILD 20 mg/kg daily for several months after clinical improvement occurs; relapse must be expected until immunity develops.

ADMINISTRATION: MEGLUMINE ANTIMONIATE MAY BE GIVEN BY DEEP INTRAMUSCULAR INJECTION. SODIUM STIBOGLUCONATE MAY BE GIVEN BY INTRAMUSCULAR INJECTION OR BY SLOW INTRAVENOUS INJECTION (OVER AT LEAST 5 MINUTES). BOTH MAY BE ADMINISTERED INTRALESIONALLY.

POM **Pentavalent antimony** *(WMF 6.4.2)*
Injection (Solution for injection), Pentavalent antimony (as Meglumine antimoniate) 85 mg/ml, 5-ml ampoule; Pentavalent antimony (as Sodium stibogluconate) 100 mg/ml, 100-ml bottle.

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POM **Meglumine antimonate** *(EDL 6.5)*
Injection, Total antimony 8.5%.

POM **Sodium Stibogluconate** *(EDL 6.5)*
Injection, Total antimony 10%.

MEGLUMINE

See under Pentavalent antimony compounds above

SODIUM STILBOGLUCONATE

See under Pentavalent antimony compounds above

PENTAMIDINE

Pentamidine isetionate is a complementary antiprotozoal and antipneumocystis drug.

Indications: Leishmaniasis (see notes, above); African trypanosomiasis (section 9.3.4.1); Pneumocystis carinii pneumonia (section 9.3.5).

Contra-indications: Severe renal impairment.

Precautions: Risk of severe hypotension following administration (establish baseline blood pressure and administer with patient lying down); monitor blood pressure during administration and treatment period; hypotension or hypertension; hypoglycaemia or hyperglycaemia; hepatic impairment; leukopenia, thrombocytopenia, anaemia; immunodeficiency—if acute deterioration in bone marrow, renal or pancreatic function, interrupt or discontinue treatment; renal impairment (Appendix 4); pregnancy—in potentially fatal visceral leishmaniasis, treat without delay (Appendix 2); breastfeeding (Appendix 3); carry out laboratory monitoring according to manufacturer's literature.

Adverse effects: Nephrotoxicity; acute hypotension—with dizziness, headache, breathlessness, tachycardia and syncope following rapid intravenous injection; hypoglycaemia—may be followed by hyperglycaemia and type I diabetes mellitus; pancreatitis; also hypocalcaemia, gastrointestinal disturbances, confusion, hallucinations, arrhythmias; thrombocytopenia, leukopenia, abnormal liver function tests; anaemia; hyperkalaemia; rash, Stevens-Johnson syndrome, reported; pain, local induration, sterile abscess and muscle necrosis at injection site.

Dose: *Visceral leishmaniasis (unresponsive to or intolerant of pentavalent antimony compounds)*, by deep intramuscular injection or by intravenous infusion, ADULT and CHILD 4 mg/kg 3 times a week for 5–25 weeks or longer, until two consecutive splenic aspirates taken 14 days apart are negative.
Cutaneous leishmaniasis (L. aethiopica, L. guyanensis), by deep intramuscular injection or by intravenous infusion, ADULT and CHILD 3–4 mg/kg once or twice a week until the lesion is no longer visible; relapse is unusual.
Diffuse cutaneous leishmaniasis (L. aethiopica), by deep intramuscular injection or by intravenous infusion, ADULT and CHILD 3–4 mg/kg once a week, continued for at least 4 months after parasites no longer detectable in slit-skin smears; relapse frequent during first few months until immunity established.
Mucocutaneous leishmanisais (L. braziliensis, L. aethiopica), by deep intramuscular injection or by intravenous infusion, ADULT and CHILD 4 mg/kg 3 times a week for 5–25 weeks or longer, until lesion no longer visible.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. DEEP INTRAMUSCULAR INJECTION IS THE PREFERRED ROUTE OF ADMINISTRATION. PENTAMIDINE ISETIONATE IS TOXIC; CARE REQUIRED TO PROTECT PERSONNEL DURING HANDLING AND ADMINISTRATION.

POM **Pentamidine** *(WMF 6.4.2)*
Injection (Powder for solution for injection), Pentamidine isetionate 200-mg vial, 300-mg vial.

POM **Pentamidine** *(EDL 6.5)*
Injection, Pentamidine 300 mg; powder in vial.

AMPHOTERICIN B

Amphotericin B is a complementary drug for the treatment of leishmaniasis.

Indications: Visceral and mucocutaneous leishmaniasis unresponsive to pentavalent antimony compounds; fungal infections (section 9.2).

Precautions: Close medical supervision throughout treatment and initial test dose required (see note below); renal impairment (Appendix 4); hepatic and renal function tests; blood counts and plasma electrolyte monitoring; corticosteroids

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(avoid except to control reactions); pregnancy (Appendix 2); breastfeeding (Appendix 3); avoid rapid infusion (risk of arrhythmias); **interactions**: Appendix 1.

ANAPHYLAXIS: ANAPHYLAXIS OCCURS RARELY WITH INTRAVENOUS AMPHOTERICIN B AND A TEST DOSE IS ADVISABLE BEFORE THE FIRST INFUSION. THE PATIENT SHOULD BE OBSERVED FOR ABOUT 30 MINUTES AFTER THE TEST DOSE.

Adverse effects: Fever, headache, anorexia, weight loss, nausea and vomiting, malaise, diarrhoea, muscle and joint pain, dyspepsia, and epigastric pain; renal function disturbances including hypokalaemia, hypomagnesaemia and renal toxicity; blood disorders; cardiovascular toxicity (including arrhythmias); neurological disorders (including peripheral neuropathy); abnormal liver function (discontinue treatment); rash; anaphylactoid reactions (see above); pain and thrombophlebitis at injection site.

Dose: *Visceral and mucocutaneous leishmaniasis (unresponsive to pentavalent antimony compounds)*, by intravenous infusion, ADULT initial test dose of 1 mg over 20–30 minutes, then, 5–10 mg, increased by 5–10 mg daily up to maximum of 0.5–1 mg/kg, which is then administered on alternate days (total cumulative dose of 1–3 g usually required).

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Amphotericin B** *(WMF 6.4.2)*
Injection (Powder for solution for injection), amphotericin B 50-mg vial.

9.3.4 Antitrypanosomal drugs

9.3.4.1 African trypanosomiasis
9.3.4.2 American trypanosomiasis

9.3.4.1 African trypanosomiasis

African trypanosomiasis, or sleeping sickness, is a protozoan infection transmitted by *Glossina* spp. (tsetse flies). Two subspecies of *Trypanosoma brucei* — *T. brucei gambiense* and *T. brucei rhodesiense*— produce distinctive clinical forms of the disease. The early stage of African trypanosomiasis results from infection of the blood stream and lymph nodes. The late meningoencephalitic stage results from infection of the central nervous system. Signs of the later stage develop within a few weeks in *T. b. rhodesiense* infection but only after several months or years in *T. b. gambiense* infection.

Treatment of early-stage infections of *T. b. rhodesiense* with **suramin sodium** and *T. b. gambiense* with **pentamidine isetionate** can be curative if started before the central nervous system has become involved. In areas where pentamidine resistance occurs, suramin sodium may be used for *T. b. gambiense* infection. **Melarsoprol** is used for confirmed cases of *T. b. gambiense* or *T. b. rhodesiense* with meningoencephalitic involvement. Several treatment regimens for adults and children are currently used in the absence of clear evidence that one is better than another. Most treatment regimens have low starting doses (especially for children and debilitated patients), increasing to a maximum of 3.6 mg/kg daily. It is given in short courses of 3–4 days with an interval of 7–10 days between courses. A severe febrile reaction may occur after the first injection, especially if patients have a large number of trypanosomes in their blood; therefore, suramin or pentamidine are often given before starting melarsoprol treatments. An increasing number of melarsoprol treatment failures have been reported in the last years in several countries. **Eflornithine** is an alternative drug which has been shown to be both effective and considerably less toxic than melarsoprol in patients with meningoencephalopathy resulting from *T. b. gambiense* trypanosomiasis.

MELARSOPROL

Indications: Treatment of meningoencephalitic stage of *T. b. gambiense* or *T. b. rhodesiense* infections.

Contra-indications: Pregnancy; avoid use during influenza epidemics.

Precautions: Hospitalization and close medical supervision required throughout treatment; episodes of reactive encephalopathy (may require treatment suspension); treat intercurrent infections such as pneumonia and malaria before malarsoprol administration; malnutrition (if possible, correct with protein-rich diet); G6PD deficiency; leprosy—may precipitate erythema nodosum.

Adverse effects: Fatal reactive

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encephalopathy characterized by headache, tremor, slurred speech, convulsions and ultimately coma (in 3–8% of patients, usually at end of first 3–4 days of treatment); myocardial damage; albuminuria; hypertension; hypersensitivity reactions; agranulocytosis; dose-related renal and hepatic impairment; hyperthermia, urticaria, headache, diarrhoea and vomiting—in late stage of treatment.

Dose: Treatment of *T. b. gambiense* and *T. b. rhodesiense* with meningoencephalitic involvement (see notes above), by slow intravenous injection, ADULT and CHILD dose gradually increased from 1.2 mg/kg to maximum of 3.6 mg/kg daily in courses of 3–4 days with intervals of 7–10 days between courses or 2.2 mg/kg daily for 10 days.

ADMINISTRATION: INJECTION VERY IRRITANT—AVOID EXTRAVASATION. PATIENTS SHOULD REMAIN SUPINE AND FASTING FOR AT LEAST 5 HOURS AFTER INJECTION.

POM **Melarsoprol** *(WMF 6.4.4.1)*
Injection (Solution for injection), Melarsoprol 3.6% in propylene glycol.

POM **Melarsoprol** *(EDL 6.5)*
Injection, Melarsoprol 3.6%.

PENTAMIDINE

Pentamidine isetionate is a complementary antitrypanosomal drug.

Indications: Treatment of haemolymphatic stage of *T. b. gambiense* infection; adjunct to melarsoprol in meningoencephalitic stage of *T. b. gambiense* infection; leishmaniasis (section 9.3.3); Pneumocystis carinii pneumonia (section 9.3.5).

Contra-indications: Severe renal impairment; *T. b. rhodesiense* infection (since primary resistance observed).

Precautions: Cerebrospinal fluid examination before treatment (pentamidine not likely to be effective if leukocyte count greater then 5 cells/mm3, total protein greater then 37 mg/100 ml, or trypanosomes detected in centrifuge deposits); risk of severe hypotension following administration (establish baseline blood pressure and administer with patient lying down); monitor blood pressure during administration and treatment period; hypotension or hypertension; hepatic impairment; hypoglycaemia or hyperglycaemia; leukopenia; thrombocytopenia; anaemia; immunodeficiency—if acute deterioration in bone marrow, renal or pancreatic function, interrupt or discontinue treatment; renal impairment (Appendix 4); pregnancy—should not be withheld, even if evidence of meningoencephalitic involvement, as melarsoprol contraindicated (Appendix 2); breastfeeding (Appendix 3).

Adverse effects: Nephrotoxicity; acute hypotension, hypoglycaemia—may be followed by hyperglycaemia and type I diabetes mellitus; pancreatitis; also hypocalcaemia, gastrointestinal disturbances, confusion, hallucinations, arrhythmias; thrombocytopenia, leukopenia, abnormal liver function tests; anaemia; hyperkalaemia; rash, Stevens-Johnson syndrome reported; pain, local induration, sterile abscess and muscle necrosis at injection site.

Dose: *Treatment of haemolymphatic stage of T. b. gambiense infection* by intramuscular injection, ADULT and CHILD 4 mg/kg daily or on alternate days for a total of 7–10 doses.
Treatment of meningoencephalitic stage of T. b. gambiense (prior to melarsoprol), by intramuscular injection, ADULT and CHILD 4 mg/kg daily on days one and two.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. PENTAMIDINE ISETIONATE IS TOXIC; CARE IS REQUIRED TO PROTECT PERSONNEL DURING HANDLING AND ADMINISTRATION.

POM **Pentamidine** *(WMF 6.4.4.1)*
Injection (Powder for solution for injection), Pentamidine isetionate 200-mg vial, 300-mg vial.

POM **Pentamidine** *(EDL 6.5)*
Injection, Pentamidine 300 mg; powder in vial.

SURAMIN

Indications: Treatment of haemolymphatic stage of T. b. gambiense and *T. b. rhodesiense* infections; adjunct to melarsoprol in meningoencephalitic stage of *T. b. gambiense* and *T. b. rhodesiense* infections; onchocerciasis (section 9.4.2.3).

Contra-indications: Previous anaphylaxis or suramin sensitivity; severe liver or renal function impairment; elderly or debilitated.

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Precautions: Administer only under close medical supervision in hospital and with general condition improved as far as possible before treatment; first dose—possible loss of consciousness (see under Dosage, below); maintain satisfactory food and fluid intake during treatment; urine tests before and weekly during treatment—reduce dose if moderate albuminuria, discontinue immediately if severe albuminuria or casts in urine; pregnancy—should not be withheld, even if evidence of meningoencephalitic involvement, as melarsoprol contraindicated.

Adverse effects: Rarely, immediate and potentially fatal reaction with nausea, vomiting, shock and loss of consciousness during first dose—see First (Test) Dose, above; albuminuria; abdominal pain; severe diarrhoea; stomal ulceration; exfoliative dermatitis; fever; tiredness; anorexia; malaise; polyuria; thirst; raised liver enzyme values; paraesthesia and hyperaesthesia of palms and soles.

Dose: *Treatment of haemolymphatic T. b. gambiense and T. b. rhodesiense infections*, by slow intravenous injection, ADULT and CHILD 5 mg/kg on day 1, 10 mg/kg on day 3 and 20 mg/kg on days 5, 11, 17, 23 and 30.

Treatment of meningoencephalitic T. b. gambiense and T. b. rhodesiense infections (prior to melarsoprol), by slow intravenous injection, ADULT and CHILD 5 mg/kg on day 1, 10 mg/kg on day 3 and in some regimens, 20 mg/kg on day 5.

RECONSTITUTION OF INJECTION: RECONSTITUTE IN WATER FOR INJECTIONS TO PRODUCE A FINAL CONCENTRATION OF 10%.

FIRST (TEST) DOSE: ADMINISTER FIRST DOSE WITH PARTICULAR CAUTION; WAIT AT LEAST 1 MINUTE AFTER INJECTING THE FIRST FEW MICROLITRES; INJECT NEXT 0.5 ML OVER 30 SECONDS AND WAIT ONE MINUTE; INJECT THE REMAINDER OVER SEVERAL MINUTES.

POM **Suramin** *(WMF 6.4.4.1)*
Injection (Powder for solution for injection), Suramin sodium 1-g vial.

POM **Suramin** *(EDL 6.3)*
Injection, Suramin 1 g; powder in vial.

EFLORNITHINE

Eflornithine HCl is a complementary drug.

Indications: Treatment of haemolymphatic and meningoencephalitic stages of *T. b. gambiense* infection.

Contra-indications: Pregnancy; breastfeeding.

Precautions: Hospitalization and close supervision throughout treatment; blood and lymph node aspirates examined daily until trypanosome negative for two consecutive days, then weekly during treatment; examination for leukocytes, total protein content and trypanosome presence in CSF after course of treatment and at intervals for following 24 months; renal impairment (Appendix 4).

Adverse effects: Diarrhoea, anaemia, leukopenia, thrombocytopenia and convulsions; impaired hearing reported; vomiting, anorexia, alopecia, abdominal pain, headache, facial oedema, eosinophilia and dizziness—less common and reversible on treatment withdrawal.

Dose: *Treatment of T. b. gambiense infections*, by intravenous infusion, ADULT 100 mg/kg over 45 minutes, every 6 hours for at least 14 days (7 days if previous treatment with melarsoprol has failed); if relapse occurs, repeat course of treatment.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Eflornithine** *(WMF 6.4.4.1)*
Infusion (Solution for dilution for infusion), Eflornithine HCl 200 mg/ml, 100-ml ampoule.

9.3.4.2 American trypanosomiasis

American trypanosomiasis (Chagas disease) is caused by the protozoan parasite *Trypanosoma cruzi* which are carried by reduviid or triatomine bugs which feed on human blood. The acute febrile phase of the disease frequently passes unrecognized. Occasionally, however, infection follows a fulminating course terminating in a fatal myocarditis and meningoencephalitis. In about half of the surviving cases, and after a latent interval ranging from 10 to more than 20 years, chronic myopathy degeneration results in arrhythmias, cardiac enlargement and less, frequently, oesophageal and colonic dilatation. At this stage, only symptomatic treatment is of benefit.

At present the only therapeutic agents of value are **benznidazole** and **nifurtimox**. Both suppress parasitaemia and are

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efficacious during the early stages of infection.

Safe use of both drugs in pregnancy has not been established and treatment should be deferred until after the first trimester. They should be instituted immediately to avoid the risk of congenital transmission.

Studies are in progress to determine whether benznidazole and nifurtimox have any influence on the later manifestations of the disease. Symptomatic treatment may be necessary in advanced cases.

BENZNIDAZOLE

Indications: Acute American trypanosomiasis (Chagas disease).
Contra-indications: Early pregnancy
Precautions: Hepatic, renal or haematological insufficiency—require close medical supervision; monitor blood count, especially leukocytes, throughout treatment.
Adverse effects: Rashes—if severe and accompanied by fever and purpura, discontinue treatment; nausea, vomiting and abdominal pain; dose-related paraesthesia and peripheral neuritis—discontinue treatment; leukopenia and rarely, agranulocytosis.
Dose: *Acute American trypanosomiasis (Chagas disease)*, by mouth, ADULT 5–7 mg/kg daily in two divided doses for 60 days; CHILD up to 12 years 10 mg/kg daily in two divided doses for 60 days.

POM **Benznidazole** *(WMF 6.4.4.2)*
Tablets, Benznidazole 100 mg.

NIFURTIMOX

Indications: Acute American trypanosomiasis (Chagas disease).
Contra-indications: Early pregnancy
Precautions: History of convulsions or psychiatric disease—requires close medical supervision; avoid alcohol—to reduce incidence and severity of adverse effects; co-administer aluminium hydroxide to reduce gastrointestinal irritation.
Adverse effects: Anorexia, loss of weight, nausea, vomiting, gastric pain, insomnia, headache, vertigo, excitability, myalgia, arthralgia, convulsions—dose-related, reduce dose; peripheral neuritis—may require discontinuation; rashes and other allergic reactions.
Dose: *Acute American trypanosomiasis (Chagas disease)*, by mouth, ADULT 8–10 mg/kg daily in 3 divided doses for 90 days; CHILD 15–20 mg/kg daily in 4 divided doses for 90 days.

POM **Nifurtimox** *(WMF 6.4.4.2)*
Tablets, Nifurtimox 30 mg, 120 mg, 250 mg.

9.3.5 Antipneumocystosis and antitoxoplasmosis drugs

PNEUMOCYSTOSIS

Pneumocystis carinii is classified as a protozoan although there is evidence to suggest that it is probably a fungus. *Pneumocystis carinii* pneumonia is probably acquired by the airborne route. In otherwise healthy persons it rarely produces signs of infection. However, it is a frequent cause of opportunistic infection in immunosuppressed, debilitated or malnourished patients; it is the commonest cause of pneumonia in AIDS and the most frequent immediate cause of death in these patients.

Sulfamethoxazole with **trimethoprim** is the treatment of choice for *Pneumocystis carinii* pneumonia and is also used for prophylaxis in high-risk patients; **pentamidine isetionate** is used in patients unresponsive to or intolerant of sulfamethoxazole with trimethoprim.

The treatment of *Pneumocystis carinii* infections must only be undertaken with specialist supervision where there are appropriate monitoring facilities.

TOXOPLASMOSIS

Toxoplasmosis is caused by infection with the protozoan parasite *Toxoplasma gondii*. Most infections are self-limiting and do not require treatment. However, in immunodeficiency, primary infection may result in encephalitis, myocarditis or pneumonitis; impairment of immunity (such as occurs in AIDS) in a previously infected person, may result in encephalitis or meningoencephalitis. Congenital transmission may occur if there is a primary infection in early pregnancy or if the mother is immunodeficient. Such cases often result in spontaneous abortion, fetal death or severe congenital disease. Ocular toxoplasmosis causes chorioretinitis and is often the result of a childhood infection that becomes apparent in adulthood.

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The treatment of choice for toxoplasmosis is **pyrimethamine** with **sulfadiazine**; a folate supplement is also given to counteract the megaloblastic anaemia associated with these drugs.

SULFAMETHOXAZOLE plus TRIMETHOPRIM

Indications: *Pneumocystis carinii* pneumonia; bacterial infections (section 9.1.2.9).

Contra-indications: Hypersensitivity to sulfonamides or trimethoprim; porphyria

Precautions: Renal impairment (avoid if severe; Appendix 4); hepatic impairment (avoid if severe; Appendix 5); maintain adequate fluid intake (to avoid crystalluria; avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rash—discontinue immediately; predisposition to folate deficiency; elderly; asthma; G6PD deficiency; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, diarrhoea, headache; hypersensitivity reactions including rashes, pruritus, photosensitivity reactions, exfoliative dermatitis and erythema nodosum; rarely, erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis; systemic lupus erythematosus, myocarditis, serum sickness; crystalluria—resulting in haematuria, oliguria, anuria; blood disorders including granulocytopenia, agranulocytosis, aplastic anaemia, purpura—discontinue immediately; also reported, liver damage, pancreatitis, antibiotic-associated colitis, eosinophilia, cough and shortness of breath, pulmonary infiltrates, aseptic meningitis, depression, convulsions, ataxia, tinnitus, vertigo, dizziness, hallucinations, and electrolyte disturbances; megaloblastic anaemia due to trimethoprim.

Dose: *Treatment of Pneumocystis carinii pneumonia (see notes above)*, by mouth or by intravenous infusion, ADULT and CHILD sulfamethoxazole up to 100 mg/kg daily with trimethoprim up to 20 mg/kg daily in 2–4 divided doses for 14–21 days.
Prophylaxis of Pneumocystis carinii pneumonia (see notes above), by mouth, ADULT and CHILD sulfamethoxazole 25 mg/kg with trimethoprim 5 mg/kg in 2 divided doses on alternate days (3 times a week).

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Sulfamethoxazole plus Trimethoprim** *(WMF 6.4.5)*
Tablets, Sulfamethoxazole 400 mg with trimethoprim 80 mg; Sulfamethoxazole 800 mg with trimethoprim 160 mg.
Oral suspension, Sulfamethoxazole 200 mg with trimethoprim 40 mg/5 ml.
Injection (Solution for dilution for infusion), Sulfamethoxazole 80 mg with trimethoprim 16 mg/ml, 5-ml and 10-ml ampoules.

POM **Co-trimoxazole** *(EDL 6.8)*
Tablets, Co-trimoxazole 120 mg, 480 mg.
Suspension, Co-trimoxazole 240 mg per 5 ml.

See section 9.1.2.9 for the proprietary preparations of Co-trimoxazole.

PENTAMIDINE

Pentamidine isetionate is a complementary antipneumocystosis drug.

Indications: *Pneumocystis carinii* pneumonia; leishmaniasis (section 9.3.3); African trypanosomiasis (section 9.3.4.1).

Contra-indications: Severe renal impairment.

Precautions: Risk of severe hypotension following administration (establish baseline blood pressure and administer with patient lying down); monitor blood pressure during administration and treatment period; hypotension or hypertension; hypoglycaemia or hyperglycaemia; hepatic impairment; renal impairment (Appendix 4); leukopenia, thrombocytopenia, anaemia; immunodeficiency—if acute deterioration in bone marrow, renal or pancreatic function, interrupt or discontinue treatment; pregnancy—in potentially fatal *P. carinii* pneumonia, treat without delay (Appendix 2); breastfeeding (Appendix 3); carry out laboratory monitoring according to manufacturer's literature.

Adverse effects: Nephrotoxicity; acute hypotension—with dizziness, headache, breathlessness, tachycardia and syncope following rapid intravenous injection; hypoglycaemia—may be followed by hyperglycaemia and type I diabetes mellitus; pancreatitis; also hypocalcaemia,

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gastrointestinal disturbances, confusion, hallucinations, arrhythmias; thrombocytopenia, leukopenia, abnormal liver function tests; anaemia; hyperkalaemia; rash, Stevens-Johnson syndrome reported; pain, local induration, sterile abscess and muscle necrosis at injection site.

Dose: *Treatment of P. carinii pneumonia (see notes above)*, by slow intravenous infusion or by deep intramuscular injection, ADULT and CHILD 4 mg/kg daily for at least 14 days.

Prophylaxis of P.carinii pneumonia (see notes above), by slow intravenous infusion, ADULT and CHILD 4 mg/kg once every 4 weeks or by inhalation of nebulized solution, ADULT 300 mg as a single dose once every 4 weeks; CHILD 4 mg/kg as a single dose once every 4 weeks.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. PENTAMIDINE ISETIONATE IS TOXIC; CARE IS REQUIRED TO PROTECT PERSONNEL DURING HANDLING AND ADMINISTRATION.

POM **Pentamidine** *(WMF 6.4.5)*

Injection (Powder for solution for injection), Pentamidine isetionate 200-mg vial, 300-mg vial.

Nebulizer solution, Pentamidine isetionate 300-mg bottle [not included on WHO Model List].

PYRIMETHAMINE

Indications: Toxoplasmosis (with sulfadiazine); malaria (with sulfadoxine) (section 9.3.1).

Contra-indications: Hepatic and renal impairment.

Precautions: Pregnancy (avoid in first trimester but give in later pregnancy if danger of congenital transmission; Appendix 2); breastfeeding (Appendix 3); blood counts required with prolonged treatment; folate supplements throughout treatment; **interactions**: Appendix 1.

Adverse effects: Depression of haematopoiesis with high doses; megaloblastic anaemia; rashes; insomnia; gastrointestinal disturbances.

Dose: *Toxoplasmosis (in second and third trimesters of pregnancy)*, by mouth, ADULT 25 mg daily for 3–4 weeks.

Toxoplasmosis in neonates, by mouth, neonate 1 mg/kg daily; duration of treatment depends on whether neonate has overt disease—continue for 6 months, or is without overt disease but, born to mother infected during pregnancy—treat for 4 weeks, followed by further courses if infection confirmed.

Toxoplasmosis in immunodeficiency, by mouth, ADULT 200 mg in divided doses on first day, then 75–100 mg daily for at least 6 weeks, followed by a suppressive dose of 25–50 mg daily.

Chorioretinitis, by mouth, ADULT 75 mg daily for 3 days then 25 mg daily for 4 weeks; in unresponsive patients, 50 mg daily for a further 4 weeks.

NOTE: FOR THE TREATMENT OF TOXOPLASMOSIS, PYRIMETHAMINE MUST ALWAYS BE TAKEN WITH SULFADIAZINE (SEE BELOW).

POM **Pyrimethamine** *(WMF 6.4.5)*

Tablets, Pyrimethamine 25 mg, 50 mg [50-mg strength not included on WHO Model List].

SULFADIAZINE

Sulfadiazine is a complementary antitoxoplasmosis drug.

Indications: Toxoplasmosis (with pyrimethamine); rheumatic fever (section 9.1.2.9).

Contra-indications: Hypersensitivity to sulfonamides; porphyria.

Precautions: Hepatic impairment (avoid if severe; Appendix 5); renal impairment (avoid if severe; Appendix 4); maintain adequate fluid intake (to avoid crystalluria); avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rashes—discontinue immediately; predisposition to folate deficiency; elderly; asthma; G6PD deficiency; pregnancy—avoid in first trimester, but may be given thereafter if danger of congenital transmission (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, diarrhoea, headache; hypersensitivity reactions including rashes, pruritus, photosensitivity reactions, exfoliative dermatitis, and erythema nodosum; rarely, erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis; systemic lupus erythematosus, myocarditis, serum sickness; crystalluria—resulting in haematuria, oliguria, anuria;

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blood disorders including granulocytopenia, agranulocytosis, aplastic anaemia, purpura—discontinue immediately; also reported, liver damage, pancreatitis, antibiotic-associated colitis, eosinophilia, cough and shortness of breath, pulmonary infiltrates, aseptic meningitis, depression, convulsions, ataxia, tinnitus, vertigo, dizziness, hallucinations, and electrolyte disturbances.

Dose: *Toxoplasmosis (in second and third trimesters of pregnancy)*, by mouth, ADULT 3 g daily in 4 divided doses.

Toxoplasmosis in neonates, by mouth, neonate 85 mg/kg daily in 2 divided doses; duration of treatment depends on whether the neonate has overt disease—continue for 6 months, or is without overt disease but born to mother infected during pregnancy—treat for 4 weeks, followed by further courses, if infection confirmed.

Toxoplasmosis in immunodeficiency, by mouth, ADULT 4–6 g daily in 4 divided doses for at least 6 weeks, followed by a suppressive dose of 2–4 g daily.

Chorioretinitis, by mouth, ADULT 2 g daily in 4 divided doses.

NOTE: FOR THE TREATMENT OF TOXOPLASMOSIS, SULFADIAZINE MUST ALWAYS BE TAKEN WITH PYRIMETHAMINE (SEE ABOVE).

POM **Sulfadiazine** *(WMF 6.4.5)*
Tablets, Sulfadiazine 500 mg.

9.4 Anthelmintics

9.4.1 Intestinal anthelmintics
9.4.2 Antifilarials
9.4.3 Trematode infections

9.4.1 Intestinal anthelmintics

9.4.1.1 Cestode infections
9.4.1.2 Intestinal nematode infections
9.4.1.3 Tissue nematode infections

9.4.1.1 Cestode infections

Cestode infections (tapeworms) include intestinal taeniasis and cysticercosis, hymenolepiasis (dwarf tapeworm), diphyllobothriasis and echinococcosis (hydatid disease). Cysticercosis is a systemic infection caused by the larval form (cysticercus) of *Taenia solium*.

Neurocysticercosis occurs when the infection involves the brain. In man, echinococcosis is due to the larval stage of *Echinococcus granulosus* or *E. multilocularis*. The larvae (oncospheres) develop by expansion (cystic echinococcosis) or tumour-like infiltration (alveolar echinococcosis), respectively, in the liver, lungs, or other organs.

DIPHYLLOBOTHRIASIS
In diphyllobothriasis, **niclosamide** or **praziquantel** in a single dose is highly effective. Hydroxocobalamin and folic acid supplements may also be required.

ECHINOCOCCOSIS
In echinococcosis, surgery (or, if this is not possible, a technique such as 'puncture-aspiration-injection-reaspiration') is the treatment of choice for operable cystic disease due to *Echinococcus granulosus* but chemotherapy with benzimidazoles, such as **mebendazole** and **albendazole**, may be of value as adjunctive therapy. Alveolar echinococcosis due to *E. multilocularis* requires both surgery and long-term treatment with either mebendazole or albendazole to inhibit spread of the infection.

In *animal* studies, albendazole and mebendazole have been found to be teratogenic. They are contraindicated for the treatment of cestode infections in pregnancy; pregnancy should be excluded before treatment with albendazole (non-hormonal contraception during and for 1 month after treatment). For single-dose or short-term use in pregnancy, see section 9.4.1.2.

HYMENOLEPIASIS
In hymenolepiasis, **praziquantel** is more effective than **niclosamide**, although resistance to praziquantel has been reported. Repeated treatment may be necessary to cure intense infections or to eliminate the parasite within a family group or institution.

TAENIASIS
In taeniasis, **praziquantel** is well tolerated and extensively absorbed and kills adult intestinal taenia worms in a single dose. Praziquantel also kills *T. solium* cysticerci when taken for 14 days in high doses. It thus offers the prospect of a cure for

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neurocysticercosis, which has been treatable only by surgery, anti-inflammatory corticosteroids and anticonvulsants. However, because dying and disintegrating cysts may induce localized cerebral oedema, treatment with praziquantel must always be undertaken in a hospital setting. In addition, a corticosteroid is usually given to reduce the inflammatory response. **Albendazole** also kills neurocysticerci when given daily for one month; a corticosteroid or an antihistamine is also given to reduce any inflammatory reaction. The longer-established **niclosamide** acts only against the adult intestinal worms. Cestode infections, due to *T. solium*, occurring during pregnancy should always be treated immediately (with praziquantel or niclosamide, but not with albendazole) because of the risk of cysticercosis.

ALBENDAZOLE

Indications: *Echinococcus multilocularis* and *E. granulosus* infections prior to or not amenable to surgery; neurocysticercosis; nematode infections (sections 9.4.1.2 and 9.4.1.3); filariasis (section 9.4.2.2).

Contra-indications: Pregnancy (Appendix 2; see notes above and Precautions).

Precautions: Liver function tests and blood counts before treatment and twice during each cycle; exclude pregnancy before starting treatment (non-hormonal contraception during and for 1 month after treatment); breastfeeding; **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances, headache, dizziness; increases in liver enzymes; reversible alopecia; rash; fever; leukopenia and rarely, pancytopenia; allergic shock if cyst leakage; convulsions and meningism in cerebral disease.

Advice to patients: See label 9 in Appendix 6.

Dose: *Cystic echinococcosis*, by mouth, ADULT over 60 kg, 800 mg daily in 2 divided doses for 28 days followed by 14 tablet-free days; ADULT less than 60 kg, 15 mg/kg daily in two divided doses (to a maximum daily dose of 800 mg) for 28 days followed by 14 tablet-free days; up to 3 courses may be given.

Alveolar echinococcosis, by mouth, ADULT as for cystic echinococcosis, but treatment cycles may need to be continued for months or years.

Neurocysticercosis, by mouth, ADULT over 60 kg, 800 mg daily in 2 divided doses for 8–30 days; ADULT less than 60 kg, 15 mg/kg daily in two divided doses (to a maximum daily dose of 800 mg) for 8–30 days.

See also under the proprietary preparations below.

Note: No fasting or purging is required. To be chewed, swallowed or crushed and mixed with food.

POM **Albendazole** *(WMF 6.1.1.1)*
Chewable tablets, Albendazole 400 mg.

POM **Albendazole** *(EDL 6.2)*
Tablet, Albendazole 200 mg.
Suspension, Albendazole 100 mg per 5 ml.

POM **ALBEZOL®** *(Farmex)*
Tablet, Albendazole BP 200 mg; uncoated tab. 200 mg - 2's (in blister).

POM **ALZOL®** *(Titan)*
Tablet, Albendazole 400 mg.
400 mg - 2 x 10.
Suspension, Albendazole 4%.
Pack - 10 ml.

POM **MESIN®** *(Unison)*
Tablet, Albendazole 200 mg; white f-c tab. marked with maker's logo on one side.
200 mg - 2.

POM **NEMOZOLE®** *(IPCA)*
Suspension, Albendazole USP 100 mg per 5 ml.
Pack - 20 ml.

POM **VERZOL®** *(St. Michael)*
Tablet, Albendazole 400 mg.
400 mg - 1.
Suspension, Albendazole 4%.
Pack - 10 ml.

POM **ZENTEL®** *(GSK)*
Tablet, Albendazole 200 mg; off-white, circular 'Tiltab' tab. with pentagonal projection on both sides.
200 mg - 2.
Suspension, Albendazole 100 mg per 5 ml; pleasant tasting, fruit flavoured susp.
Pack - 20 ml.

Dose: Adult and Children over 2 years, 2 tabs or 20 ml susp. (400 mg) as single dose. *Strongyloidiasis* or *Taeniasis*, 2 tabs or 20 ml susp. (400 mg) as single dose for 3 consecutive days; second course may

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be given after 3 weeks if necessary
Child (under 2 years), 10 ml susp. or ½ tab. (200 mg) as single dose for common hehminth infections.
Hymenolepis nana infection, 2 tabs or 20 ml susp. (400 mg) for 3 consecutive days.

POM **ZOLAT**® *(Emzor)*
Caplet, Albendazole 200 mg.
200 mg - 2.
Suspension, Albendazole 100 mg per 5 ml; pleasant tasting, fruit flavoured susp.
Pack - 20 ml.

MEBENDAZOLE

Mebendazole is a representative benzimidazole carbamate derivative anthelminthic. Various drugs can serve as alternatives.

Indications: *Echinococcus granulosus* and *E. multilocularis* infections before surgery or not amenable to surgery; nematode infections (sections 9.4.1.2 and 9.4.1.3).

Contra-indications: Pregnancy (Appendix 2; see also notes above).

Precautions: Blood counts and liver function tests (with high-dose regimens); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances, headache, dizziness; with high doses, allergic reactions, raised liver enzymes, alopecia, bone marrow depression.

Advice to patients: Tablets may be chewed, swallowed whole, or crushed and mixed with food to minimise GI upset; hygienic precautions should be taken to prevent reinfection such as wearing shoes and washing hands; wash all fruits and vegetables before eating; a second course of therapy may be needed after 3 weeks if necessary; deworm all family members; dietary restrictions, enamas or laxatives are not necessary.

Nursing considerations: •No dietary restrictions, laxatives, or enemas are necessary. Treat all family members.
•Teach patient about the need for good personal hygiene, especially good handwashing technique. To avoid reinfection, teach him to wash perianal area daily. Change undergarments and bedclothes daily. Wash hands and clean fingernails before meals and after bowl movements.
•Advise patient to avoid preparing food during infestation.

Dose: *Cystic echinococcosis*, alveolar echinococcosis, by mouth, ADULT 4.5 g daily in 3 divided doses for 6 months; in alveolar echinococcosis, treatment may be required for up to 2 years after radical surgery, or indefinitely in inoperable cases.

PATIENT ADVICE: DOSES SHOULD BE TAKEN BETWEEN MEALS.

POM **Mebendazole** *(WMF 6.1.1.1)*
Chewable tablets, Mebendazole 100 mg, 500 mg.

POM **Mebendazole** *(EDL 6.2)*
Tablet, Mebendazole 100 mg.

POM **DANAMEB**® *(Dana)*
Tablet, Mebendazole 100 mg.
100 mg - 20 x 6's.

POM **EXPELL**® *(Ranbaxy)*
Suspension, Mebendazole 100 mg per 5 ml.
Pack - 30 ml.

POM **MEBENDEX**® *(Titan)*
Tablet, Mebendazole 100 mg.
100 mg - 10 x 6.

POM **MEBEZOLE**® *(Greenlife)*
Tablet, Mebendazole 100 mg; uncoated tab.
100 mg - 6.

POM **VERMOX**® *(Janssen-Cilag)*
Tablet, Mebendazole 100 mg (light-brown scored tab), 500 mg (biconvex tab. marked 'VERMOX 500')
100 mg - 6; 240.
500 mg - 1
Suspension, Mebendazole 100 mg per 5 ml.
Pack - 30 ml.

POM **WORMIN**® *(Interpharma)*
Tablets, Mebendazole 100 mg, 500 mg.
100 mg - 24 x 6's.
500 mg - 20 x 1's.
Suspension, Mebendazole 100 mg per 5 ml.
Pack - 30 ml.

POM **X-PELL**® *(Jawa)*
Suspension, Mebendazole 100 mg per 5 ml
Pack - 30 ml.

NICLOSAMIDE

Indications: *Taenia saginata*, *T. solium*, *Hymenolepis nana*, and *Diphyllobothrium latum* infections.

Precautions: Chronic constipation (restore regular bowel movement before treatment); give antiemetic before

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treatment; not effective against larval worms; pregnancy (Appendix 2).

Adverse effects: Nausea, retching, abdominal pain; lightheadedness; pruritus.

Advice to patients: See Labels 4 and 24 in Appendix 6. Chew tablets thoroughly before washing down with water; tablets can be pulverised and mixed with water to form a paste for administration to children; can be taken with food; a mild laxative can be used for constipation.

Nursing considerations: •Administer a laxative 2-3 hours after the niclosamide dose if treating *Taenia solium* infections to prevent the development of cysticercosis.

•Fruit juice can aid the expulsion of dwarf tapeworms lodged in the intestinal mucous. Patient is regarded cured when 3 negative stool results have been received.

•Teach patient proper hygiene methods.

Dose: *Taenia solium infection*, by mouth, ADULT and CHILD over 6 years 2 g as a single dose after a light breakfast, followed by a purgative after 2 hours; CHILD under 2 years 500 mg, 2–6 years 1 g.

T. saginata and *Diphyllobothrium latum* infections, by mouth, as for *T. solium* but half the dose may be taken after breakfast and the remainder 1 hour later followed by a purgative 2 hours after last dose.

Hymenolepis nana infection, by mouth, ADULT and CHILD over 6 years 2 g as a single dose on first day then 1 g daily for 6 days; CHILD under 2 years 500 mg on the first day then 250 mg daily for 6 days, 2–6 years, 1 g on first day then 500 mg daily for 6 days.

PATIENT ADVICE: TABLETS SHOULD BE CHEWED THOROUGHLY (OR CRUSHED) BEFORE WASHING DOWN WITH WATER.

POM **Niclosamide** *(WMF 6.1.1.1)*
Chewable tablets, Niclosamide 500 mg.

POM **Niclosamide** *(EDL 6.2)*
Tablet (Chewable), Niclosamide 500 mg.

POM **YOMESAN®** *(Gemini)*
Tablet, Niclosamide 500 mg; yellow, chewable tab. marked 'BAYER' and 'FE'.
500 mg - 4.

PRAZIQUANTEL

Pharmacology: Praziquantel increases cell membrane permeability in susceptible worms, resulting in a loss of intracellular calcium, massive contractions and paralysis of their musculature. There is further vacuolization and disintegration of the schistosome tegument followed by attachment of phagocytes to the parasite and death.

Indications: Taenia saginata, T. solium, Hymenolepis nana and Diphyllobothrium latum infections; trematode infections (sections 9.4.3.1 and 9.4.3.2).

Contra-indications: Ocular cysticercosis.

Precautions: Neurocysticercosis (corticosteroid cover with monitoring, in hospital); pregnancy (Appendix 2); breastfeeding (avoid during and for 72 hours after treatment); **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Abdominal discomfort, nausea, vomiting, diarrhoea, malaise; headache, dizziness, drowsiness; rarely hypersensitivity reactions including fever, urticaria, pruritus, eosinophilia (may be due to dead and dying parasites); in neurocysticercosis, headache, hyperthermia, seizures, intracranial hypertension (inflammatory response to dead and dying parasites in CNS).

Advice to patients: Do not chew tablets due to bitter taste; take with food; caution should be used when performing tasks requiring mental alertness, may impair judgement and co-ordination.

Dose: *Taenia saginata and T. solium infections*, by mouth, ADULT and CHILD over 4 years 5–10 mg/kg as a single dose

Hymenolepis nana infection, by mouth, ADULT and CHILD over 4 years, 15–25 mg/kg as a single dose.

Diphyllobothrium latum infection, by mouth, ADULT and CHILD over 4 years, 10–25 mg/kg as a single dose.

Cysticercosis, by mouth, ADULT and CHILD over 4 years, 50 mg/kg daily in 3 divided doses for 14 days with prednisolone (or similar corticosteroid) given 2–3 days before and throughout treatment period.

Dermal cysticercosis, by mouth, ADULT and CHILD over 4 years, 60 mg/kg daily in 3 divided doses for 6 days.

Note: The tablets should be taken unchewed with some liquid during meals. Keeping the tablets or its segments in the mouth can give a bitter taste which can promote gagging or vomiting.

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POM **Praziquantel** *(WMF 6.1.1.1)*
Tablets, Praziquantel 150 mg, 600 mg.

POM **Praziquantel** *(EDL 6.4)*
Tablet, Praziquantel 600 mg.

POM **AZITEL®** *(Panvij Biotec)*
Tablet, Praziquantel 600 mg; white to orange tinged, oblong, f-c tab. marked 'AZITEL' on one side and 'PBL' with two score lines on the reverse.
600 mg - 8.
Dose: *Schistosomiasis*, 3 doses of 20 mg/kg given 4-6 hours apart as one day treatment.
Clonorchiasis and Opisthorchiasis, 3 doses of 25 mg/kg given 4-6 hours apart as one day treatment.

POM **BILTRICIDE®** *(Gemini)*
Tablet, Praziquantel 600 mg.
600 mg - 1000.

9.4.1.2 Intestinal nematode infections

Intestinal nematode infections include ascariasis, capillariasis, enterobiasis, hookworm infection, strongyloidiasis, trichostrongyliasis and trichuriasis.

ASCARIASIS
Ascariasis is an infection, usually of the small intestine, caused by *Ascaris lumbricoides* (roundworm). Single doses of **levamisole** or **pyrantel** are effective; the broad-spectrum anthelminthics, **albendazole** or **mebendazole** are also effective.

CAPILLARIASIS
Capillariasis is caused by infection of the intestine with Capillaria philippinensis . Prolonged treatment with **mebendazole** or **albendazole** offers the only prospect of cure.

ENTEROBIASIS
Enterobiasis is an infection of the large intestine caused by *Enterobius vermicularis* (pinworm, threadworm). All household members should be treated concurrently with a single dose of **mebendazole**, **albendazole** or **pyrantel**. Since reinfection readily occurs, at least one further dose should be given 2–4 weeks later. Piperazine is also effective but must be taken regularly for at least 7 consecutive days.

HOOKWORM INFECTIONS
Hookworm infections are caused by *Ancylostoma duodenale* (ancylostomiasis) and *Necator americanus* (necatoriasis); they are a major cause of iron-deficiency anaemia in the tropics and sub-tropics. Ideally all cases of hookworm infection should be treated. However, when this is impracticable, priority should be given to women in second- and third-trimester of pregnancy, children and debilitated patients. In hookworm, broad-spectrum anthelminthics are preferred wherever other nematode infections are endemic. Both **mebendazole** and **albendazole** are effective.

In *animal* studies, **albendazole** and **mebendazole** have been found to be teratogenic. There is some evidence to suggest that the use of mebendazole in pregnancy is not associated with an increased incidence of adverse effects on the fetus. However, neither mebendazole nor albendazole should be used during the first trimester of pregnancy to treat nematode infections. Both drugs are contraindicated for the treatment of cestode infections in pregnancy (see section 9.4.1.1).

Levamisole is effective in the treatment of mixed *Ascaris* and hookworm infections and **pyrantel** has been highly effective in some community-based control programmes, although several doses are often needed to eliminate *Necator americanus* infection. Patients with iron-deficiency anaemia caused by hookworm infection require supplementary iron salts and should receive ferrous sulfate (200 mg daily for adults) for at least 3 months after the haemoglobin concentration of 12 g/100 ml is obtained.

STRONGYLOIDIASIS
Strongyloidiasis is an infection of the small intestine caused by *Strongyloides stercoralis*. All infected patients should be treated. **Ivermectin** in a single dose of 200 micrograms/kg or 200 micrograms/kg/day on two consecutive days is the treatment of choice for chronic strongyloidiasis but it may not be available in all countries. **Albendazole** 400 mg once or twice daily for 3 days is well tolerated by both adults and children aged over 2 years and it may eradicate up to 80% of infections. **Mebendazole** has also been used but, to

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be effective, it must be administered for longer periods as it has a limited effect on larvae and hence the prevention of autoinfection.

TRICHOSTRONGYLIASIS
Trichostrongyliasis is an infection of the small intestine caused by *Trichostrongylus* spp. In symptomatic trichostrongyliasis, a single dose of **pyrantel** (10 mg/kg) or **albendazole** (400 mg) is effective.

TRICHURIASIS
Trichuriasis is an infection of the large intestine caused by *Trichuris trichiura* (whipworm). Chemotherapy is required whenever symptoms develop or when faecal samples are found to be heavily contaminated (up to 10 000 eggs per gram). A single dose of **albendazole** (400 mg) or **mebendazole** (500 mg) can be effective in mild to moderate infections; heavier infections require a 3-day course.

ALBENDAZOLE

Indications: Ascariasis, hookworm infections, strongyloidiasis, enterobiasis, trichuriasis, trichostrongyliasis, and capillariasis; cestode infections (section 9.4.1.1); tissue nematode infections (section 9.4.1.3); filariasis (9.4.2.2).
Precautions: Pregnancy (see notes above and Appendix 2; also section 9.4.1.1); **interactions**: Appendix 1.
Adverse effects: Gastrointestinal discomfort, headache; adverse effects associated with use in cestode infections (section 9.4.1.1).
Dose: *Ascariasis, hookworm infections, enterobiasis, and trichostrongyliasis*, by mouth, ADULT and CHILD over 2 years, 400 mg as a single dose; child 12 months–2 years, 200 mg as a single dose.
Trichuriasis, by mouth, ADULT and CHILD over 2 years, 400 mg as a single dose (for moderate infections) or 400 mg daily for 3 days (severe infections); child 12 months–2 years, 200 mg as a single dose (for moderate infections) or 200 mg initially then 100 mg twice daily for 3 days (severe infections).
Strongyloidiasis, by mouth, ADULT and CHILD over 2 years, 400 mg once or twice daily for 3 days.
Capillariasis, by mouth, ADULT and CHILD over 2 years, 400 mg daily for 10 days.

POM **Albendazole** *(WMF 6.1.1.2)*
Chewable tablets, Albendazole 400 mg.

POM **Albendazole** *(EDL 6.2)*
Tablet, Albendazole 200 mg.
Suspension, Albendazole 100 mg per 5 ml.

See section 9.4.1.1 for the proprietary preparations of Albendazole.

LEVAMISOLE

Indications: Ascariasis, hookworm, and mixed ascariasis with hookworm infections; malignant disease (section 12.1).
Contra-indications: Breastfeeding (Appendix 3).
Precautions: Pregnancy (Appendix 2); **interactions**: Appendix 1.
Adverse effects: Abdominal pain, nausea, vomiting, dizziness, and headache
Dose: *Ascariasis, hookworm, and mixed ascariasis with hookworm infections*, by mouth, ADULT and CHILD 2.5 mg/kg as a single dose; in severe hookworm infection, a second dose may be given after 7 days.

POM **Levamisole** *(WMF 6.1.1.2)*
Tablets, Levamisole (as HCl) 40 mg, 50 mg, 150 mg.

POM **Levamisole** *(EDL 6.2)*
Tablet, Levamisole 40 mg (as HCl)
Syrup, Levamisole 40 mg (as HCl) per 5 ml.

POM **KETRAX®** *(Reals)*
Tablet, Levamisole 40 mg; red tab. marked 'KETRAX'.
Syrup, Levamisole 40 mg per 5 ml; cherry red with raspberry odour.

POM **SAMTREX®** *(Sam)*
Tablet, Levamisole 40 mg; red tab.
40 mg - 2 x 10.

MEBENDAZOLE

Mebendazole is a representative benzimidazole carbamate derivative anthelminthic. Various drugs can serve as alternatives.
Indications: Ascariasis, hookworm infections, enterobiasis, trichuriasis, and capillariasis; cestode infections (section 9.4.1.1); tissue nematode infections (section 9.4.1.3).
Precautions: Pregnancy (Appendix 2; see also notes above and section 9.4.1.1);

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breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Gastrointestinal disturbances, headache, and dizziness; adverse effects associated with use in cestode infections (section 9.4.1.1).

Advice to patients: Tablets may be chewed, swallowed whole, or crushed and mixed with food to minimise GI upset; hygienic precautions should be taken to prevent reinfection such as wearing shoes and washing hands; wash all fruits and vegetables before eating; a second course of therapy may be needed after 3 weeks if necessary; deworm all family members; dietary restrictions, enamas or laxatives are not necessary.

Dose: *Ascariasis*, by mouth, ADULT and CHILD over 1 year, 500 mg as a single dose or 100 mg twice daily for 3 days.

Hookworm infections, trichuriasis, by mouth, ADULT and CHILD over 1 year, 100 mg twice daily for 3 days; if eggs persist in the faeces, second course after 3–4 weeks; alternatively (especially for mass treatment control programmes), by mouth, ADULT and CHILD over 1 year, 500 mg as a single dose.

Enterobiasis, by mouth, ADULT and CHILD over 2 years, 100 mg as a single dose, repeated after interval of 2–3 weeks; all household members over 2 years should be treated at the same time.

Capillariasis, by mouth, ADULT and CHILD over 2 years, 200 mg daily for 20–30 days; for mass treatment control programmes, by mouth, ADULT and CHILD over 2 years, 500 mg as a single dose 4 times a year.

PATIENT ADVICE: DOSES SHOULD BE TAKEN BETWEEN MEALS.

POM **Mebendazole** *(WMF 6.1.1.2)*
Chewable tablets, Mebendazole 100 mg, 500 mg.

POM **Mebendazole** *(EDL 6.2)*
Tablet, Mebendazole 100 mg.

See section 9.4.1.1 for the proprietary preparations of Mebendazole.

PIPERAZINE

Therapeutic category: Anthelmintic

Pharmacology: Piperazine is effective against round-worms (ascaris) and threadworms (enterobius). It produces reversible muscle paralysis in roundworms which takes at least 5 hours to develop; the worms are then easily dislodged by gut movement.

Indications: Treatment of enterobiasis and ascariasis.

Contra-indications: Liver disease, epilepsy, renal failure.

Precautions: Impaired renal function, latent epilepsy, chronic disorders of CNS.

Adverse effects: Nausea, vomiting; colic, diarrhoea; headache, dizziness, convulsion, muscular incoordination and weakness.

Advice to patients: See Label 24 for tablets and Label 13 for oral granules in Appendix 6. Take on an empty stomach for best absorption; if severe or persistent headache, loss of balance or co-ordination, dizziness, vomiting, diarrhoea, or rash occurs, contact physician. If used for pinworm infections, all members of family should be treated.

Nursing considerations: •Administer drug crushed or chewed if patient is unable to swallow it whole; may be given with food, but for best absorption give on an empty stomach.
•Give laxative if patient is constipated.
•Teach patient proper hygiene after bowel movement, to avoid reinfection.
•Discontinue if CNS or significant GI reactions occur.
•Because of potential for neurotoxicity, avoid prolonged or repeated treatment, especially in children.

Dose: *Ascariasis*, Adult and children over 10 years, 30 ml elixir; 6-10 years, 20 ml; under 2 years, 120 mg piperazine hydrate per kg. body-wt.
To be taken as a single dose.
Enterobiasis, Adult and children over 12 years, 15 ml elixir; 5-12 years, 10 ml; 2-4 years, 5 ml; under 2 years 50-75 mg piperazine hydrate per kg body-wt.
To be taken once daily for 7 days.
See lit. for dose equivalents of tablets and granules.

OTC **Piperazine** *(EDL 6.2)*
Tablet, Piperazine (as Adipate or Citrate) 500 mg.
Granules, Piperazine (as Adipate or citrate) 5 g/Cachet.
Elixir/syrup, Piperazine (as Adipate or Citrate) 500 mg per 5 ml.

OTC **ANTEPAR®** *(SKG Pharma)*
Elixir Piperazine hydrate 750 mg per 5 ml (as hydrate and citrate).
Pack - 30 ml

OTC **MATHEWWORM®** *(Daily Need)*
Elixir, Piperazine (as citrate) 937.5 mg per 5

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ml.
Pack - 30 ml.

OTC **MOKO WORM ELIXIR**® *(New Healthway)*
Elixir, Piperazine (as citrate) 0.9375%.
Pack - 30 ml.

OTC **PADRAX**® *(GSK)*
Oral powder, Piperazine citrate 5 g per sachet.
Pack - 10

OTC **PENTA-ELIX**® *(Morison)*
Elixir, Piperazine 500 mg (as citrate) per 5 ml; clear orange liquid.
Pack - 30 ml.

OTC **Piperazine** *(Emzor)*
Tablet, Piperazine (as citrate) 500 mg
500 mg - 3; 100; 500; 1000.

OTC **UVILON**® *(Gemini)*
Syrup, Piperazine hydrate 750 mg per 5 ml.
Pack - 30 ml.

PYRANTEL

Indications: Ascariasis, hookworm infections, enterobiasis, and trichostrongyliasis; tissue nematode infections (section 9.4.1.3).
Precautions: Pregnancy; breastfeeding; liver disease (reduce dose).
Adverse effects: Mild gastrointestinal disturbances, headache, dizziness, drowsiness, insomnia, rash, and elevated liver enzymes.
Advice to patients: May mix drug with food, milk or fruit juice; strict hygiene is essential to prevent reinfection.
Nursing considerations: •Shake well before pouring to assure acurate dosage; treat other members of the family.
•Teach patient proper hygiene after bowel movement especially handwashing, scrubbing of finger nails before and after eating, washing of the perineal area and change of under pant.
•Instruct patient to wash all fruits and vegetables well before eating.
•No dietary restrictions, laxatives, or enemas are necessary.
Dose: *Ascariasis, trichostrongyliasis*, by mouth, ADULT and CHILD 10 mg/kg as a single dose.
Hookworm infections, by mouth, ADULT and CHILD 10 mg/kg as a single dose; in severe infections, 10 mg/kg daily for 4 days.
Enterobiasis, by mouth, ADULT and CHILD 10 mg/kg as a single dose with a second dose after 2–4 weeks.

POM **Pyrantel** *(WMF 6.1.1.2)*
Chewable tablet, Pyrantel (as embonate) 250 mg.
Oral suspension, Pyrantel (as embonate) 50 mg/ml.

OTC **Pyrantel** *(EDL 6.2)*
Tablets, Pyrantel 125 mg (as pamoate) per 5 ml.
Suspension, Pyrantel 250 mg (as pamoate) per 5 ml.

OTC **COMBANTRIN**® *(Neimeth)*
Tablet, Pyrantel pamoate 125 mg; orange tab.
125 mg - 6; 1000.
Caplet, Pyrantel pamoate 250 mg; orange caplet.
250 mg - 3; 75.
Suspension, Pyrantel pamoate 250 mg per 5 ml; yellow caramel flavoured susp.
Pack - 15 ml.

OTC **COMBIWORM**® *(Vitabiotics)*
Tablet, Pyrantel pamoate 125 mg.
125 mg - 12 x 6's.

OTC **D-WORM P**® *(Farmex-Meyer)*
Suspension, Pyrantel pamoate 250 mg per 5 ml.
Pack - 15 ml.

OTC **THELMIN**® *(Hovid)*
Tablet, Pyrantel pamoate 125 mg; f-c tab.
125 mg - 100.

TIABENDAZOLE

Synonym: Thiabendazole
Indications: Strongyloidiasis, cutaneous larva migrans (creeping eruption); dracunculiasis (guinea worm), visceral larva migrans; enterobiasis (threadworm); trichinosis; also for hookworm, whipworm (trichuriasis), ascariasis.
Precautions: Renal or hepatic dysfunction, pregnancy, breast-feeding.
Interactions: Xanthines.
Adverse effects: Anorexia, nausea, vomiting, dizziness, diarrhoea, epigastric distress, hypersensitivity reactions, lymphadenopathy; rarely Stevens Johnson's Syndrome.
Advice to patients: See Labels 3, 21 and 24 in Appendix 6. Take after meals, chew chewable tablets well, shake suspension well before measuring; may decrease alertness, avoid driving or operating machinery; drinking of fruit juice aids in expulsion of worms by removing the mucous to which the intestinal

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tapeworms attach themselves.

Nursing considerations: •No dietary restrictions, laxatives, or enemas are necessary.
•Treat all family members.
•Teach patient proper hygiene methods to prevent reinfection.

Dose: By mouth, Adult 60 kg and above, 1.5 g 1-2 times daily for 2-4 days; max. daily dose is 3 g.
Less than 60 kg, 25 mg/kg per dose.

POM **Tiabendazole** *(EDL 6.2)*
Tablet Chewable, Tiabendazole 500 mg.
Syrup, Tiabendazole 500 mg per 5 ml.

POM **MINTEZOL®** *(Bolax/BPP)*
Tablet, Tiabendazole 500 mg; orange, chewable tab. marked 'MSD 907'
500 mg - 6; 12.
Suspension, Tiabendazole 500 mg per 5 ml
Pack - 30 ml

9.4.1.3 Tissue nematode infections

Tissue nematode infections include angiostrongyliasis, anisakiasis, cutaneous larva migrans, dracunculiasis, trichinellosis, and visceral larva migrans.

ANGIOSTRONGYLIASIS
Angiostrongyliasis is caused by infection with the larvae of the rat lungworm, *Parastrongylus cantonensis* (*Angiostrongylus cantonensis*). Symptomatic treatment pending spontaneous recovery is often all that is required.

ANISAKIASIS
Anisakiasis is caused by infection with seafood containing larvae of *Anisakis*, *Contracaecum*, or *Pseudoterranova* spp. In anisakiasis, anthelminthic treatment is rarely necessary. Prevention is dependent upon informing communities of the hazards of eating raw or inadequately prepared salt-water fish; and early evisceration of fish after capture and freezing of seafood at -20°C for at least 60 hours before sale.

CUTANEOUS LARVA MIGRANS
Cutaneous larva migrans (creeping eruption) is caused by infection with larvae of animal hookworms, usually *Ancylostoma braziliense* and *A. caninum* which infect cats and dogs. **Albendazole** (section 9.4.1) in a single dose of 400 mg is effective.

DRACUNCULIASIS
Dracunculiasis (dracontiasis, guinea-worm infection) is caused by infection with *Dracunculus medinensis*, acquired through drinking water containing larvae that develop in small freshwater crustaceans. **Metronidazole** (section 9.3.2) (25 mg/kg daily for 10 days, with a daily maximum of 750 mg for children) provides rapid symptomatic relief. It also weakens the anchorage of the worms in the subcutaneous tissues, and they can then be removed by traction. However, since it has no effect on the larvae of pre-emergent worms, it does not immediately prevent transmission.

TRICHINELLOSIS
Trichinellosis (trichinosis) is caused by infection with the larvae of *Trichinella spiralis*. Each case of confirmed or even suspected trichinellosis infection should be treated in order to prevent the continued production of larvae. In both adults and children, **mebendazole** (section 9.4.1) (200 mg daily for 5 days), **albendazole** (section 9.4.1) (400 mg daily for 3 days), and **pyrantel** (section 9.4.1) (10 mg/kg daily for 5 days) are all effective. Prednisolone (40–60 mg daily) may be needed to alleviate the allergic and inflammatory symptoms.

VISCERAL LARVA MIGRANS
Visceral larva migrans (toxocariasis) is caused by infection with the larval forms of *Toxocara canis* and less commonly, *T. cati* (which infect dogs and cats). Treatment should be reserved for symptomatic infections. A 3-week oral course of **diethylcarbamazine** (section 9.4.2) kills the larvae and arrests the disease, but established lesions are irreversible. To reduce the intensity of allergic reactions induced by dying larvae, dosage is commonly commenced at 1 mg/kg twice daily and raised progressively to 3 mg/kg twice daily (adults and children).

Ocular larva migrans occurs when larvae invade the eye, causing a granuloma which may result in blindness. In order to suppress allergic inflammatory responses in patients with ophthalmic lesions, prednisolone should be administered concurrently, either topically or systemically.

9.4.2 Antifilarials

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9.4.2.1 Loiasis
9.4.2.2 Lymphatic filariasis
9.4.2.3 Onchocerciasis

9.4.2.1 Loiasis

Loiasis is an infection with the filarial nematode *Loa loa* and is transmitted by the biting tabanid fly *Chrysops*. **Diethylcarbamazine** is effective against both adult worms and larvae; a single weekly dose is normally effective as prophylaxis. During individual treatment, particularly of persons with heavy microfilaraemia (>50 000 microfilariae/ml blood), a condition simulating meningoencephalitis occasionally occurs. This probably results from sludging of moribund microfilariae within cerebral capillaries. The frequency of meningoencephalitis associated with diethylcarbamazine therapy of loiasis is reported as 1.25%, with a mortality rate of about 50% in affected patients; treatment with diethylcarbamazine should be stopped at the first sign of cerebral involvement (and specialist advice sought). Permanent cerebral damage is common among patients who survive and this possibility should be considered when deciding on treatment. Treatment of heavily infected patients should thus begin at low dosage and corticosteroid and antihistamine cover should be provided for the first 2 to 3 days.

DIETHYLCARBAMAZINE

Diethylcarbamazine citrate is a complementary antifilarial drug.

Indications: Treatment of loiasis; prophylaxis of loiasis in temporary residents in endemic areas; tissue nematode infections (section 6.1.1.3); lymphatic filariasis (section 6.1.2.2).

Contra-indications: Pregnancy (delay treatment until after delivery); infants, elderly, debilitated (usually excluded from mass treatment programmes; see also Precautions).

Precautions: Renal impairment (reduce dose; Appendix 4); cardiac disorders; other severe acute diseases—delay diethylcarbamazine treatment until after recovery; risk of meningoencephalitis in severe infection (see notes above).

Adverse effects: Headache, dizziness, drowsiness, nausea and vomiting; immunological reactions, within a few hours of the first dose, subsiding by fifth day of treatment, and including fever, headache, joint pain, dizziness, anorexia, malaise, nausea and vomiting, urticaria, and asthma in asthmatics (similar to Mazzotti reaction—see section 9.4.2.3), induced by disintegrating microfilariae; microencephalitis (with heavy microfilaraemia, see notes above); reversible proteinuria.

Advice to patients: See label 9 in Appendix 6.

Dose: *Loiasis, treatment*, by mouth,
ADULT 1 mg/kg as a single dose on the first day, doubled on two successive days, then adjusted to 2–3 mg/kg 3 times daily for a further 18 days.
Loiasis, prophylaxis, by mouth,
ADULT 300 mg weekly for as long as exposure occurs.

PATIENT ADVICE: COMPLETE THE PRESCRIBED COURSE AS DIRECTED TO MIMIMIZE ALLERGIC REACTIONS TO DYING PARASITES.

POM **Diethylcarbamazine** *(WMF 6.1.2.1)*
Tablets, Diethylcarbamazine citrate 50 mg, 100 mg.

POM **Diethylcarbamazine** *(EDL 6.3)*
Tablet, Diethylcarbamazine (as citrate) 50 mg.

POM **BANOCIDE®** *(SKG)*
Tablet, Diethylcarbamazine citrate 50 mg; white scored tab. marked 'WELLCOME S2A'. 50 mg - 100.

Dose: *Treatment of Filariasis*, initially 1 mg/kg in 3 divided doses on day one; increase gradually over 2-3 days to 6 mg /kg in 3 divided doses for 21 days.
Prophylaxis against Malayian and Bancroftian Filariasis, 50 mg as a single dose monthly.
Prophylaxis against Loiasis, 5 mg/kg as a single dose for 3 consecutive days; repeat every month.

9.4.2.2 Lymphatic filariasis

Lymphatic filariasis is caused by infection with *Wuchereria bancrofti* (bancroftian filariasis), *Brugia malayi* or *B. timori* (brugian filariasis). Occult filariasis (tropical pulmonary eosinophilia) is a clinical variant of *W. bancrofti* infection. Individual treatment with **diethylcarbamazine** which has both microfilaricidal and macrofilaricidal activity is effective. Total

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cumulative dosages of 72 mg/kg are generally recommended for *Wuchereria bancrofti* infections with half this dose used for *Brugia malayi* and *B. timori* infections. In all cases treatment is best initiated with smaller doses for 2–3 days to avoid the danger of immunological reactions. Rigorous hygiene to the affected limbs with adjunctive measures to minimize infection and promote lymph flow are important for reducing acute episodes of inflammation.

In communities where filariasis is endemic, annual administration of single doses of **albendazole** 400 mg with either diethylcarbamazine (6 mg/kg) or **ivermectin** (200 micrograms/kg) is effective for interrupting transmission; this treatment is continued for at least 5 years. Trials in India and China have shown that the consistent use for 6–12 months of table salt containing diethylcarbamazine 0.1% can eliminate *W. bancrofti*; a concentration of 0.3% for 3–4 months may be required where *B. malayi* is endemic.

DIETHYLCARBAMAZINE

Diethylcarbamazine citrate is a complementary antifilarial drug.

Indications: Systemic lymphatic filariasis and occult filariasis; loiasis (section 9.4.2.1); tissue nematode infections (section 9.4.1.3).

Contra-indications: Pregnancy (delay treatment until after delivery).

Precautions: Renal impairment (reduce dose; Appendix 4); cardiac disorders; other severe acute disease—delay diethylcarbamazine treatment until after recovery.

Adverse effects: headache, dizziness, drowsiness, nausea and vomiting; immunological reactions, within a few hours of the first dose, subsiding by fifth day of treatment, including fever, headache, joint pain, dizziness, anorexia, malaise, transient haematuria, urticaria, vomiting, asthma in asthmatics (similar to Mazzotti reaction—see section 6.1.2.3) induced by disintegrating microfilariae; nodules (palpable subcutaneously and along spermatic cord—formed by recently killed worms); transient lymphangitis and exacerbation of lymphoedema.

Dose: *Lymphatic filariasis (bancroftian)*, by mouth, ADULT and CHILD over 10 years, 6 mg/kg daily, preferably in divided doses after meals, for 12 days; CHILD under 10 years, half the adult dose; mass treatment control programmes, ADULT and CHILD over 10 years, 6 mg/kg in divided doses over 24 hours, once a year; CHILD under 10 years, half the adult dose.

Lymphatic filariasis (brugian), by mouth, ADULT and CHILD over 10 years, 3–6 mg/kg, preferably in divided doses after meals, for 6–12 days; CHILD under 10 years, half the adult dose; mass treatment control programmes, ADULT and CHILD over 10 years, 3–6 mg/kg in divided doses over 24 hours, 6 times at weekly or monthly intervals; CHILD under 10 years, half the adult dose.

Occult filariasis, by mouth, ADULT 8 mg/kg daily for 14 days, repeated as necessary if symptoms return.

NOTE: THE ABOVE DOSE REGIMENS ARE INTENDED ONLY AS A GUIDE, SINCE MANY COUNTRIES HAVE DEVELOPED SPECIFIC TREATMENT REGIMENS.

POM **Diethylcarbamazine** *(WMF 6.1.2.2)*
Tablets, Diethylcarbamazine citrate 50 mg, 100 mg.

POM **Diethylcarbamazine** *(EDL 6.3)*
Tablet, Diethylcarbamazine (as citrate) 50 mg.

See section 9.4.2.1 for the proprietary preparations of Diethylcarbamazine.

9.4.2.3 Onchocerciasis

Onchocerciasis (river blindness) is caused by infection with the filarial nematode *Onchocerca volvulus*. The vector is the blackfly which breeds near fast-flowing rivers. **Ivermectin** has transformed suppressive treatment of onchocerciasis and is now used extensively in control programmes in many countries. Its microfilaricidal action is more persistent and less liable to provoke adverse reactions than that of diethylcarbamazine. A single oral dose reduces the microfilarial count to low levels for up to a year. It appears both to kill microfilariae and to inhibit their expulsion from the uterus of female worms. A single annual dose may suppress the microfilaraemia to a degree that prevents development of clinical disease. Although the drug is generally well tolerated, it is advisable to have medical support available during treatment programmes. Patients with a heavy

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microfilarial load occasionally react adversely and, rarely, transient severe postural hypotension has occurred within 12–24 hours of treatment.

Treatment of pregnant women with ivermectin should be limited to those situations where the risk of complications from untreated onchocerciasis exceeds the potential risk to the fetus from treatment. Mass treatment programmes should not include children under 15 kg, pregnant patients or those with severe illness.

Diethylcarbamazine is now largely superseded as a microfilaricide in onchocerciasis because of the frequency with which it induces severe host (Mazzotti) reactions characterized by itching, rash, oedema, pain and swelling of the lymph nodes, fever and severe eye lesions.

Suramin is the only macrofilaricide that is currently available for use against *Onchocerca volvulus*. Administered intravenously over a period of several weeks suramin also kills microfilariae. It is, however, one of the most toxic substances used in clinical medicine and should always be given under medical supervision in a hospital. A careful assessment must always be made of the patient's capacity to withstand the effects of suramin treatment both before and during administration.

IVERMECTIN

Indications: Suppressive treatment of onchocerciasis; filariasis (section 9.4.2.2).
Contra-indications: Pregnancy (delay treatment until after delivery).
Precautions: Breastfeeding (avoid treating mother until infant is 1 week old).
Adverse effects: Mild ocular irritation; somnolence; raised liver enzymes; rarely postural hypotension; mild Mazzotti reaction within 3 days of treatment, resulting from death of microfilariae—fever, headache, sore throat, cough, pruritus, rash, conjunctivitis, arthralgia, myalgia, lymphadenopathy, lymphadenitis, oedema, weakness, tachycardia, nausea and vomiting, diarrhoea.
Advice to patients: To be taken with water on empty stomach. No food must be taken for at least 2 hours before or after the dose.
Dose: *Suppression of microfilariae*, by mouth, ADULT and CHILD over 5 years (and weighing over 15 kg), 150 micrograms/kg as a single dose once a year.

PATIENT ADVICE: AVOID FOOD OR ALCOHOL FOR AT LEAST 2 HOURS BEFORE AND AFTER A DOSE.

POM **Ivermectin** *(WMF 6.1.2.3)*
Tablets, Ivermectin 3 mg, 6 mg.

POM **Ivermectin** *(EDL 6.3)*
Tablet, Ivermectin 6 mg.

POM **MECTIZAN®** *(Bolax/BPP)*
Tablet, Ivermectin 6 mg.

SURAMIN

Suramin sodium is a complementary drug.
Indications: Curative treatment of onchocerciasis; trypanosomiasis (section 9.3.4.1).
Contra-indications: Previous anaphylaxis or suramin sensitivity; pregnancy (delay treatment until after delivery); severe liver or renal function impairment; elderly or debilitated; total blindness (unless required for relief from intensely itchy lesions).
Precautions: Administer only under close medical supervision in hospital and with general condition of patient improved as far as possible before treatment (see notes above); first dose—possible loss of consciousness (see under Dosage, below); maintain satisfactory food and fluid intake during treatment; urine tests before and weekly during treatment—reduce dose if moderate albuminuria, discontinue immediately if severe albuminuria or casts in urine.
Adverse effects: Rarely, immediate and potentially fatal reaction with nausea, vomiting, shock and loss of consciousness during first dose—see First (Test) Dose, above; albuminuria; abdominal pain; severe diarrhoea; stomal ulceration; exfoliative dermatitis; fever; tiredness; anorexia; malaise; polyuria; thirst; raised liver enzyme values; paraesthesia and hyperaesthesia of palms and soles; swelling, tenderness and abscess formation around adult worms; urticopapular rash, painful hip, hand and foot joints, inflammatory and degenerative changes in optic nerve and retina—due to dying microfilariae.
Dose: *Curative treatment of onchocerciasis*, by slow intravenous injection, ADULT 3.3 mg/kg as a single dose (see First (Test) Dose administration, below), followed at weekly intervals by incremental

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doses of 6.7 mg/kg, 10.0 mg/kg, 13.3 mg/kg, 16.7 mg/kg, and 16.7 mg/kg on weeks 2 to 6 respectively (total dose 66.7 mg/kg over 6 weeks).

RECONSTITUTION OF INJECTION: RECONSTITUTE IN WATER FOR INJECTIONS TO PRODUCE A FINAL CONCENTRATION OF 10%.

FIRST (TEST) DOSE: ADMINISTER FIRST DOSE WITH PARTICULAR CAUTION; WAIT AT LEAST 1 MINUTE AFTER INJECTING THE FIRST FEW MICROLITRES; INJECT THE NEXT 0.5 ML OVER 30 SECONDS AND WAIT 1 MINUTE; INJECT THE REMAINDER OVER SEVERAL MINUTES.

POM **Suramin** *(WMF 6.1.2.3)*
Injection (Powder for solution for injection), suramin sodium 1-g vial.

9.4.3 Trematode infections

9.4.3.1 Schistosomiasis
9.4.3.2 Fluke infections

9.4.3.1 Schistosomiasis

Schistosomiasis, a waterborne parasitic infection, is caused by several species of trematode worms (blood flukes). Its socioeconomic impact as a parasitic disease is outstripped only by that of malaria. Intestinal schistosomiasis is caused principally by *Schistosoma mansoni* as well as *S. japonicum*, *S. mekongi*, and *S. intercalatum*. Urinary schistosomiasis is caused by *S. haematobium*. The latter is an important predisposing cause of squamous cell cancer of the bladder.

Praziquantel has transformed the treatment of schistosomiasis and is often effective in a single dose, against all species of the parasite. It can be of particular value in patients with mixed infections and those who do not respond adequately to other drugs. It is also extremely well tolerated and well suited for mass treatment control programmes. Extensive use over several years has provided no evidence of serious adverse effects or long-term toxicity, nor has mutagenic or carcinogenic activity been shown in experimental animals.

Drugs still widely used in the treatment of schistosomiasis include **oxamniquine**, which is effective against *S. mansoni*. Strains resistant to oxamniquine, which have been reported in South America, have been effectively treated with praziquantel. It is preferable to delay treatment with oxamniquine in pregnant women until after delivery unless immediate intervention is essential. Due to lack of information on whether oxamniquine is excreted in breast milk, it is preferable not to administer it to nursing mothers.

METRIFONATE

Therapeutic category: Schistosomicide
Pharmacology: It is an organophosphorous compound which is only effective against *S. haematobium*. As it reduces plasma-cholinesterase concentrations, it should be used with caution in patients likely to be frequently exposed to organophosphorous insecticides.
Indications: Urinary Schistosomiasis due to *S. haematobium*.
Dose: By mouth, 7.5 mg/kg in 3 doses at intervals of 2 weeks.

POM **Metrifonate** *(EDL 6.4)*
Tablet, Metrifonate 100 mg.

OXAMNIQUINE

Oxamniquine is a complementary drug.
Therapeutic category: Schistosomicide
Pharmacology: It is a quinoline compound active against *Schistosoma mansoni*. It causes the worms to shift from the mesenteric veins to the liver where they are destroyed. It has no significant activity against *S. haematobium*.
Indications: Intestinal schistosomiasis due to *Schistosoma mansoni* (acute stage and chronic hepatosplenic disease).
Precautions: Epilepsy—close observation, may precipitate seizures; pregnancy and breastfeeding (see notes above).
SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.
Adverse effects: Commonly, dizziness and drowsiness; headache, nausea, vomiting, diarrhoea; intense reddish discoloration of urine; rarely, urticaria, hallucinations, epileptiform convulsions; raised liver enzyme values; transient fever, eosinophilia, scattered pulmonary infiltrates (Loeffler syndrome)—after 3-day course in patients in Egypt and eastern Mediterranean.
Nursing considerations: •Give orally, after meals for improved GI tolerance.
•Teach patient to avoid driving and other hazardous activities if he feels drowsy.
•Teach patient proper personal hygiene; tell patient that urine may turn orange or red.
•Use cautiously in patients with a history of seizure disorders. Epileptiform seizure have rarely been

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observed within the first few hours after ingestion.

Dose: *Intestinal schistosomiasis due to S. mansoni (West Africa, South America, Caribbean islands)*, by mouth, ADULT 15 mg/kg as a single dose; CHILD under 30 kg, 20 mg/kg in 2 divided doses.
Intestinal schistosomiasis due to S. mansoni (East and central Africa, Arabian peninsula), by mouth, ADULT and CHILD 30 mg/kg in 2 divided doses.
Intestinal schistosomiasis due to S. mansoni (Egypt and southern Africa), ADULT and CHILD 60 mg/kg in divided doses over 2–3 days (maximum single dose 20 mg/kg).

POM **Oxamniquine** *(WMF 6.1.3.1)*
Capsules, Oxamniquine 250 mg.
Oral suspension, Oxamniquine 250 mg/5 ml.

POM **Oxamniquine** *(EDL 6.4)*
Capsule, Oxamniquine 250 mg.

PRAZIQUANTEL

Therapeutic category: Schistosomicide.

Pharmacology: Praziquantel increases cell membrane permeability in susceptible worms, resulting in a loss of intracellular calcium, massive contractions and paralysis of their musculature. There is further vacuolization and disintegration of the schistosome tegument followed by attachment of phagocytes to the parasite and death.

Indications: Intestinal schistosomiasis; urinary schistosomiasis; cestode infections (section 9.4.1.1); fluke infections (section 9.4.3.2).

Contra-indications: Ocular cysticercosis (see section 9.4.1.1).

Precautions: Pregnancy (Appendix 2); breastfeeding (Appendix 3); areas endemic for cysticercosis—possible oedematous reaction; **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Abdominal discomfort, nausea, vomiting, malaise, headache, dizziness, drowsiness, rectal bleeding; rarely hypersensitivity reactions, including fever, pruritus, eosinophilia (may be due to dead and dying parasites).

Advice to patients: Do not chew tablets due to bitter taste; take with food; caution should be used when performing tasks requiring mental alertness, may impair judgement and co-ordination.

Nursing considerations: •Tablets can be halved or quartered; laxatives may be given before treatment to cleanse bowel.
•Teach patient proper hygiene techniques.
•Patient should not breast-feed on the day of treatment and 72 hours after.

Dose: *Schistosomiasis*, by mouth, ADULT and CHILD over 4 years 40–60 mg/kg as a single dose; alternatively 3 doses of 20 mg/kg on one day at intervals of 4–6 hours.

Note: The tablets should be taken unchewed with some liquid during meals. Keeping the tablets or its segments in the mouth can give a bitter taste which can promote gagging or vomiting.

POM **Praziquantel** *(WMF 6.1.1.1)*
Tablets, Praziquantel 150 mg, 600 mg.

POM **Praziquantel** *(EDL 6.4)*
Tablet, Praziquantel 600 mg.

POM **AZITEL®** *(Panvij Biotec)*
Tablet, Praziquantel 600 mg; white to orange tinged, oblong, f-c tab. marked 'AZITEL' on one side and 'PBL' with two score lines on the reverse.
600 mg - 8.

Dose: *Schistosomiasis*, 3 doses of 20 mg/kg given 4-6 hours apart as one day treatment.
Clonorchiasis and Opisthorchiasis, 3 doses of 25 mg/kg given 4-6 hours apart as one day treatment.

POM **BILTRICIDE®** *(Gemini)*
Tablet, Praziquantel 600 mg.
600 mg - 1000.

9.4.3.2 Fluke infections

The intestinal flukes include *Fasciolopsis buski*, *Metagonimus yokogawai*, *Heterophyes heterophyes*, *Echinostoma* spp. and *Gastrodiscoides hominis*. The liver flukes include *Clonorchis sinensis*, *Opisthorchis viverrini*, *O. felineus* and *Fasciola hepatica*. In some areas *C. sinensis* and *Opisthorchis* spp. infections are strongly associated with cholangiocarcinoma (cancer of the bile ducts). The lung flukes are of the genus *Paragonimus*.

Praziquantel has transformed the therapy of most fluke infections. Parasitological cure has been obtained in virtually all cases (with the exception of *Fasciola* infections)

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without significant adverse effect but it needs to be taken for several days in the treatment of *Paragonimus* infections.

Triclabendazole, a benzimidazole compound is highly effective and well tolerated, as a single dose or two divided doses, for both *Fasciola* and *Paragonimus* infections.

PRAZIQUANTEL

Indications: Intestinal flukes, liver flukes, and lung flukes; cestode infections (section 9.4.1.1); schistosomiasis (section 9.4.3.1).

Contra-indications: Ocular cysticercosis (see section 9.4.1.1).

Precautions: *Paragonimus* infections—treatment in hospital as may be central nervous system involvement; pregnancy (unless immediate treatment required, delay treatment until after delivery; Appendix 2); breastfeeding (avoid during and for 72 hours after treatment); areas endemic for cysticercosis—possible oedematous reaction; **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Abdominal discomfort, nausea, vomiting, malaise, headache, dizziness, drowsiness, rectal bleeding; rarely hypersensitivity reactions, including fever, pruritus.

Advice to patients: Do not chew tablets due to bitter taste; take with food; caution should be used when performing tasks requiring mental alertness, may impair judgement and co-ordination.

Dose: *Intestinal fluke infections*, by mouth, ADULT and CHILD over 4 years, 25 mg/kg as a single dose.
Liver and lung fluke infections, by mouth, ADULT and CHILD over 4 years, 25 mg/kg 3 times daily for 2 consecutive days; alternatively 40 mg/kg as a single dose; treatment may need to be extended for several days in paragonimiasis.

Note: The tablets should be taken unchewed with some liquid during meals. Keeping the tablets or its segments in the mouth can give a bitter taste which can promote gagging or vomiting.

POM **Praziquantel** *(WMF 6.1.3.2)*
Tablets, Praziquantel 600 mg.

POM **Praziquantel** *(EDL 6.4)*
Tablet, Praziquantel 600 mg.

See section 9.4.3.1 for the proprietary preparations of Praziquantel.

TRICLABENDAZOLE

Indications: Fascioliasis; paragonimiasis

Precautions: Paragonimus infections—treatment in hospital as may be central nervous system involvement; severe fascioliasis—biliary colic, due to obstruction by dying worms.

Adverse effects: Gastrointestinal discomfort; headache.

Dose: *Fascioliasis*, by mouth, ADULT and CHILD over 4 years, 10 mg/kg as a single dose.
Paragonimiasis, by mouth, ADULT and CHILD over 4 years, 20 mg/kg given in 2 divided doses.

POM **Triclabendazole** *(WMF 6.1.3.2)*
Tablets, Triclabendazole 250 mg.

9.5 Antiviral drugs

9.5.1 Herpes and cytomegalovirus infections
9.5.2 Antiretroviral drugs

9.5.1 Herpes and cytomegalovirus infections

HERPES SIMPLEX VIRUS (HSV)

Aciclovir is active against herpes viruses but does not eradicate them. It is only effective if started at onset of infection; it is also used for prevention of recurrence in the immunocompromised. Genital lesions, oesophagitis and proctitis may be treated with oral aciclovir. HSV encephalitis or pneumonitis should be treated with intravenous aciclovir.

Valaciclovir [not included on WHO Model List], a prodrug of aciclovir, can be given by mouth as an alternative treatment for herpes simplex infections of the skin and mucous membranes (including initial and recurrent genital herpes).

HERPES ZOSTER VIRUS

While most HIV positive patients with zoster experience only one self-limiting course, some will experience repeated episodes. Treatment should be reserved for debilitating disease and when there is high risk of serious complications, such as in advanced HIV disease. Aciclovir is the

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treatment of choice and it can be administered in high oral dose or in the case of lack of response to oral therapy or CNS involvement, it should be given intravenously.

CYTOMEGALOVIRUS (CMV)
Parenteral antiviral **ganciclovir** arrests retinochoroiditis and enteritis caused by CMV in HIV infected patients. Maintenance therapy with oral ganciclovir should be given to prevent relapse of retinitis. Alternative therapy with intravenous **foscarnet** can be used if necessary.

ACICLOVIR

Aciclovir is a representative drug active against herpes simplex virus and varicella–zoster virus. Various drugs can serve as alternatives.

Indications: Treatment of primary genital herpes; disseminated varicella–zoster in immunocompromised patients; herpes simplex encephalitis.

Indications: Maintain adequate hydration; renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3).

Adverse effects: Nausea, vomiting, abdominal pain, diarrhoea, headache, fatigue, rash, urticaria, pruritus, photosensitivity; rarely hepatitis, jaundice, dyspnoea, angioedema, anaphylaxis; neurological reactions (including dizziness, confusion, hallucinations, drowsiness), acute renal failure; decreases in haematological indices; on intravenous infusion, severe local inflammation (sometimes resulting in ulceration), fever, agitation, tremor, psychosis, and convulsions.

Advice to patients: See Label 9 in Appendix 6. Patients are contagious only when viral shedding is occurring; recurrences tend to appear within 3 months of original infection; acyclovir is NOT a cure; avoid sexual intercourse when lesions are present; may take with food.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.
•Administer tablet with or without food with a full glass of water. Shake suspension before use.
•Avoid giving by bolus I.V. injection; infusion must be administered over at least 1 hour to prevent renal tubular damage.
•Maintain adequate fluid intake to prevent deposit in kidneys.
•Discontinue drug therapy and inform the physician if severe abdominal pain and bleeding occur.
•Teach patient that drug does not cure infection but symptoms will be controlled.

Dose: *Treatment of primary genital herpes*, by mouth, ADULT 200 mg 5 times daily for 7–10 days or 400 mg 3 times daily for 7–10 days.
Prevention of recurrence of genital herpes, by mouth, ADULT 400 mg twice daily.
Disseminated varicella–zoster in immunocompromised patients, by intravenous infusion, ADULT 10 mg/kg 3 times daily for 7 days.
Herpes simplex encephalitis, by intravenous infusion, ADULT 10 mg/kg 3 times daily for 10 days.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Aciclovir** *(WMF 6.5.1)*
Tablets, Aciclovir 200 mg.
Oral suspension, Aciclovir 200 mg/5 ml [not included on WHO Model List].
Infusion (Powder for solution for infusion), Aciclovir (as sodium salt) 250-mg vial.

POM **Acyclovir** *(EDL 6.12)*
Tablets, Aciclovir 200 mg, 400 mg
Injection, Acyclovir (as Sodium salt) 250 mg in vial.

POM **APO-ACYCLOVIR®** *(Lahams)*
Tablet, Aciclovir 200 mg; blue, shield-shaped tab. marked 'APO 200'.
200 mg - 100.

POM **LOVIR®** *(Ranbaxy)*
Tablets, Aciclovir 200 mg, 400 mg.
200 mg - 5 x 5 (in blisters)
400 mg - 5 x 5 (in blisters).

POM **VIREST®** *(Hovid)*
Tablets, Aciclovir 200 mg, hexagon-shaped, blue-uncoated tab.; 400 mg, hexagon-shaped, pink uncoated tab.
200 mg - 100; blisters of 5 x 5
400 mg - 150, blisters of 5 x 5.

POM **VIVORAX®** *(Interpharma)*
Tablet, Aciclovir BP 200 mg.
200 mg - 10's.

Dose: *Primary genital herpes*, 200 mg 5 times daily for 5-10 days.
Prevention of recurrence of genital herpes, 200 mg 4 times daily for 12 weeks.
Herpes zoster, 800 mg 5 times daily for 7-10 days.
Mucotaneous herpes simplex infection, 200 mg 5 times daily for 5 days.

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POM **ZOVIRAX®** *(GSK)*
Tablet, Aciclovir 200 mg
200 mg - 25.
Suspension, Aciclovir 200 mg per 5 ml.
Injection, Aciclovir (as sodium salt) 250 mg; powder in vial.

POM **ZOYLEX®** *(Pharmabox)*
Tablet, Aciclovir BP 200 mg; pale blue, hexagonal tablet.
200 mg – 25's; 50's; 100's; 300's

IDOXURIDINE

See under Section 13.1

LAMIVUDINE

Indications: Treatment of chronic hepatitis B virus infection in adult and children over 16 years of age.
Contra-indications, Precautions, etc: See Lamivudine under HIV below.
Dose: By mouth, 100 mg once daily. To be swallowed whole with water and with or without food.

POM **ZEFFIX®** *(GSK)*
Tablet, Lamivudine 100 mg; capsule shaped and butterscotch coloured f-c tab.

9.5.2 Antiretroviral drugs

9.5.2.1 Nucleoside reverse transcriptase inhibitors
9.5.2.2 Non-nucleoside reverse transcriptase inhibitors
9.5.2.3 Protease inhibitors

ANTIRETROVIRAL DRUGS DO NOT CURE HIV (HUMAN IMMUNODEFICIENCY VIRUS) INFECTION; THEY ONLY TEMPORARILY SUPPRESS VIRAL REPLICATION AND IMPROVE SYMPTOMS. PATIENTS RECEIVING THESE DRUGS REQUIRE CAREFUL MONITORING BY APPROPRIATELY TRAINED HEALTH PROFESSIONALS IN AN ADEQUATELY RESOURCED SETTING. RIGOROUS PROMOTION OF MEASURES TO PREVENT NEW INFECTIONS REMAINS ESSENTIAL AND ITS NEED IS NOT DIMINISHED BY THE AVAILABILITY OF ANTIRETROVIRAL DRUGS. EFFECTIVE THERAPY REQUIRES THE SIMULTANEOUS USE OF 3 OR 4 DRUGS; ALTERNATIVE REGIMENS ARE NECESSARY TO MEET SPECIFIC REQUIREMENTS AT START-UP, TO SUBSTITUTE FOR FIRST-LINE REGIMENS IN CASES OF INTOLERANCE, OR TO REPLACE FAILING REGIMENS. THE USE OF A 3- OR 4-DRUG COMBINATION AS SPECIFIED IN THE WHO TREATMENT GUIDELINES IS RECOMMENDED. THE USE OF FIXED-DOSE PREPARATIONS FOR THESE COMBINATIONS IS ALSO RECOMMENDED IF THE PHARMACEUTICAL QUALITY IS ASSURED AND INTERCHANGEABILITY WITH THE SINGLE PRODUCTS IS DEMONSTRATED AS SPECIFIED BY THE RELEVANT DRUG REGULATORY AUTHORITY.

SELECTION OF 2 OR 3 PROTEASE INHIBITORS FROM THE MODEL LIST WILL NEED TO BE DETERMINED BY EACH COUNTRY AFTER CONSIDERATION OF LOCAL TREATMENT GUIDELINES AND EXPERIENCE, AS WELL AS COMPARATIVE COSTS OF AVAILABLE PRODUCTS. LOW-DOSE RITONAVIR IS USED IN COMBINATION WITH INDINAVIR, LOPINAVIR OR SAQUINAVIR AS A 'BOOSTER'; RITONAVIR IS NOT RECOMMENDED AS A DRUG IN ITS OWN RIGHT.

PRINCIPLES OF TREATMENT

Treatment is aimed at reducing the plasma viral load as much as possible and for as long as possible; it should be started before the immune system is irreversibly damaged. The need for early drug treatment should, however, be balanced against the development of toxicity. Commitment to treatment and strict adherence over many years are required; the regimen chosen should take into account convenience and the patient's tolerance of it. The development of resistance is reduced by using a combination of 3 or 4 drugs; such combinations should have additive or synergistic activity while ensuring that their toxicity is not additive. Testing for resistance to antiviral drugs, particularly in therapeutic failure, should be considered.

Women of childbearing age receiving antiretroviral therapy must have available effective contraceptive methods to prevent unintended pregnancy. Women who are taking non-nucleoside reverse transcriptase inhibitors or protease inhibitors which can lower blood concentration of hormonal oral contraceptives, should be advised to use additional or alternative contraceptives.

DRUGS USED TO TREAT HIV INFECTION

Zidovudine, a nucleoside reverse transcriptase inhibitor (or 'nucleoside analogue'), was the first anti-HIV drug to be introduced. Other nucleoside reverse transcriptase inhibitors include **abacavir**, **didanosine**, **lamivudine**, **stavudine**, and zalcitabine.

The protease inhibitors include amprenavir, **indinavir**, **lopinavir**, **nelfinavir**, **ritonavir** and **saquinavir**. Ritonavir in low doses is used in combination with indinavir, lopinavir or saquinavir as a booster. The small amount of ritonavir in such combinations has no intrinsic antiviral activity but it increases the antiviral activity of the other protease

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inhibitors by reducing their metabolism. Indinavir, nelfinavir, ritonavir and possibly saquinavir inhibit the cytochrome P450 enzyme system and therefore have a potential for significant drug interactions. Protease inhibitors are associated with lipodystrophy and metabolic effects (see below).

The non-nucleoside reverse transcriptase inhibitors include **efavirenz** and **nevirapine**. They interact with a number of drugs metabolized in the liver; the doses of protease inhibitors may need to be increased when they are given with efavirenz or nevirapine. Nevirapine is associated with a high incidence of rash (including Stevens-Johnson syndrome) and occasionally fatal hepatitis. Rash is also associated with efavirenz but it is usually milder. Efavirenz treatment has also been associated with an increased plasma cholesterol concentration.

INITIATION OF TREATMENT

The time for initiating antiviral treatment is determined by the clinical stage of the HIV infection as indicated by symptoms, and where available, by the CD4-cell count or total lymphocyte count; the plasma viral load, if available, is also a valuable guide for staging the disease (see Monitoring, below).

Recommended initial treatment with a combination of drugs ('highly active antiretroviral therapy', HAART) includes:

2 nucleoside reverse transcriptase inhibitors (section 9.5.2.1)
plus
a non-nucleoside reverse transcriptase inhibitor (section 9.5.2.2)
or a third nucleoside reverse transcriptase inhibitor (section 9.5.2.1)
or a protease inhibitor which may be combined with ritonavir as booster (section 9.5.2.3).

MONITORING

In resource-limited settings the basic clinical assessment before initiating antiretroviral therapy includes documentation of past medical history, identification of current and past HIV-related illnesses, identification of co-existing medical conditions that may influence the choice of therapy (for example, pregnancy or tuberculosis) as well as current symptoms and physical signs.

The *absolute minimum laboratory tests* before initiating antiretroviral therapy are an HIV antibody test (in patients over 18 months of age) and a haemoglobin or haematocrit measurement.

Additional basic testing should include:

- white blood cell count;
- differential cell count (to identify a decline in neutrophils and the possibility of neutropenia);
- total lymphocyte count;
- serum alanine or aspartate aminotransferase concentration to assess the possibility of hepatitis co-infection and to monitor for hepatotoxicity;
- serum creatinine and/or blood urea nitrogen to assess baseline renal function;
- serum glucose;
- pregnancy tests for women.

Desirable supplemental tests include measurement of bilirubin, amylase and serum lipids. CD4-cell determinations are, of course, very desirable and efforts should be made to make these widely available. Viral load testing is currently considered optional because of constraints on resources.

CHANGING THERAPY

Deterioration of the condition (including clinical and virological changes) usually calls for replacement of the failing drugs. Intolerance to adverse effects and drug-induced organ dysfunction usually require change in therapy.

The choice of an alternative regimen depends on factors such as the response to previous treatment, tolerance and the possibility of cross-resistance. If treatment fails, a new second-line regimen will be needed. If toxicity occurs, either a new second-line regimen is indicated or, if the toxicity is related to an identifiable drug in the regimen, the offending drug can be replaced with another drug that does not have the same adverse effects.

PREGNANCY

Treatment of HIV infection in pregnancy aims to:

- minimize the viral load and disease progression in the mother;
- reduce the risk of toxicity to the fetus (although the teratogenic potential of most antiretroviral drugs is unknown);
- prevent transmission of infection to the neonate.

In pregnant women, it may be desirable to initiate antiretroviral therapy after the first trimester, although for pregnant women who are severely ill, the benefit of early therapy outweighs the potential risk to the fetus. All treatment options require careful assessment by a specialist.

The use of zidovudine, lamivudine, nevirapine, nelfinavir and saquinavir are

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recommended for women of child-bearing potential or who are pregnant. Efavirenz should be avoided because of its potential teratogenic effect on the fetus in the first trimester. First-line treatment in pregnant women should when possible include zidovudine and lamivudine. Monotherapy with either zidovudine or with nevirapine reduces transmission of infection to the neonate (see also below), but combination antiretroviral therapy maximizes the chance of preventing transmission and represents optimal therapy for the mother. Low-dose ritonavir is required if either indinavir or saquinavir is used in pregnancy because adequate drug concentration is achieved only with ritonavir boosting. Information is lacking on the use of lopinavir with ritonavir in pregnancy.

Lactic acidosis and hepatic steatosis associated with nucleoside reverse transcriptase inhibitors may be more frequent in pregnant women and therefore the combination of stavudine and didanosine should be used in pregnancy only when no alternatives are available. Protease inhibitors have been associated with glucose intolerance and pregnant women should be instructed to recognize symptoms of hyperglycaemia and to seek health care advice if they occur.

Various regimens have been used to specifically prevent the transmission of HIV from mother to the neonate at term. More information is available in *New Data on the Prevention of Mother-to-Child Transmission of HIV and their Policy Implications: Conclusions and Recommendations* (WHO/RHR/01.28), which reflects an inter-agency consultation held on 11–13 October 2000.

BREASTFEEDING

Antiretroviral drugs may be present in breastmilk, and may reduce viral load in breastmilk and reduce the risk of transmission through breastfeeding. However, the concentration of antiretroviral drugs in breastmilk may not be adequate to prevent viral replication and there is therefore the possibility of promoting the development of drug-resistant virus which could be transmitted to the infant.

Women with HIV infection should be counselled about the risks of breastfeeding and, where possible, they should limit or avoid breastfeeding; in particular, breastfeeding should be avoided where replacement feeding is acceptable, affordable, sustainable, and safe. HIV-infected women should be counselled on infant feeding options and they should be supported in their choice.

POST-EXPOSURE PROPHYLAXIS

Treatment with antiretroviral drugs may be appropriate following occupational exposure to HIV-contaminated material. Immediate expert advice should be sought in such cases; national guidelines on post-exposure prophylaxis for healthcare workers have been developed and local ones may also be available.

LIPODYSTROPHY AND METABOLIC EFFECTS

Combination antiretroviral therapy, including regimens containing a protease inhibitor, is associated with redistribution of body fat in some patients (for example, decreased fat under the skin, increased abdominal fat, 'buffalo humps' and breast enlargement). Protease inhibitors are also associated with metabolic abnormalities such as hyperlipidaemia, insulin resistance, and hyperglycaemia. Clinical examination should include an evaluation of fat distribution; measurement of serum lipids and blood glucose should be considered.

9.5.2.1 Nucleoside reverse transcriptase inhibitors

IN SOME SETTINGS IT MAY NOT BE POSSIBLE TO CARRY OUT FULL MONITORING DESCRIBED UNDER EACH DRUG ENTRY; IN SUCH CASES THE LEVEL OF MONITORING SHOULD BE DETERMINED BY LOCAL GUIDELINES (SEE ALSO NOTES ABOVE).

ABACAVIR

Synonym: ABC

Indications: HIV infection in combination with at least two other antiretroviral drugs.

Precautions: Hepatic impairment (see below and Appendix 5); renal impairment (Appendix 4); pregnancy (see notes above and Appendix 2); breastfeeding (see notes above).

HYPERSENSITIVITY REACTIONS: LIFE-THREATENING HYPERSENSITIVITY REACTIONS REPORTED—CHARACTERIZED BY FEVER OR RASH AND POSSIBLY NAUSEA, VOMITING, DIARRHOEA, ABDOMINAL PAIN, LETHARGY, MALAISE, HEADACHE, MYALGIA AND RENAL FAILURE; LESS FREQUENTLY MOUTH ULCERATION, OEDEMA, HYPOTENSION, DYSPNOEA, SORE THROAT, COUGH, PARAESTHESIA, ARTHRALGIA, CONJUNCTIVITIS, LYMPHADENOPATHY, LYMPHOCYTOPENIA AND ANAPHYLAXIS

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(HYPERSENSITIVITY REACTIONS PRESENTING AS SORE THROAT, INFLUENZA-LIKE ILLNESS, COUGH AND BREATHLESSNESS IDENTIFIED); RARELY MYOLYSIS; LABORATORY ABNORMALITIES MAY INCLUDE RAISED LIVER ENZYMES (SEE BELOW) AND CREATINE KINASE; SYMPTOMS USUALLY APPEAR IN THE FIRST 6 WEEKS, BUT MAY OCCUR AT ANY TIME; MONITOR FOR SYMPTOMS EVERY 2 WEEKS FOR 2 MONTHS; DISCONTINUE IMMEDIATELY IF ANY SYMPTOM OF HYPERSENSITIVITY DEVELOPS AND DO NOT RECHALLENGE (RISK OF MORE SEVERE HYPERSENSITIVITY REACTION); DISCONTINUE IF HYPERSENSITIVITY CANNOT BE RULED OUT, EVEN WHEN OTHER DIAGNOSES POSSIBLE—IF RECHALLENGE NECESSARY IT MUST BE CARRIED OUT IN HOSPITAL SETTING; IF ABACAVIR IS STOPPED FOR ANY REASON OTHER THAN HYPERSENSITIVITY, EXCLUDE HYPERSENSITIVITY REACTION AS THE CAUSE AND RECHALLENGE ONLY IF MEDICAL ASSISTANCE IS READILY AVAILABLE; CARE NEEDED WITH CONCOMITANT USE OF DRUGS WHICH CAUSE SKIN TOXICITY.

PATIENT ADVICE: PATIENTS SHOULD BE TOLD THE IMPORTANCE OF REGULAR DOSING (INTERMITTENT THERAPY MAY INCREASE SENSITIZATION), HOW TO RECOGNIZE SIGNS OF HYPERSENSITIVITY, AND ADVISED TO SEEK IMMEDIATE MEDICAL ATTENTION IF SYMPTOMS DEVELOP OR BEFORE RE-STARTING TREATMENT.

HEPATIC DISEASE: POTENTIALLY LIFE-THREATENING LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS REPORTED—CAUTION IN LIVER DISEASE, LIVER ENZYME ABNORMALITIES, OR RISK FACTORS FOR LIVER DISEASE (PARTICULARLY IN OBESE WOMEN); SUSPEND OR DISCONTINUE IF DETERIORATION IN LIVER FUNCTION TESTS, HEPATIC STEATOSIS, PROGRESSIVE HEPATOMEGALY OR UNEXPLAINED LACTIC ACIDOSIS.

Adverse effects: Hypersensitivity reactions (see above), nausea, vomiting, diarrhoea, anorexia, lethargy, fatigue, fever, headache, pancreatitis, lactic acidosis (see hepatic disease, above); rash and gastrointestinal disturbances more common in children.

Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT 300 mg twice daily; CHILD 3 months–16 years, 8 mg/kg twice daily (maximum 600 mg daily).

POM **Abacavir** *(WMF 6.5.2.1)*
Tablets, Abacavir (as sulfate) 300 mg.
Oral solution, Abacavir (as sulfate) 100 mg/5 ml.

DIDANOSINE

Synonym: ddI, DDI

Indications: HIV infection in combination with at least two other antiretroviral drugs.

Precautions: History of pancreatitis (preferably avoid, otherwise extreme caution, see also below); peripheral neuropathy or hyperuricaemia (see under Adverse effects); history of liver disease (see below); renal and hepatic impairment (see Appendices 4 and 5); pregnancy and breastfeeding (see notes above); dilated retinal examinations recommended (especially in children) every 6 months, or if visual changes occur; **interactions**: Appendix 1.

PANCREATITIS: IF SYMPTOMS OF PANCREATITIS DEVELOP OR IF SERUM AMYLASE OR LIPASE IS RAISED (EVEN IF ASYMPTOMATIC) SUSPEND TREATMENT UNTIL DIAGNOSIS OF PANCREATITIS EXCLUDED; ON RETURN TO NORMAL VALUES RE-INITIATE TREATMENT ONLY IF ESSENTIAL (USING LOW DOSE INCREASED GRADUALLY IF APPROPRIATE). WHENEVER POSSIBLE AVOID CONCOMITANT TREATMENT WITH OTHER DRUGS KNOWN TO CAUSE PANCREATIC TOXICITY (FOR EXAMPLE INTRAVENOUS PENTAMIDINE ISETIONATE); MONITOR CLOSELY IF CONCOMITANT THERAPY UNAVOIDABLE. SINCE SIGNIFICANT ELEVATIONS OF TRIGLYCERIDES CAUSE PANCREATITIS MONITOR CLOSELY IF ELEVATED.

HEPATIC DISEASE: POTENTIALLY LIFE-THREATENING LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS REPORTED THEREFORE CAUTION IN LIVER DISEASE, EXCESSIVE ALCOHOL INTAKE, LIVER ENZYME ABNORMALITIES, OR RISK FACTORS FOR LIVER DISEASE (PARTICULARLY IN OBESE WOMEN); SUSPEND OR DISCONTINUE IF DETERIORATION IN LIVER FUNCTION TESTS, HEPATIC STEATOSIS, PROGRESSIVE HEPATOMEGALY OR UNEXPLAINED LACTIC ACIDOSIS.

Adverse effects: Pancreatitis (see also under Precautions); peripheral neuropathy especially in advanced HIV infection–suspend (reduced dose may be tolerated when symptoms resolve); hyperuricaemia (suspend treatment if significant elevation); diarrhoea (occasionally serious); also reported, nausea, vomiting, dry mouth, asthenia, headache, hypersensitivity reactions, retinal and optic nerve changes (especially in children), diabetes mellitus, raised liver enzymes (see also under Precautions), liver failure.

Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT under 60 kg 250 mg daily in 1–2 divided doses, body weight over 60 kg 400 mg daily in 1–2 divided doses; CHILD under 3 months, 50 mg/m2 twice daily; 3 months–13 years, 90 mg/m^2 twice daily or 240 mg/m^2 once daily.

PATIENT ADVICE: TO ENSURE SUFFICIENT ANTACID FROM TABLETS CONTAINING ANTACID, EACH DOSE TO BE TAKEN AS 2 TABLETS (CHILD UNDER 1 YEAR 1 TABLET) CHEWED THOROUGHLY, CRUSHED OR DISPERSED IN WATER; TABLETS SHOULD BE TAKEN AT LEAST 1 HOUR BEFORE FOOD OR ON AN EMPTY STOMACH.

POM **Didanosine** *(WMF 6.5.2.1)*
Chewable tablets, Didanosine (with calcium and magnesium antacids) 25 mg, 50 mg; 100 mg, 150 mg, 200 mg.

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Oral solution (Powder for oral solution), Didanosine (with calcium and magnesium antacids) 100 mg/sachet, 167 mg/sachet, 250 mg/sachet.
Enteric-coated capsules (Gastro-resistant capsules), Didanosine 125 mg, 200 mg, 250 mg, 400 mg.
NOTE: ANTACIDS IN FORMULATION MAY AFFECT ABSORPTION OF OTHER DRUGS—SEE **INTERACTIONS**: APPENDIX 1 (ANTACIDS).

LAMIVUDINE

Synonym: 3TC
Therapeutic category: Antiviral Agent; Reverse Transcriptase Inhibitor.
Indications: HIV infection in combination with at least two other antiretroviral drugs.
Precautions: Renal impairment (Appendix 4), hepatic disease (see below); pregnancy and breastfeeding (see notes above); **interactions**: Appendix 1.
HEPATIC DISEASE: POTENTIALLY LIFE-THREATENING LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS REPORTED THEREFORE CAUTION (PARTICULARLY IN OBESE WOMEN) IN LIVER DISEASE, LIVER ENZYME ABNORMALITIES, OR RISK FACTORS FOR LIVER DISEASE; SUSPEND OR DISCONTINUE IF DETERIORATION IN LIVER FUNCTION TESTS, HEPATIC STEATOSIS, PROGRESSIVE HEPATOMEGALY OR UNEXPLAINED LACTIC ACIDOSIS. RECURRENT HEPATITIS IN PATIENTS WITH CHRONIC HEPATITIS B MAY OCCUR ON DISCONTINUATION OF LAMIVUDINE.
Adverse effects: Nausea, vomiting, diarrhoea, abdominal pain; cough; headache, fatigue, insomnia; malaise, fever, rash, alopecia, muscle disorders; nasal symptoms; peripheral neuropathy reported; rarely pancreatitis (discontinue); neutropenia, anaemia, thrombocytopenia and red-cell aplasia; lactic acidosis; raised liver enzymes and serum amylase reported.
Advice to patients: Lamivudine is not a cure for HIV infection and does not reduce risk of transmission to others; patient may still experience illness associated with HIV infection; to be taken exactly as prescribed and on an empty stomach if possible; children should be monitored for symptoms of pancreatitis.
Nursing considerations: •Administer twice daily with or without food; usually given with other antiretrovirals.
•Monitor children for pancreatitis viz abdominal pain, nausea, vomiting.
•Evaluate frequently for opportunistic infection and other complications of HIV.
•Teach patient that drug does not cure infection but symptoms will be controlled.
Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT 150 mg twice daily or 300 mg once daily; INFANT under 1 month, 2 mg/kg twice daily; CHILD 1 month or over, 4 mg/kg twice daily (maximum 300 mg daily).

POM **Lamivudine** *(WMF 6.5.2.1)*
Tablets, Lamivudine 150 mg.
Oral solution, Lamivudine 50 mg/5 ml.

POM **AVOLAM®** *(Ranbaxy)*
Tablet, Lamivudine 150 mg.
150 mg - 60.

POM **EPIVIR®** *(GSK)*
Tablet, Lamivudine 150 mg; white diamond-shaped f-c tab. marked "150" on one side and "GXCJ7" on the reverse side.
150 mg - 60.
Oral Solution, Lamivudine 10 mg per ml; clear, colourless to pale yellow, strawberry-banana flavoured liquid.
Pack - 240 ml.

POM **Lamivudine** *(Strides Vital)*
Tablet, Lamivudine 150 mg.
150 mg – 60's.

STAVUDINE

Synonym: d4T
Therapeutic category: Antiviral agent; Nucleoside reverse transcriptase inhibitor.
Indications: HIV infection in combination with at least two other antiretroviral drugs.
Indications: History of peripheral neuropathy (see below); history of pancreatitis or concomitant use with other drugs associated with pancreatitis; hepatic disease (see below); renal impairment (Appendix 4); pregnancy and breastfeeding (see notes above); **interactions**: Appendix 1.
PERIPHERAL NEUROPATHY: SUSPEND IF PERIPHERAL NEUROPATHY DEVELOPS—CHARACTERIZED BY PERSISTENT NUMBNESS, TINGLING OR PAIN IN FEET OR HANDS; IF SYMPTOMS RESOLVE SATISFACTORILY ON WITHDRAWAL, AND IF STAVUDINE NEEDS TO BE CONTINUED, RESUME TREATMENT AT HALF PREVIOUS DOSE.
HEPATIC DISEASE: POTENTIALLY LIFE-THREATENING LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS REPORTED THEREFORE CAUTION IN LIVER DISEASE, LIVER ENZYME ABNORMALITIES, OR RISK FACTORS FOR LIVER DISEASE (PARTICULARLY IN OBESE WOMEN); SUSPEND OR DISCONTINUE IF DETERIORATION IN LIVER FUNCTION TESTS, HEPATIC STEATOSIS, PROGRESSIVE HEPATOMEGALY OR UNEXPLAINED LACTIC ACIDOSIS.

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Adverse effects: Peripheral neuropathy (dose-related, see above); pancreatitis; nausea, vomiting, diarrhoea, constipation, anorexia, abdominal discomfort; chest pain; dyspnoea; headache, dizziness, insomnia, mood hanges; asthenia, musculoskeletal pain; influenza-like symptoms, rash and other allergic reactions; lymphadenopathy; neoplasms; elevated liver enzymes (see hepatic disease, above) and serum amylase; neutropenia, thrombocytopenia.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.

•Administer 12 hrly around-the-clock preferably 1 hr before meals.

•Teach patient that drug does not cure infection but symptoms will be controlled; to avoid OTC medications unless prescribed.

Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT under 60 kg, 30 mg twice daily preferably at least 1 hour before food; body weight over 60 kg, 40 mg twice daily; CHILD over 3 months, under 30 kg, 1 mg/kg twice daily; body weight over 30 kg, 30 mg twice daily.

POM **Stavudine** *(WMF 6.5.2.1)*
Capsules, Stavudine 15 mg, 20 mg, 30 mg, 40 mg.
Oral solution (Powder for oral solution), stavudine 5 mg/5 ml.

POM **AVOSTAV®** *(Ranbaxy)*
Capsule, Stavudine 40 mg.
40 mg - 60.

POM **Stavudine** *(Strides Vital)*
Tablets, Stavudine 30 mg, 40 mg.
30 mg – 60's.
40 mg – 60's.

POM **Stavudine + Lamivudine + Nevirapine** *(Strides Vital)*
Tablet, Stavudine 30 mg, Lamivudine 150 mg, Nevirapine 200 mg.
Pack – 60's.
Tablet, Stavudine 40 mg, Lamivudine 150 mg, Nevirapine 200 mg.
Pack – 60's.

ZALCITABINE

Synonym.: Dideoxycytidine; ddc.

Therapeutic category: Antiviral Agent; Reverse Transcriptase Inhibitor.

Indications: Treatment as monotherapy in HIV-infected adults with advanced disease who cannot tolerate Zidovudine or whose disease has progressed despite it; for the treatment of selected patients with advanced AIDS in combination with Zidovudine.

Contra-indications: Hypersensitivity to Zalcitabine; avoid in pregnancy.

Precautions: Monitor pancreatic enzymes and liver function tests in patients with history of pancreatitis, increased amylase, those on parenteral nutrition or with a history of alcohol abuse; discontinue immediately if pancreatitis is suspected; hepatic impairment (may exacerbate existing liver dysfunction); peripheral neuropathy (avoid use if possible); safety and efficacy not yet established in children less than 13 years of age.

Interactions:

• Increased risk of peripheral neuropathy or other toxicities with amphotericin, aminoglycosides, chloramphenicol, cisplatin, dapsone, ethionamide, isoniazid, metronidazole, vincristine, phenytoin, nitrofurantoin.

Adverse effects: Oral ulcers, chest pain, headache, dizziness, myalgia, anaemia, granulocytopenia,skin rash, pruritus, nausea, dysphagia, abdominal pain, vomiting, diarrhoea, body weight reduction, oedema, palpitations, increased heart rate, pancreatitis, hepatic disorders, peripheral neuropathy, tremors, confusion, increased micturition frequency.

Advice to patients: Zalcitabine is not a cure for AIDS; if numbness or tingling occurs, or if persistent, severe abdominal pain, nausea, or vomiting occur, notify your doctor. Women of childbearing age should use effective contraceptive while on Zalcitabine; take on an empty stomach, if possible.

Nursing considerations: •Recommend the use of wig if hair is lost during treatment.

Dose: Monotherapy, by mouth, Adult, 0.75 mg every 8 hours, given together with 200 mg Zidovudine (Total daily dose is 2.25 mg Zalcitabine and 600 mg Zidovudine); if Zalcitabine is discontinued due to toxicities decrease Zidovudine dose to 100 mg every 4 hours.

Note: Safety and efficacy in children less than 13 years of age have not been established. Dosage should be adjusted in renal and hepatic impairment.

POM **HIVID®** *(Swipha)*
Tablets, Zalcitabine 0.375 mg, 0.75 mg; f-c

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tabs.
0.375 mg - 100
0.750 mg - 100

ZIDOVUDINE

Synonym: Azidothymidine; AZT, ZDV

NOTE: THE ABBREVIATION AZT WHICH HAS SOMETIMES BEEN USED FOR ZIDOVUDINE HAS ALSO BEEN USED FOR ANOTHER DRUG.

Therapeutic category: Antiviral Agent; Reverse Transcriptase Inhibitor.

Indications: HIV infection in combination with at least two other antiretroviral drugs; monotherapy for prevention of maternal-fetal HIV transmission (but see notes above under Pregnancy).

Contra-indications: Abnormally low neutrophil counts or haemoglobin (consult product literature); neonates either with hyperbilirubinaemia requiring treatment other than phototherapy or with raised transaminase (consult product literature).

Precautions: Haematological toxicity; vitamin B_{12} deficiency (increased risk of neutropenia); reduce dose or interrupt treatment according to product literature if anaemia or myelosuppression; renal impairment (Appendix 4); hepatic impairment (see below and Appendix 5); risk of lactic acidosis, (see below); elderly; pregnancy and breastfeeding (see notes above); **interactions**: Appendix 1.

HEPATIC DISEASE: POTENTIALLY LIFE-THREATENING LACTIC ACIDOSIS AND SEVERE HEPATOMEGALY WITH STEATOSIS REPORTED THEREFORE CAUTION IN LIVER DISEASE, LIVER ENZYME ABNORMALITIES, OR RISK FACTORS FOR LIVER DISEASE (PARTICULARLY IN OBESE WOMEN), SUSPEND OR DISCONTINUE IF DETERIORATION IN LIVER FUNCTION TESTS, HEPATIC STEATOSIS, PROGRESSIVE HEPATOMEGALY OR UNEXPLAINED LACTIC ACIDOSIS.

Adverse effects: Anaemia (may require transfusion), neutropenia, and leukopenia (all more frequent with high dose and advanced disease); also nausea and vomiting, abdominal pain, dyspepsia, diarrhoea, flatulence, taste disturbance, pancreatitis, liver disorders including fatty change and raised bilirubin and liver enzymes (see hepatic disease, above); chest pain, dyspnoea, cough; influenza-like symptoms, headache, fever, paraesthesia, neuropathy, convulsions, dizziness, somnolence, insomnia, anxiety, depression, loss of mental acuity, malaise, anorexia, asthenia, myopathy, myalgia; pancytopenia, thrombocytopenia; gynaecomastia; urinary frequency; rash, pruritus, pigmentation of nail, skin and oral mucosa.

Advice to patients: Take 30 minutes before or 1 hour after a meal with a glass of water; limit paracetamol containing analgesics; maternal/foetal transmission may appear in some cases despite therapy.

Nursing considerations: • Ensure that patient adheres to the 4 hourly dosage schedule; suggest the use of alarm clock if necessary.
• Advise patient that blood transfusion, dosage modifications and even drug discontinuation may be needed if blood disorders such as anaemia occur.
• Zidovudine is neither a cure for HIV infection nor does it prevent the risk of transmission of HIV to others.

Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT 500–600 mg daily in 2–3 divided doses; INFANT under 4 weeks, 4 mg/kg twice daily; CHILD 4 weeks–13 years 180 mg/m^2 twice daily.
Patients temporarily unable to take zidovudine, by mouth, by intravenous infusion over 1 hour, adult 1–2 mg/kg every 4 hours (approximating to 1.5–3 mg/kg every 4 hours by mouth) usually for not more than 2 weeks; child 80–160 mg/m^2 every 6 hours (120 mg/m^2 every 6 hours approximates to 180 mg/m^2 every 6 hours by mouth).
Prevention of maternal-fetal HIV transmission, see notes above under Pregnancy.

ADMINISTRATION AND DILUTION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Zidovudine** *(WMF 6.5.2.1)*
Capsules, Zidovudine 100 mg, 250 mg.
Tablets, Zidovudine 300 mg.
Syrup (Oral solution), Zidovudine 50 mg/5 ml.
Infusion (Concentrate for solution for infusion), Zidovudine 10 mg/ml, 20-ml vial.

POM **APO-ZIDOVUDINE®** *(Lahams)*
Capsules, Zidovudine 100 mg; white cap. marked 'APO 100'.
100 mg - 100.

POM **AVIRO-Z®** *(Ranbaxy)*
Tablet, Zidovudine 300 mg.
300 mg - 60.

POM **RETROVIR®** *(GSK)*
Capsules, Zidovudine 100 mg, white cap with a central dark-blue band marked "Wellcome" "100" and "Y9C"; 250 mg, white/blue cap with

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a central dark-blue band marked "Wellcome" "250" and "H2F."
Tablet, Zidovudine 300 mg; white scored f-c tab. marked "Wellcome X4F"
Oral Solution, Zidovudine 50 mg per 5 ml; pale yellow strawberry-flavoured sugar-free solution containing 10 ml oral-dosing syringe.

With Lamivudine
POM **COMBIVIR®** *(GSK)*
Tablet, Lamivudine 150 mg, Zidovudine 300 mg; white to off-white f-c tab.
Indications: Treatment of HIV infected adults and children over 12 years of age.
Contra-indications, Precautions, etc: See under Lamivudine and Zidovudine.
Dose: One tab. twice daily; to be taken with or without food.

POM **Lamivudine + Zidovudine** *(Strides Vital)*
Tablet, Lamivudine 150 mg, Zidovudine 300 mg.
Pack – 60's.

9.5.2.2 Non-nucleoside reverse transcriptase inhibitors

IN SOME SETTINGS IT MAY NOT BE POSSIBLE TO CARRY OUT FULL MONITORING DESCRIBED UNDER EACH DRUG ENTRY; IN SUCH CASES THE LEVEL OF MONITORING SHOULD BE DETERMINED BY LOCAL GUIDELINES (SEE ALSO NOTES ABOVE).

EFAVIRENZ

Synonym : EFV, EFZ
Indications: HIV infection in combination with at least two other antiretroviral drugs.
Contra-indications: Pregnancy (see notes above and Appendix 2; substitute nevirapine for efavirenz in pregnant women or women for whom effective contraception cannot be assured).
Precautions: Hepatic impairment (avoid if severe; Appendix 5); severe renal impairment (Appendix 4); breastfeeding (see notes above); elderly; history of mental illness or substance abuse; **interactions**: Appendix 1.
RASH: RASH, USUALLY IN THE FIRST 2 WEEKS, IS THE MOST COMMON ADVERSE EFFECT; DISCONTINUE IF SEVERE RASH WITH BLISTERING, DESQUAMATION, MUCOSAL INVOLVEMENT OR FEVER; IF RASH MILD OR MODERATE, MAY CONTINUE WITHOUT INTERRUPTION—RASH USUALLY RESOLVES WITHIN 1 MONTH.
Adverse effects: Rash including Stevens-Johnson syndrome (see also above); dizziness, headache, insomnia, somnolence, abnormal dreams, fatigue, impaired concentration (administration at bedtime especially in the first 2–4 weeks reduces CNS effects); nausea; less frequently vomiting, diarrhoea, hepatitis, depression, anxiety, psychosis, amnesia, ataxia, stupor, vertigo; also reported raised serum cholesterol, elevated liver enzymes (especially if seropositive for hepatitis B or C), pancreatitis.
Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT 600 mg once daily; CHILD over 3 years, body weight 10–15 kg, 200 mg once daily; body weight 15–19 kg, 250 mg once daily; body weight 20–24 kg, 300 mg once daily; body weight 25–32 kg, 350 mg once daily; body weight 33–39 kg, 400 mg once daily; body weight 40 kg and over, adult dose.

POM **Efavirenz** *(WMF 6.5.2.2)*
Capsules, Efavirenz 50 mg, 100 mg, 200 mg
Oral solution, Efavirenz 150 mg/5 ml.

NEVIRAPINE

Synonym: NVP
Therapeutic category: Antiviral agent; Nucleoside reverse transcriptase inhibitor.
Indications: HIV infection, in combination with at least two other antiretroviral drugs; prevention of mother-to-child transmission in HIV-infected patients (but see notes above under Pregnancy).
Precautions: Hepatic impairment (see below and Appendix 5); history of chronic hepatitis (greater risk of hepatic adverse effects), pregnancy and breastfeeding (see notes above); **interactions**: Appendix 1.
HEPATIC DISEASE: POTENTIALLY LIFE-THREATENING HEPATOTOXICITY INCLUDING FATAL FULMINANT HEPATITIS REPORTED USUALLY OCCURRING IN FIRST 8 WEEKS; MONITOR LIVER FUNCTION BEFORE LONG-TERM TREATMENT THEN EVERY 2 WEEKS FOR 2 MONTHS THEN AFTER 1 MONTH AND THEN EVERY 3–6 MONTHS; DISCONTINUE PERMANENTLY IF ABNORMALITIES IN LIVER FUNCTION TESTS ACCOMPANIED BY HYPERSENSITIVITY REACTION (RASH, FEVER, ARTHRALGIA, MYALGIA, LYMPHADENOPATHY, HEPATITIS, RENAL IMPAIRMENT, EOSINOPHILIA, GRANULOCYTOPENIA); SUSPEND IF SEVERE ABNORMALITIES IN LIVER FUNCTION TESTS BUT NO HYPERSENSITIVITY REACTION—DISCONTINUE PERMANENTLY IF SIGNIFICANT LIVER FUNCTION ABNORMALITIES RECUR; MONITOR PATIENT CLOSELY IF MILD TO MODERATE ABNORMALITIES IN LIVER FUNCTION TESTS WITH NO HYPERSENSITIVITY REACTION.
RASH: RASH, USUALLY IN FIRST 8 WEEKS, IS MOST COMMON ADVERSE EFFECT; INCIDENCE REDUCED IF

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INTRODUCED AT LOW DOSE AND DOSE INCREASED GRADUALLY; DISCONTINUE PERMANENTLY IF SEVERE RASH OR IF RASH ACCOMPANIED BY BLISTERING, ORAL LESIONS, CONJUNCTIVITIS, SWELLING, GENERAL MALAISE OR HYPERSENSITIVITY REACTIONS; IF RASH MILD OR MODERATE MAY CONTINUE WITHOUT INTERRUPTION BUT DOSE SHOULD NOT BE INCREASED UNTIL RASH RESOLVES.

PATIENT ADVICE: PATIENTS SHOULD BE TOLD HOW TO RECOGNIZE HYPERSENSITIVITY REACTIONS AND ADVISED TO SEEK IMMEDIATE MEDICAL ATTENTION IF SYMPTOMS DEVELOP.

Adverse effects: Rash including Stevens-Johnson syndrome and rarely, toxic epidermal necrolysis (see also Precautions above); hepatitis or jaundice reported (see also Precautions above); nausea, vomiting, abdominal pain, diarrhoea, headache, drowsiness, fatigue, fever; hypersensitivity reactions (may involve hepatic reactions and rash, see Precautions above); anaphylaxis, angioedema, urticaria also reported.

Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.

•Administer around-the-clock in equal intervals to promote less variation in peak and trough serum levels.

•Administer tablet with or without food.

•Teach patient that drug does not cure infection but symptoms will be controlled; to avoid OTC medications unless prescribed.

•Monitor patient for allergic reactions.

Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT 200 mg once daily for first 14 days then (if no rash present) 200 mg twice daily; INFANT 15–30 days old, 5 mg/kg once daily for 14 days, then (if no rash present) 120 mg/m2 twice daily for 14 days, then 200 mg/m^2 twice daily; CHILD 1 month–13 years, 120 mg/m^2 twice daily for first 14 days, then (if no rash present) 200 mg/m^2 twice daily.

Prevention of mother-to-child transmission of HIV (see also notes above under Pregnancy), by mouth, ADULT 200 mg as a single dose at onset of labour; NEONATE 2 mg/kg as a single dose within 72 hours of birth.

NOTE: IF TREATMENT INTERRUPTED FOR MORE THAN 7 DAYS REINTRODUCE WITH 200 MG DAILY (INFANT 15–30 DAYS OLD, 5 MG/KG; CHILD OVER 1 MONTH, 120 MG/M^2) AND INCREASE DOSE CAUTIOUSLY.

POM **Nevirapine** *(WMF 6.5.2.2)*
Tablets, Nevirapine 200 mg.
Oral suspension, Nevirapine 50 mg/5 ml.

POM **NEVIPAN**® *(Ranbaxy)*
Tablet Nevirapine 200 mg.
200 mg - 60.

POM **Nevirapine** *(Strides Vital)*
Tablet, Nevirapine 200 mg.
200 mg – 60's.

9.5.2.3 Protease inhibitors

IN SOME SETTINGS IT MAY NOT BE POSSIBLE TO CARRY OUT FULL MONITORING DESCRIBED UNDER EACH DRUG ENTRY; IN SUCH CASES THE LEVEL OF MONITORING SHOULD BE DETERMINED BY LOCAL GUIDELINES (SEE ALSO NOTES ABOVE)

INDINAVIR

Synonym: IDV

Indications: HIV infection in combination with two nucleoside reverse transcriptase inhibitors and usually with low-dose ritonavir booster.

Precautions: Hepatic impairment (Appendix 5); ensure adequate hydration to reduce risk of nephrolithiasis; diabetes mellitus; haemophilia; pregnancy (see notes above and Appendix 2); breastfeeding (see notes above); metabolism of many drugs inhibited if administered concomitantly; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, diarrhoea, abdominal discomfort, dyspepsia, flatulence, pancreatitis, dry mouth, taste disturbances; headache, dizziness, insomnia; myalgia, myositis, rhabdomyolysis, asthenia, hypoaesthesia, paraesthesia; hyperglycaemia; anaphylactoid reactions, rash (including Stevens-Johnson syndrome), pruritus, dry skin, hyperpigmentation, alopecia, paronychia; interstital nephritis, nephrolithiasis (may require interruption or discontinuation; more frequent in children), dysuria, haematuria, crystalluria, proteinuria, pyuria (in children); hepatitis, transient hyperbilirubinaemia; blood disorders including neutropenia, haemolytic anaemia; lipodystrophy and metabolic effects, see notes above.

Dose: *HIV infection (in combination with nucleoside reverse transcriptase inhibitors and low-dose ritonavir booster)*, by mouth, ADULT indinavir 800 mg and ritonavir 100 mg both twice daily.

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HIV infection (in combination with nucleoside reverse transcriptase inhibitors but without ritonavir booster), by mouth, ADULT 800 mg every 8 hours; CHILD and ADOLESCENT 4–17 years, 500 mg/m² every 8 hours (maximum 800 mg every 8 hours); CHILD under 4 years, safety and efficacy not established.

PATIENT ADVICE: ADMINISTER 1 HOUR BEFORE OR 2 HOURS AFTER A MEAL; MAY BE ADMINISTERED WITH LOW-FAT, LIGHT MEAL; WHEN GIVEN WITH DIDANOSINE TABLETS, ALLOW 1 HOUR BETWEEN THE DRUGS (ANTACIDS IN DIDANOSINE REDUCE ABSORPTION OF INDINAVIR).

POM **Indinavir** *(WMF 6.5.2.3)*
Capsules, Indinavir (as sulfate) 200 mg, 333 mg, 400 mg.

POM **Indinavir** *(Strides Vital)*
Capsule, Indinavir sulfate 400 mg.
400 mg – 60's.

LOPINAVIR plus RITONAVIR

Synonym: LPV/r

Indications: HIV infection in combination with two other antiretroviral drugs.

NOTE: RITONAVIR INCREASES EFFECT OF LOPINAVIR (SEE NOTES ABOVE); LOW DOSE IN COMBINATION DOES NOT HAVE INTRINSIC ANTIVIRAL ACTIVITY.

Precautions: Hepatic impairment—avoid if severe (Appendix 5); renal impairment (Appendix 4); haemophilia; pregnancy (see notes above and Appendix 2); breastfeeding (see notes above and Appendix 3); diabetes mellitus; oral solution contains propylene glycol—avoid in hepatic and renal impairment, and in pregnancy, increased susceptibility to propylene glycol toxicity in slow metabolizers; **interactions**: Appendix 1.

PANCREATITIS: SIGNS AND SYMPTOMS SUGGESTIVE OF PANCREATITIS (INCLUDING RAISED SERUM AMYLASE AND LIPASE) SHOULD BE EVALUATED—DISCONTINUE IF PANCREATITIS DIAGNOSED.

Adverse effects: Diarrhoea, nausea, vomiting, colitis, abdominal discomfort, asthenia, headache, insomnia; rash; less frequently, dry mouth, hepatic dysfunction, pancreatitis (see also Precautions), dyspepsia, dysphagia, oesophagitis, influenza-like syndrome, appetite changes; hypertension, palpitations, thrombophlebitis, vasculitis, chest pain, dyspnoea, agitation, anxiety, ataxia, hypertonia, confusion, depression, dizziness, dyskinesia, paraesthesia, peripheral neuritis, somnolence; Cushing syndrome, hypothyroidism, sexual dysfunction, anaemia, leukopenia, dehydration, oedema, lactic acidosis; arthralgia, myalgia, abnormal vision, otitis media, taste disturbances, tinnitus; acne, alopecia, dry skin, pruritus, skin discoloration, nail disorders, sweating; lipodystrophy and metabolic effects (see notes above); raised bilirubin and lowered sodium, low platelet and low neutrophil counts also reported in children.

Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT and ADOLESCENT with body surface area of 1.3 m² or greater, 3 capsules or 5 ml twice daily (lopinavir 400 mg and ritonavir 100 mg twice daily); CHILD 6 months–13 years, lopinavir 225 mg/m² and ritonavir 57.5 mg/m² twice daily (or body weight 7–15 kg lopinavir 12 mg/kg and ritonavir 3 mg/kg twice daily, body weight 15–40 kg lopinavir 10 mg/kg and ritonavir 5 mg/kg twice daily).

NOTE: INCREASE DOSE BY 33% IF USED WITH EFAVIRENZ OR WITH NEVIRAPINE

PATIENT ADVICE: EACH DOSE TO BE TAKEN WITH FOOD.

POM **Lopinavir plus Ritonavir** *(WMF 6.5.2.3)*
Capsules, Lopinavir 133.3 mg and ritonavir 33.3 mg.
Oral solution, Lopinavir 400 mg and ritonavir 100 mg/5 ml.

NOTE: 5 ML ORAL SOLUTION ≡ 3 CAPSULES; WHERE APPROPRIATE CAPSULES MAY BE USED INSTEAD OF ORAL SOLUTION; ORAL SOLUTION EXCIPIENTS INCLUDE PROPYLENE GLYCOL AND ALCOHOL 42%.

NELFINAVIR

Synonym: NFV

Therapeutic category: Antiviral agent; Protease Inhibitor

Indications: HIV infection in combination with two other antiretroviral drugs.

Precautions: Hepatic and renal impairment; diabetes mellitus; haemophilia; pregnancy and breastfeeding (see notes above); **interactions**: Appendix 1.

Adverse effects: Diarrhoea, nausea, vomiting, flatulence, abdominal pain; rash; reports of elevated creatine kinase, hepatitis, pancreatitis, neutropenia, hypersensitivity reactions including bronchospasm, fever, pruritus and facial oedema, lipodystrophy and metabolic effects, see notes above.

Advice to patients: See label 21 in Appendix

RETURN

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Nursing considerations: •Obtain specimen for C&S test before first dose; therapy may begin pending test results.

•Administer tablet with food.

•Discontinue drug therapy and inform the physician if severe abdominal pain and bleeding occur.

•Teach patient that drug does not cure infection but symptoms will be controlled; to avoid other medications unless prescribed.

•Monitor patient for allergic reactions.

Dose: *HIV infection (in combination with other antiretroviral drugs)*, by mouth, ADULT 1.25 g twice daily or 750 mg 3 times daily; CHILD under 1 year, 40–50 mg/kg 3 times daily or 65–75 mg/kg twice daily; 1–13 years, 55–65 mg/kg twice daily.

PATIENT ADVICE: ADMINISTER WITH OR AFTER FOOD; POWDER MAY BE MIXED WITH WATER, MILK, FORMULA FEEDS OR PUDDING; IT SHOULD **NOT** BE MIXED WITH ACIDIC FOODS OR JUICES OWING TO ITS TASTE.

POM **Nelfinavir** *(WMF 6.5.2.3)*
Tablets, Nelfinavir (as mesilate) 250 mg.
Oral powder, Nelfinavir (as mesilate) 50 mg/g.

POM **VIRACEPT®** *(Swipha)*
Tablet, Nelfinavir (as mesylate) 250 mg.
250 mg - 270.

RITONAVIR

Synonym: r, RTV

Indications: HIV infection, as a booster to increase effect of indinavir, lopinavir or saquinavir and in combination with two other antiretroviral drugs.

Contra-indications: Severe hepatic impairment.

Precautions: Hepatic impairment; diabetes mellitus; haemophilia; pregnancy and breastfeeding (see notes above); **interactions**: Appendix 1.

PANCREATITIS: SIGNS AND SYMPTOMS SUGGESTIVE OF PANCREATITIS (INCLUDING RAISED SERUM AMYLASE AND LIPASE) SHOULD BE EVALUATED—DISCONTINUE IF PANCREATITIS DIAGNOSED.

Adverse effects: Nausea, vomiting, diarrhoea (may impair absorption—close monitoring required), abdominal pain, taste disturbances, dyspepsia, anorexia, throat irritation; vasodilatation; headache, circumoral and peripheral paraesthesia, hyperaesthesia, dizziness, sleep disturbances, asthenia, rash, hypersensitivity reactions, leukopenia; raised liver enzymes, bilirubin, and uric acid; occasionally flatulence, eructation, dry mouth and ulceration, cough, anxiety, fever, pain, myalgia, weight loss, decreased thyroxine, sweating, pruritus, electrolyte disturbances, anaemia, neutropenia, increased prothrombin time; pancreatitis (see also Pancreatitis, above); lipodystrophy and metabolic effects, see notes above.

Dose: *HIV infection (as a booster with other antiretroviral drugs)*, by mouth, ADULT 100 mg twice daily; CHILD 6 months–13 years 57.5 mg/m2 twice daily (or 3–5 mg/kg twice daily) (maximum 100 mg twice daily).

POM **Ritonavir** *(WMF 6.5.2.3)*
Capsules, Ritonavir 100 mg.
Oral solution, Ritonavir 400 mg/5 ml.

SAQUINAVIR

Synonym: SQV

Therapeutic category: Antiviral agent; Protease Inhibitor.

Indications: HIV infection in combination with two other antiretroviral drugs and usually with low-dose ritonavir booster.

Contra-indications: Severe hepatic impairment (Appendix 5).

Precautions: Hepatic impairment (Appendix 5); renal impairment (Appendix 4); diabetes mellitus; haemophilia; pregnancy and breastfeeding (see notes above); **interactions**: Appendix 1.

Adverse effects: Diarrhoea, buccal and mucosal ulceration, abdominal discomfort, nausea, vomiting; headache, peripheral neuropathy, paraesthesia, dizziness, insomnia, mood changes, ataxia, musculoskeletal pain, asthenia; fever, pruritus, rash and other skin eruptions, rarely Stevens-Johnson syndrome; other rare adverse effects include thrombocytopenia and other blood disorders, liver damage, pancreatitis and nephrolithiasis; reports of elevated creatine kinase, raised liver enzymes and neutropenia when used in combination therapy; lipodystrophy and metabolic effects (see notes above)

Advice to patients: See label 21 in Appendix 6. Saquinavir is not a cure for HIV infection nor does it reduce the transmission of HIV; opportunistic infections and other illnesses associated with AIDS may still occur; take saquinavir within 2 hours after a full meal; avoid direct sunlight when taking saquinavir.

Nursing considerations: •See under Nelfinavir.

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Dose: *HIV infection (in combination with nucleoside reverse transcriptase inhibitors and low-dose ritonavir booster)*, by mouth, ADULT saquinavir 1 g and ritonavir 100 mg twice daily.
HIV infection (in combination with other antiretroviral drugs but without ritonavir booster), by mouth, ADULT 1.2 g every 8 hours after a meal; CHILD under 16 years, safety and efficacy not established.

PATIENT ADVICE: ADMINISTER WITH OR AFTER FOOD.
NOTE. TO AVOID CONFUSION BETWEEN THE DIFFERENT FORMULATIONS OF SAQUINAVIR, PRESCRIBERS SHOULD SPECIFY THE BRAND TO BE DISPENSED; ABSORPTION FROM GEL-FILLED CAPSULES CONTAINING SAQUINAVIR IS MUCH GREATER THAN FROM CAPSULES CONTAINING SAQUINAVIR MESILATE. TREATMENT SHOULD GENERALLY BE INITIATED WITH GEL-FILLED CAPSULES.

POM **Squinavir** *(WMF 6.5.2.3)*
Capsules (gel-filled), Saquinavir 200 mg.

POM **FORTOVASE®** *(Swipha)*
Capsule, Saquinavir 200 mg; soft gel capsule.
200 mg - 180.
Dose: 1.2 g (6 caps.) 3 times daily.

POM **INVIRASE®** *(Swipha)*
Capsule, Saquinavir mesylate 200 mg; hard gel capsule.
200 mg - 270.
Dose: 600 mg (3 caps.) 3 times daily.

9.6 Insect repellents

Diethyltoluamide, an effective insect repellent, is used for the prevention of infections transmitted by insect bites, ticks, harvest mites and fleas. One application offers protection for 4 to 8 hours.

DIETHYLTOLUAMIDE

Indications: Insect repellent against mosquitoes, biting flies, ticks, harvest mites and fleas.
Precautions: Avoid contact with eyes or mouth, mucous membranes, areas of flexures, wounds, broken or irritated skin
Adverse effects: Systemic toxicity—reported with application of large topical doses, especially in children; occasionally, hypersensitivity reactions.
Administration: Apply sparingly to exposed skin and when treatment no longer needed, wash skin thoroughly with soap and water.

OTC **Diethyltoluamide** *(WMF 6.6)*
Cutaneous solution, Diethyltoluamide 50%, 75%.

10. Endocrine system drugs

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10.1 Antidiabetic drugs
10.1.1 Insulins
10.1.2 Hypodermic equipment
10.1.3 Oral antidiabetic drugs
10.1.3.1 Sulfonylureas
10.1.3.2 Biguanides
10.1.3.3 Other antidiabetics
10.2 Thyroid hormones and antithyroid drugs
10.2.1 Thyroid hormones
10.2.2 Antithyroid drugs
10.3 Corticosteroids
10.4 Sex hormones
10.4.1 Estrogens (Female sex hormones)
10.4.2 Progestogens (Female sex hormones)
10.4.3 Androgens (Male sex hormones)
10.5 Drugs acting on pituitary ovarian axis
10.5.1 Anti-estrogens (Ovulation inducers)
10.5.2 Anterior pituitary hormones (Gonadotrophins)
10.5.3 Posterior pituitary hormones
10.6 Other endocrine drugs

10.1 Antidiabetic drugs

10.1.1 Insulins
10.1.2 Hypodermic equipment
10.1.3 Oral antidiabetic drugs

Diabetes mellitus is characterized by hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism. There are 2 principal types of diabetes.

Type 1 diabetes or insulin-dependent diabetes mellitus is due to a defiency of insulin caused by autoimmune destruction of pancreatic beta cells. Patients require administration of insulin.

Type 2 diabetes or non-insulin dependent diabetes mellitus is due to reduced secretion of insulin or to peripheral resistance to the action of insulin. Patients may be controlled by diet alone, but often require administration of oral antidiabetic drugs or insulin. The energy and carbohydrate intake must be adequate but obesity should be avoided. In type 2 diabetes, obesity is one of the factors associated with insulin resistance. Diets high in complex carbohydrate and fibre and low in fat are beneficial. Emphasis should be placed on exercise and increased activity.

The aim of treatment is to achieve the best possible control of plasma glucose concentration and prevent or minimize complications including microvascular complications (retinopathy, albuminuria, neuropathy). Diabetes mellitus is a strong risk factor for cardiovascular disease; other risk factors such as smoking, hypertension, obesity and hyperlipidaemia should also be addressed.

Nursing Considerations:- Antidiabetics

•Give insulin after warming to room temp by rotating in palms to prevent lipodystrophy from injecting cold insulin. Change to human insulin if patient is allergic to beef or pork.

•Rotate injection sites when giving insulin within anyone of these regions: abdomen, upper back, thighs, upper arm, buttocks. Keep a record of sites.

•Give oral antidiabetics 30 min before meals.

•Monitor blood and urine glucose levels, fasting blood sugar, 2 hr PP.

•Advise patient to avoid alcohol and salicylates except on doctor's prescription; to maintain weight

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control, dietary restrictions, exercise, hygiene; to go for eye check yearly.

•Ensure patient understands symptoms of hypoglycaemia namely headache, tremors, fatigue, weakness; and to carry candy or sugar to treat hypoglycaemia.

10.1.1 Insulins

Appropriate insulin regimens should be worked out for each patient. Insulin requirements may be affected by variations in lifestyle (diet and exercise)—drugs such as corticosteroids, infections, stress, accidental or surgical trauma, puberty and pregnancy (second and third trimesters) may increase insulin requirements; renal or hepatic impairment and some endocrine disorders (for example Addison disease, hypopituitarism) or coelic disease may reduce requirements. In pregnancy insulin requirements should be monitored frequently.

If possible patients should monitor their own blood-glucose concentration using blood glucose strips. Since blood-glucose concentration varies throughout the day, patients should aim to maintain blood-glucose concentration between 4 and 10 mmol/litre for most of the day while accepting that on occasions it will be higher; strenuous efforts should be made to prevent blood-glucose concentrations falling below 4 mmol/litre because of the risk of hypoglycaemia. Patients should be advised to look for troughs and peaks of blood glucose and to adjust their insulin dosage only once or twice a week. Insulin doses are determined on an individual basis, by gradually increasing the dose to optimise blood-glucose concentration while avoiding hypoglycaemia.

In the absence of blood-glucose monitoring strips, urine-glucose monitoring strips can be used; in fact this is the method of personal choice for many patients with Type 2 diabetes mellitus. It is less reliable than blood glucose but is easier and costs much less. All patients should monitor either blood- or urine-glucose concentration daily.

Hypoglycaemia is a potential complication in all patients treated with insulin or oral hypoglycaemic agents. The consequences of hypoglycaemia, include confusion, seizures, coma and cerebral infarction.

Loss of warning of hypoglycaemia is common among insulin-treated patients and can be a serious hazard especially for drivers and those in dangerous occupations. Very tight control lowers the blood glucose concentration needed to trigger hypoglycaemic symptoms; increase in the frequency of hypoglycaemic episodes reduces the warning symptoms experienced by patients. Beta-blockers can also blunt hypoglycaemic awareness (and delay recovery). Some patients report loss of hypoglycaemic warning after transfer to human insulin. Clinical studies do not confirm that human insulin decreases hypoglycaemic awareness. If a patient believes that human insulin is responsible for loss of warning it is reasonable to revert to animal insulin. To restore warning signs, episodes of hypoglycaemia must be reduced to a minimum; this involves appropriate adjustment of insulin dose and frequency, and suitable timing and quantity of meals and snacks.

Drivers need to be particularly careful to avoid hypoglycaemia. They should check their blood-glucose concentration before driving and, on long journeys, at intervals of approximately two hours; they should ensure that a supply of sugar is always readily available. If hypoglycaemia occurs, the driver should stop the vehicle in a safe place, ingest a suitable sugar supply and wait until recovery is complete (may be 15 minutes or longer). Driving is particularly hazardous when hypoglycaemic awareness is impaired.

For sporadic physical activity, extra carbohydrate may need to be taken to avert hypoglycaemia. Blood glucose should be monitored before, during and after exercise. Hypoglycaemia can develop in patients taking oral antidiabetics, notably the sulfonylureas, but this is uncommon and usually indicates excessive dosage. Sulfonylurea-induced hypoglycaemia may persist for several hours and must be treated in hospital.

Diabetic ketoacidosis is a potentially lethal condition caused by an absolute or relative lack of insulin; it commonly occurs when adjustments to insulin dosage fail to compensate for increases in insulin requirements, for example during severe infection or major intercurrent illness. Diabetes ketoacidosis occurs mostly in patients with Type 1 diabetes mellitus. It also occurs in Type 2 diabetics who have a temporary need for insulin. Diabetic

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ketoacidosis is characterized by hyperglycaemia, hyperketonaemia and acidaemia with dehydration and electrolyte disturbances. It is essential that soluble insulin (and intravenous fluids) is readily available for its treatment.

Infections are more likely to develop in patients with poorly controlled diabetes mellitus. These should be treated promptly and effectively to avoid diabetic ketoacidosis.

Surgery. Particular attention should be paid to insulin requirements when a patient with diabetes undergoes surgery that is likely to need an intravenous infusion of insulin for longer than 12 hours. Soluble insulin should be given in intravenous infusion of glucose and potassium chloride (provided the patient is not hyperkalaemic), and adjusted to provide a blood-glucose concentration of between 7 and 12 mmol/litre. The duration of action of intravenous insulin is only a few minutes therefore the infusion must not be stopped unless the patient becomes frankly hypoglycaemic. For non-insulin dependent diabetics, insulin treatment is almost always required during surgery (oral hypoglycaemic drugs having been omitted).

Insulin must be given by injection because it is inactivated by gastrointestinal enzymes. Generally, insulin is given by subcutaneous injection into the upper arms, thighs, buttocks, or abdomen. There may be increased absorption from a limb, if the limb is used in strenuous exercise following the injection. It is essential to use only syringes calibrated for the particular concentration of insulin administered.

There are three main types of insulin preparations, classified according to duration of action after subcutaneous injection:

- those of short duration which have a relatively rapid onset of action, for example soluble or neutral insulin;
- those with an intermediate action, for example isophane insulin and insulin zinc suspension;
- those with a relatively slow onset and long duration of action, for example crystalline insulin zinc suspension.

Soluble insulin, when injected subcutaneously, has a rapid onset of action (after 30–60 minutes), a peak action between 2 and 4 hours, and a duration of action up to 8 hours. Soluble insulin by the intravenous route is reserved for urgent treatment and fine control in serious illness and perioperatively. When injected intravenously, soluble insulin has a very short half-life of only about 5 minutes.

When injected subcutaneously, **intermediate-acting insulins** have an onset of action of approximately 1–2 hours, a maximal effect at 4–12 hours and a duration of action of 16–24 hours. They can be given twice daily together with short-acting insulin or once daily, particularly in elderly patients. They can be mixed with soluble insulin in the syringe, essentially retaining properties of each component.

The duration of action of different insulin preparations varies considerably from one patient to another and this needs to be assessed for every individual. The type of insulin used and its dose and frequency of administration depend on the needs of each patient. For patients with acute onset diabetes mellitus, treatment should be started with soluble insulin given 3 times daily with medium-acting insulin at bedtime. For those less seriously ill, treatment is usually started with a mixture of pre-mixed short- and medium-acting insulins (for example 30% soluble insulin with 70% isophane insulin) given twice daily. The proportions of soluble insulin can be increased in patients with excessive post-prandial hyperglycaemia.

Regimens should be developed by each country.

Further information on Insulin

Insulin is an anabolic hormone in man produced exclusively by the beta-cells of the islets of Langerhans in the Pancrease. The major effects of insulin are on carbohydrate, fat and protein metabolism. Insulin reduces blood sugar concentration by (a) increasing glucose uptake by peripheral tissues namely muscle and fat cells, and (b) reducing hepatic glucose release through inhibiting glycogen breakdown (glycogenolysis) and suppressing gluconeogenesis, a process in which pyruvate, lactate and amino acids such as alanine are converted into glucose.

Sources of insulin include Pork, beef and human. Beef insulins are now rarely used. All insulin preparations are to a greater or lesser extent immunogenic in man.

Insulin is needed by all patients, regardless of age, presenting with ketoacidosis, and most of those with rapid onset of Symptoms: weight loss, weakness and sometimes vomiting often

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associated with Ketonuria.

Almost all children with diabetes require insulin therapy. The latter is also needed for type 2 diabetes when other methods have failed to achieve good control, and temporarily in the presence of intercurrent illness or preoperatively. Pregnant women with type 2 diabetes should be treated with insulin when diet alone fails.

Insulin Kinetics: Insulin is destroyed by gastro-intestinal enzymes and therefore always given parenterally. The absorption of Insulin into the blood stream and, consequently, the onset of hypoglycaemic effect are among other factors influenced by route of administration (I.V., I.M., S.C.), site of injection (abdomen, thighs, buttocks), ambient temperature, injection volume (dose), strength of insulin, and individual patient factors such as reactions at the injection site.

Method of Administration: Insulin is usually administered subcutaneously (S.C.), however, I.M. or I.V. administration is possible, e.g. in diabetic emergencies such as Ketoacidosis or surgery if a more rapid effect is wanted.

Subcutaneous injection into the abdominal wall ensures a faster absorption than from other regions of the body. Injection into a lifted skin fold minimizes the risk of I.M. injection.

An injection should be followed by a meal or snack containing carbohydrate within 30 minutes.

Injection Technique: A volume of air corresponding to the prescribed dose of insulin is injected into the vial. Turn vial and syringe upside down and draw up the prescribed dose of insulin. Remove syringe from vial and expel any air from syringe. Lift up a skin fold and inject the insulin under the skin. Keep the needle under the skin for a few seconds to make sure that all insulin has been injected. If blood appears after withdrawing the needle, press the injected site lightly with a finger.

Insulin Types/Duration of Action: Insulin preparations are of three types:

(a) Short-acting, soluble, regular or neutral insulin. The effect begins after approximately ½ hour, is maximal between 1 and 3 hours and terminates after approximately 8 hours.

(b) Intermediate-acting insulin. The effect begins after approximately 1½-2 ½ hours, is maximal between 4 and 5 hours and terminates after approximately 24 hours. Examples are Insulin Zinc suspensuon, Isophane insulin.

(c) Long-acting insulin. The effect begins after approximately 4 hours,is maximal between 8 and 30 hours and terminates after 36 hours. Examples include Protamine Zinc Insulin (PZI). Long acting insulins are rarely used today as they do not offer good control of the blood glucose.

The duration of action of a particular type of insulin varies considerably from one patient to another and needs to be assessed individually. Short-acting Insulin is a crystalline zinc-Insulin complex dispensed as a clear solution at neutral pH. All other commercial insulins have been modified to provide prolonged action and are dispensed as turbid suspensions at neutral pH with either protamine in phosphate buffer (Protamine Zinc and NPH insulin) or varying concentrations of Zinc in acetate buffer (ultralente, lente, and semilente insulins).

Colour: Short-acting, soluble, regular or neutral insulin must be as clear as water, while others are milky and cloudy when properly shaken. When drawing, the vial should be gently shaken or turned upside down ten times to ensure the even dispersal of the active ingredients. If particles or undissolved substances are formed in the vial, it should not be used.

Mixing of Insulin: When mixing insulin is required, the soluble portion should be drawn first into the syringe before the intermediate - acting insulin is drawn. The mixture should be administered immediately most especially the Zinc suspensions.

Insulin Dosing: The dose, frequency or administration and combination of insulin formulations used depend on numerous factors which vary greatly between individuals. Concomitant disease, especially if the patient is febrile, usually increases the patient's requirement. Blood glucose monitoring is recommended.

Total daily dose of insulin is 0.6-1 mcg/kg body-weight. 2/3 of total insulin dose is usually given in the morning before breakfast and the remaining 1/3 in the evening before supper. The overall dose is usually adjusted according to response. When short and medium acting insulins are mixed, the ratio of the short to the medium is normally 1:3.

Most patients are best started on insulin of intermediate action twice daily and a short-acting insulin can be added later to cover any hyperglycaemia which may follow breakfast or evening meal.

Insulin requirements may be increased by infection, stress, accidental or surgical trauma, puberty and, during the second and third trimesters of pregnancy.

Requirements may be decreased in patients with renal or hepatic impairment and in those with some endocrine disorders (e.g. Addison's disease, hypopituitrism) or coeliac disease.

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For intensive insulin regimens, multiple injections (3 to 4 times daily) are usually recommended; soluble insulin can also be given by continuous subcutaneous infusion using an infusion pump.

Warnings and Precautions for use: Insulin is contra-indicated in hypoglycaemia and in the presence of insulinoma. Patients should be able to differentiate the warning symptoms of too low blood glucose (hypoglycaemia) from those indicating too high blood glucose (hyperglycaemia). Significant deficiency of insulin may lead to diabetic Ketoacidosis, a fatal complication of hyper-glycaemia. An overdose of insulin can cause hypoglycaemia with early symptoms such as cold sweat, fatigue, nausea, trembling of hands, hunger and rapid heart beat. Sugar or food rich in carbohydrate can ameliorate the symptoms at this stage. Severe hypoglycaemia can result in temporary or permanent impairment of brain function and death. Diabetics should be advised always to carry some sugar lumps or biscuits with them.

Insulin does not pass the placental barrier (safe in pregnancy) and it does not pose any risk to the breast-fed baby. Diabetes may become more difficult to manage during pregnancy and lactation, and hence, closer supervision is necessary.

The ability to drive or operate machinery can be impaired during the initial period of insulin therapy, as well as upon change of product, or if the patient is under exceptional physical or mental stress and/or unaware of symptoms of hypoglycaemia.

Drivers need to be particularly careful to avoid hypoglycaemia and should be warned of the problems. They should normally check their blood-glucose concentration before driving and, on long journeys, at intervals of approximately 2 hours. If hypoglycaemia occurs, a driver should switch off the ignition until recovery is complete.

Interactions with other drugs: The following substances may enhance the hypoglycaemic effect of insulin: Non-selective beta-blocking agents, ACE-inhibitors, alcohol, anabolic steroids, salicylate, MAOIs. The following drugs may increase insulin requirements: Oral contraceptives, thiazides, corticosteroids, thyroid hormones and sympathomimetics.

Storage Conditions: Insulin preparations not in use should be stored in a refrigerator, between 2°C and 8°C, at which temperature they will retain the biological and antimicrobial effect until the date of expiry printed on the pack.

Insulin stored in a refrigerator must not be stored in or near the freezing compartment. Insulin which has been frozen must not be used. Insulin vials may be stored at room temperature (up to 25°C) for up to six weeks after first use but should be protected from excessive heat or direct sunlight. Never keep insulin in an unventilated vehicle that is parked in the sunlight. Do not place insulin in the same room with dry ice (carbon dioxide).

Insulin vials in use may be stored in the refrigerator for three months after first use.

Positioning of Insulin Preparations: Insulin vials should be stored horizontally. This is because the insulin in certain preparations, e.g. suspensions, can settle during storage. If this should occur while the bottles are stored in an upright position, it can be difficult to redisperse the insulin uniformly in the liquid.

SOLUBLE INSULIN

Synonym: Neutral Insulin; Insulin Injection; Regular Insulin.

Indications: Diabetes mellitus; diabetic emergencies and at surgery; diabetic ketoacidosis or coma.

Precautions: See notes above; reduce dose in renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.

Adverse effects: Hypoglycaemia in overdose; localized, and rarely generalized allergic reactions; lipoatrophy at injection site.

Nursing considerations: •Administer after warming vial by rotating in palms to prevent lipodystrophy from injecting cold insulin.

•Use S.C. route for administration because absorption rate and pain are less than with I.M. injections. Press but do not rub site after injection; rotate injection site to avoid overuse of one area.

•Do not interchange insulin sources (human or beef or pork) or insulin brands without physicians approval.

•Teach patient to be able differentiate between symptoms of hypoglycaemia and hyperglycaemia.

•Advise patient to carry a lump of sugar, crackers biscuit or sweetened chewing gum on hand for emergency.

•Cigarette smoking decreases insulin absorption; advise patient not to smoke at least 30 minutes after taking insulin injection.

•Insulin requirement increases drastically in pregnancy and declines during postpartum.

•Ensure that patient knows that insulin relieves symptoms but does not cure disease.

•Instruct patient on how to monitor urine glucose and use of equipment for performing self-monitoring of blood glucose.

•Store insulin in a cool area; refrigeration is desirable but not essential.

•Check expiration date on the vial before using the

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contents.
•Instruct patient about the nature of disease; the importance of adhering to therapeutic regimen, adhering to recommended diet, weight reduction, exercise and personal hygiene to prevent infection, and timing of injection and eating (meals must not be omitted).

Dose: *Diabetes mellitus*, by subcutaneous injection, by intramuscular injection, by intravenous injection or by intravenous infusion, ADULT and CHILD according to individual requirements.

Note: Injection should be followed by a meal within 30 minutes of administration.

POM **Soluble insulin** *(WMF 18.7)*
Injection (Solution for injection), Soluble insulin 40 units/ml, 10-ml vial; 100 units/ml, 10-ml vial.

Animal Insulin (highly purified)
POM **Soluble Insulin** *(EDL 19.7.1)*
Injection, Soluble insulin 40 units, 80 units, 100 units per ml; in 10 ml vials.

POM **ACTRAPID®** *(Zoomota)*
Injection, Neutral insulin (porcine, highly purified) 40 units, 100 units per ml; in 10 ml vials.

Biosynthetic Human Insulin
POM **Human Insulin** *(EDL 19.7.1)*
Injection, Human insulin 100 units per ml.

POM **ACTRAPID HM®** *(Zoomota)*
Injection, Soluble insulin (human monocomponent) 40 units, 100 units per ml; clear solution in 10 ml vials.

POM **ACTRAPID HM Penfill®** *(Zoomota)*
Injection, Soluble insulin (human monocomponent) 100 units per ml; 3 ml penfill cartridge for use only in NovoPen® metered–dose injection device.

POM **BIOSULIN-R®** *(Fidson)*
Injection, Soluble human insulin EP 40 units, 100 units per ml; in 10 ml vials.

POM **HUMULIN R®** *(CHI/Eli Lilly)*
Injection, Soluble human insulin 100 units per ml; in 10 ml vial.

INSULIN ZINC SUSPENSION

Synonym: Insulin Zinc suspension (mixed); I.Z.S.

Indications: Diabetes mellitus.

Contra-indications: Intravenous administration.

Precautions: See notes above; reduce dose in renal impairment (Appendix 4); pregnancy and breastfeeding (Appendix 2 and Appendix 3); **interactions**: Appendix 1

Adverse effects: Hypoglycaemia in overdose; localized, and rarely generalized allergic reactions; lipoatrophy at injection site.

Nursing considerations: •*See under Soluble Insulin*.

Dose: *Diabetes mellitus*, by subcutaneous injection, ADULT and CHILD according to individual requirements.

IMPORTANT: INTRAVENOUS INJECTION CONTRAINDICATED

POM **Insulin zinc suspension** *(WMF 18.7)*
Injection (Suspension for injection), Insulin zinc (mixed) 40 units/ml, 10-ml vial; 100 units/ml, 10-ml vial.

Animal Insulin (highly purified)
POM **Insulin Zinc Suspension** *(EDL 19.7.1)*
Injections, Insulin zinc suspension 40 units, 80 units, and 100 units per ml; in 10 ml vials.

Biosynthetic Human Insulin
POM **BIOSULIN-L®** *(Fidson)*
Injection, Human insulin zinc suspension EP 40 units, 100 units per ml; in 10 ml vials.

POM **HUMULIN L®** *(CHI/Eli Lilly)*
Injection, Human insulin zinc suspension 100 units per ml; in 10 ml vial.

POM **MONOTARD HM®** *(Zoomota)*
Injection, Insulin zinc suspension (human monocomponent) 100 units per ml; in 10 ml vial.

Currently recommended regimens using Monotard HM

The choice of regimen is determined not only by the severity of the metabolic disorder, but should also take into account motivation, ability and compliance of the patient.

1. Conventional treatment
   Monotard HM is usually given once or twice daily. The injection should be followed by a meal approx. 45 minutes after administration.
2. Mixing
   Monotard HM can be mixed with rapid-acting insulin for 1-2 daily injections in cases where a fixed mixture does not suit the requirements of the patient.
3. Basal/bolus
   An intermediate-acting insulin (e.g. Monotard HM) is injected in the late evening as an overnight

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or basal insulin. During daytime, bolus injection of rapid-acting insulin, e.g. Actrapid HM is given 15-30 minutes before each major meal. The dose of rapid-acting insulin before each meal should be determined based on pre- and post-prandial measurements of blood glucose.

ISOPHANE INSULIN

Indications: Diabetes mellitus.
Contra-indications: Intravenous administration.
Precautions: See notes above; reduce dose in renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); **interactions**: Appendix 1.
Adverse effects: Hypoglycaemia in overdose; localized, and rarely generalized allergic reactions; lipoatrophy at injection site.
Nursing considerations: •*See under Soluble Insulin*.
Dose: *Diabetes mellitus*, by subcutaneous injection, ADULT and CHILD according to individual requirements.
IMPORTANT: INTRAVENOUS INJECTION CONTRAINDICATED

POM **Isophane insulin** *(WMF 18.7)*
Injection (Suspension for injection), Isophane insulin 40 units/ml, 10-ml vial; 100 units/ml, 10-ml vial.

Biosynthetic Human Insulin
POM **BIOSULIN-N**® *(Fidson)*
Injection, Human isophane insulin EP 40 units, 100 units per ml; in 10 ml vials.

POM **HUMULIN N**® *(CHI/Eli Lilly)*
Injection, Human isophane insulin 100 units per ml; in 10 ml vial.

POM **INSULATARD HM**® *(Zoomota)*
Injections, Isophane insulin (human monocomponent) 40 units, 100 units per ml; cloudy or milky suspension in 10 ml vials.

POM **INSULATARD HM Penfill**® *(Zoomota)*
Injection, Isophane insulin (human monocomponent) 100 units per ml; in 3 ml Novopen penfill cartridge.
Pack - 3 ml x 5.

BIPHASIC ISOPHANE INSULIN

Synonym: Biphasic Isophane Insulin Injection.
Indications: Diabetes mellitus (intermediate acting).
Contra-indications, Precautions, etc: See Isophane insulin above.
Dose: By S.C. injection, according to patient's requirements.

Biosynthetic Human Insulin
POM **BIOSULIN 30/70**® *(Fidson)*
Injection, Mixture of human soluble insulin (30%) and human isophane insulin (70%), 40 units, 100 units per ml; in 10 ml vials.

POM **HUMULIN 70/30**® (*CHI/Eli Lilly)*
Injection, A mixture of highly purified 70% intermediate-acting human isophane insulin and 30% rapid-acting human soluble insulin, 100 units per ml; in 10 ml vial.

POM **MIXTARD 30/70 HM**® *(Zoomota)*
Injection, A mixture of 30% rapid-acting soluble insulin and 70% intermediate-acting isophane insulin purified according to monocomponent specifications 40 units, 100 units per ml; in 10 ml vials.

POM **MIXTARD 30/70 HM Penfill**® *(Zoomota)*
Injection, A mixture of 30% rapid-acting soluble insulin and 70% intermediate-acting isophane insulin purified according to monocomponent specifications, 100 units per ml; in 3 ml Novopen penfill cartridge.
Pack - 3 ml x 5's.

PROTAMINE ZINC INSULIN

Indications: Diabete mellitus.
Precautions: Reduce dose in renal impairment; over dosage may cause serious hypoglycaemia and insulin shock
Interactions: Alcohol, Oral contraceptives; corticosteriods
Adverse effects: Local reactions and fat hypertrophy at site of injection.
Nursing considerations: •*See under soluble insulin*.
Dose: By S.C. injection, according to patients requirements.

POM **Protamine Zinc Insulin** *(EDL 19.7.1)*
Injection, Protamine zinc insulin 40 units, 80 units, 100 units per ml; in 10 ml vials.

10.1.2 Hypodermic Equipment

NOVOPEN 3 ® *(Zoomota)*
Portable pen-like device for administration of insulin.

NOVOFINE 30G® *(Zoomota)*
Needle tips for use with Novopen.

10.1.3 Oral antidiabetic drugs

10.1.3.1Sulphonylureas

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10.1.3.2Biguanides
10.1.3.3Other antidiabetics

Oral antidiabetic (hypoglycaemic) drugs are used for non-insulin-dependent diabetes mellitus in patients who do not respond to dietary adjustment and an increase in physical exercise. They are used to supplement the effect of diet and exercise. There are various types of oral antidiabetic agents. The most commonly used are the **sulfonylureas** and the **biguanide**, metformin.

10.1.3.1Sulfonylureas

Sulfonylureas act mainly by augmenting insulin secretion and are therefore only effective if there is some residual pancreatic beta-cell activity. They may occasionally lead to hypoglycaemia 4 hours or more after food. This may be dose-related and usually indicates excessive dose and it occurs more frequently with long-acting sulfonylureas such as **glibenclamide** and occurs particularly in the elderly. The sulfonylureas have the disadvantage that they may encourage weight gain. They should not be used during breastfeeding and caution is required in the elderly and those with renal or hepatic insufficiency because of the risk of hypoglycaemia. Insulin therapy is generally required during intercurrent illness such as myocardial infarction, coma, infection, and trauma, during surgery and also during pregnancy.

CHLORPROPAMIDE

Therapeutic category: Oral hypoglycaemic; Sulfonylurea.

Pharmacology: Chlorpropamide is a long-acting sulfonylurea. It acts by stimulation of synthesis and release of endogenous insulin. Extrapancreatic effects may play a part in the mechanism of action of oral sulfonylureas.

Indications: Non-insulin-dependent diabetes mellitus (type II, NIDDM) or maturity onset diabetes.

Contra-indications: Hypersensitivity to the drug, diabetic ketoacidosis (with or without coma), insulin-dependent (juvenile) diabetes mellitus.

Precautions: Hypoglycaemia, loss of control of blood glucose, pregnancy, breast feeding, elderly, obesity.

Interactions: NSAIDs such as phenylbutazone; drugs that are highly protein bound like sulphonamides, probenecid, chloramphenicol, beta-blockers; drugs that cause hyperglycaemia like diuretics, corticosteroids, phenothiazines, oral contraceptives, isoniazid, sympathomimetics, calcium channel blockers; alcohol.

Adverse effects: Hypoglycaemia, Gl reactions, (e.g cholestatic jaundice rarely, dermatological reactions, haematological reactions, metabolic reactions (disulfiram-like reaction with alcohol), endocrine reactions, headache.

Advice to patients: See Label 4 in Appendix 6. Avoid alcohol; take at the same time each day; avoid hypoglycaemia, eat regularly, do not skip meals; carry a quick source of sugar.

Nursing considerations: •Administer 30 minutes before meal.

•Ensure patient understands nature of the disease and the importance of following therapeutic regimen, adhering to specific diet, weight reduction, exercise and personal hygiene to prevent infection.

•Explain how and when to monitor urinary and blood sugar levels.

•Teach patient to differentiate between symptoms of hypoglycaemia and hyperglycaemia.

•Ensure that patient understands that therapy relieves symptoms but does not cure disease.

•Evaluate therapeutic response viz decrease in polyuria, polydipsia, polyphagia.

•Patient needs no transition period should there be need to change to another sulfonylurea antidiabetic agent.

•Patient may require hospitalization during transition from insulin to oral antidiabetic agent; monitor patient's blood sugar.

•Tell patient to avoid ingesting alcohol, since headache, light-headedness, and occasional breathlessness may occur.

•Observe for signs of impending renal insufficiency such as dysuria, anuria, haematuria, and report to doctor immediately.

•Advise patient to avoid taking other drugs without clearance from the doctor.

•Advise patient to carry sweets to treat mild hypoglycaemia.

•Patient on oral antidiabetic therapy may require insulin during periods of increased stress, such as infection, fever, surgery, or trauma.

•Elderly patients are particularly prone to the dangers of hypoglycaemia when long-acting sulfonylureas are used namely Chlorpropamide and Glibenclamide.

Dose: Initial therapy, 250 mg daily; 100-125 mg daily for elderly patients; increased or decreased according to patient's response. See lit. for details.

POM **Chlorpropamide** *(EDL 19.7.2)*
Tablet, Chlorpropamide 250 mg.

POM **APO-CHLORPROPAMIDE®** *(Lahams)*
Tablet, Chlorpropamide 250 mg; white, f-c,

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scored, oval tab. marked 'AP0250'.
250 mg - 1000.

POM **DIABINESE**® *(Neimeth)*
Tablet, Chlorpropamide 250 mg
250 mg - 20; 100.

POM **DIPROMID**® *(Hovid)*
Tablet, Chlorpropamide 250 mg.
250 mg - 1000.

POM **SUCRANASE**® *(Supreme Pharm.)*
Tablet, Chlorpropamide 250 mg.
250 mg - 30.

GLIBENCLAMIDE

Synonym: Glyburide
Therapeutic category: Oral hypoglycaemic; Sulfonylurea.
Indications: Diabetes mellitus.
Contra-indications: Ketoacidosis; porphyria; pregnancy (Appendix 2); breastfeeding (Appendix 3).
Precautions: Renal impairment (Appendix 4); hepatic impairment (Appendix 5); elderly; substitute insulin during severe infection, trauma, surgery (see notes above); **interactions**: Appendix 1
Adverse effects: Mild and infrequent, including gastrointestinal disturbances and headache; liver disorders; hypersensitivity reactions usually in first 6–8 weeks; rarely, erythema multiforme, exfoliative dermatitis, fever and jaundice; hypoglycaemia, particularly in the elderly; rarely blood disorders including leukopenia, thrombocytopenia, agranulocytosis, pancytopenia, haemolytic anaemia, and aplastic anaemia.
Advice to patients: Eat regularly, do not skip meals; carry a quick source of sugar.
Nursing considerations: •Patients who are anorexic or NPO, may need to have their dose held to avoid hypoglycaemia.
•*See also under Chlorpropamide*.
Dose: *Diabetes mellitus*, by mouth, ADULT initially 5 mg once daily with or immediately after breakfast (ELDERLY 2.5 mg, but avoid—see notes above), adjusted according to response (maximum 15 mg daily).

POM **Glibenclamide** *(WMF 18.7)*
Tablets, Glibenclamide 2.5 mg, 5 mg.

POM **Glibenclamide** *(EDL 19.7.2)*
Tablet, Glibenclamide 5 mg.

POM **CLAMIDE**® *(Hovid)*
Tablet, Glibenclamide 5 mg.
5 mg - 1000.

POM **DAONIL**® *(May & Baker)*
Tablet, Glibenclamide 5 mg; almost white scored oblong tab.
5 mg - 30; 100.

POM **GILEMAL**® *(Sanofi)*
Tablet, Glibenclamide 5 mg.
5 mg - 28; 500; 1000.

POM **GLANIL**® *(NGC)*
Tablet, Glibenclamide 5 mg; almost white scored oblong tab.
5 mg - 30; 100.

POM **GLIBEN-J**® *(Juhel)*
Caplet, Glibenclamide 5 mg; white scored caplet marked 'GLI/5' on one side and 'Juhel' on the reverse.
5 mg – 10 x 10's (in blister); 500's (in jars).

POM **GLIBENOL**® *(Afrab-Chem)*
Tablet, Glibenclamide 5 mg; white scored tab. marked "af".

GLICLAZIDE

Therapeutic category: Oral Hypoglycaemic
Indications: Non-insulin-dependent diabetes mellitus (NIDDM)
Contra-indications, Precautions, etc: See under chlorpropamide and notes above.
Dose: By mouth, 80-320 mg daily depending on blood glucose response; 160 mg daily in majority of cases usually in 2 divided doses.

POM **Gliclazide** *(EDL 19.7.2)*
Tablet, Gliclazide 80 mg.

POM **GLIMICRON**® *(Hovid)*
Tablet, Gliclazide 80 mg; white, uncoated tab. cross scored on one side.
80 mg - 10 x 10 (in blister pack); 500

10.1.3.2Biguanides

Metformin exerts its effect by decreasing gluconeogenesis and by increasing peripheral utilization of glucose. Metformin can only act in the presence of endogenous insulin therefore is effective only in diabetics with some residual functioning pancreatic islet cells. It is used as a first-line treatment in overweight non-

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insulin-dependent diabetic patients and in others when strict dieting and sulfonylureas have failed to control the disease. Gastrointestinal adverse effects are common on initial treatment and may persist, particularly when very high doses (such as 3 g daily) are given. In order to reduce gastrointestinal effects, treatment should be initiated with a low dose which may be gradually increased. Metformin may provoke lactic acidosis which is most likely to occur in patients with renal impairment; it should not be used in patients with even mild renal impairment. One major advantage of metformin is that it does not usually cause hypoglycaemia. It may be used together with insulin (but weight gain and hypoglycaemia can be problems) or sulfonylureas (but possibility of increased adverse effects with such combinations). During medical and surgical emergencies insulin treatment is almost always required; insulin should be substituted for metformin before elective surgery and in pregnancy.

METFORMIN

Therapeutic category: Oral hypoglycaemic; Biguanide.

Indications: Diabetes mellitus (see notes above).

Contra-indications: Renal impairment (withdraw if renal impairment suspected; Appendix 4); withdraw if tissue hypoxia likely (for example sepsis, respiratory failure, recent myocardial infarction, hepatic impairment), use of iodine-containing X-ray contrast media (do not restart metformin until renal function returns to normal) and use of general anaesthesia (suspend metformin 2 days beforehand and restart when renal function returns to normal); alcohol dependence; pregnancy (Appendix 2).

Precautions: Measure serum creatinine before treatment and once or twice annually during treatment; substitute insulin during severe infection, trauma, surgery (see notes above and contraindications); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Anorexia, nausea and vomiting, diarrhoea (usually transient), abdominal pain, metallic taste; lactic acidosis most likely in patients with renal impairment (discontinue); decreased vitamin B_{12} absorption.

Advice to patients: See Label 21 in Appendix 6. Eat regularly, do not skip meals; carry quick source of sugar; avoid alcohol.

Nursing considerations: •Ensure patient understands the disease and its treatment; patients who are NPO may need to have their dose held to avoid hypoglycaemia.
•Administer with food to decrease GI irritation.
•Warn patient to avoid excessive alcohol consumption to prevent excessive elevation of blood lactate.
•Discontinue therapy and report to doctor immediately if vomiting occurs; may be due to lactic acidosis potentially fatal complication of biguanide therapy.

Dose: *Diabetes mellitus*, by mouth, ADULT initially 500 mg with breakfast for at least 1 week then 500 mg with breakfast and evening meal for at least 1 week, then 500 mg with breakfast, lunch and evening meal or 850 mg every 12 hours with or after food (maximum 2 g daily in divided doses).

POM **Metformin** *(WMF 18.7)*
Tablets, Metformin HCl 500 mg, 850 mg [850-mg strength not included in WHO Model list].

POM **Metformin** *(EDL 19.7.2)*
Tablet, Metformin HCl 500 mg.

POM **DIABETMIN®** *(Hovid)*
Tablet, Metformin HCl 500 mg; f-c tab.
500 mg - 1000.
Retard tablet, Metformin HCl 850mg; s-r tab.
850 mg – 10 x 10; 100.

Dose: By mouth, Adult, initially 850 mg twice daily with or after meals; increased gradually to 2.55 g daily if necessary. Avoid use in the elderly with impaired renal function.

POM **FORMET®** *(Strides Vital)*
Tablet, Metformin 500 mg.
Pack – 3 x 10's.

POM **GLUCOPHAGE®** *(Biofem)*
Tablets, Metformin HCl 500 mg, 850 mg; white f-c tabs.
500 mg - 84's
850 mg - 30's.

POM **GLUFORMIN®** *(NGC)*
Tablet, Metformin HCl 500 mg.
500 mg - 10; 100.

POM **MIFORMIN®** *(Didachons)*

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Tablet, Metformin HCI 500 mg.

With Glibenclamide

POM **GLUCOVANCE**® *(Biofem)*

Tablet, Metformin HCl 500 mg, Glibenclamide 2.5 mg; white f-c tab marked '2.5 mg' on one side.

Pack - 30's.

Tablet, Metformin HCl 500 mg, Glibenclamide 5 mg; white f-c tab marked '5 mg' on one side.

Pack: 30's.

10.1.3.3Other antidiabetics

Rosiglitazone, a member of the thiazolidinedione class of antidiabetic agents, reduces blood-glucose concentration by increasing insulin sensitivity. It is used in the management of Type 2 diabetes mellitus (also known as non-insulin-dependent diabetes mellitus [NIDDM] or adult-onset diabetes). It improves glycaemic control while reducing circulating insulin levels.

ROSIGLITAZONE

Indications: Management of type 2 diabetes mellitus alone as an adjunct to diet and exercise or in combination with metformin, sulfonylurea or insulin.

Management of type 2 diabetes should include diet control. Caloric restriction, weight loss, and exercise are essential for the proper treatment of the diabetic patient becauses they help improve insulin sensitivity. This is important not only in the primary treatment of type 2 diabetes, but also in maintaining the efficacy of drug therapy. Prior to initiation of therapy with rosiglitazone, secondary causes of poor glycaemic control e.g. infection, should be investigated and treated.

Contra-indications: History of hypersensitivity to rosiglitazone or any other ingredient of the preparation.

Precautions: Rosiglitazone is active only in the presence of endogenous insulin (avoid use in patients with type 1 diabetes for the treatment of diabetic ketoacidosis); may cause resumption of ovulation in premenopausal anovulatory women with insulin resistance and as a result of improved insulin sensitivity, risk of pregnancy may be increased (ensure adequate contraception is used); thiazolidinediones can cause fluid retention/ oedema which can exacerbate or lead to CHF; may cause weight gain which probably involves a combination of fluid retention and fat accumulation; avoid use if patient shows clinical evidence of active liver disease or increased serum transaminase levels; pregnancy and lactation.

Interactions: Rosiglitazone is predominantly metabolized by CYP2C8, and to a lesser extent, 2C9. Co-administration with CYP2C8 inhibitors may cause inceased rosiglitazone plasma concentration while the inducers may produce opposite effect (close monitoring of glycaemic control and rosiglitazone dose adjustment may be needed).

Adverse effects: Oedema, anaemia, hypercholesterolaemia, weight gain, hypoglycaemia, CHF/pulmonary oedema, cardiac ischaemia; hepatic dysfunction evidenced primarily by elevated hepatic enzymes.

Advice to patients: May be taken with or without meals.

Inform patient that management of of type 2 diabetes should include diet control. Caloric restriction, weight loss, and exercise are essential for the proper treatment of the diabetic patient becauses they help improve insulin sensitivity. This is important not only in the primary treatment of type 2 diabetes, but also in maintaining the efficacy of drug therapy.

Instruct patient to adhere to the diet and to regularly check blood glucose and Hgb levels; it can take up to 2 weeks to see a reduction in blood glucose and 2-3 months to see full effect.

Advise patient to report immediately any unexplained symptoms of nausea, vomiting, abdominal pain, fatigue, anorexia, or dark urine. Patient should also be told to report unusually rapid increase in weight or oedema, or shortness of breath or other symptoms of heart failure.

Explain to patient that rosiglitazone when used alone or in combination with other hypoglycaemic agents can cause hypoglycaemia; teach patient the symptoms, treatment and predisposing factors.

Ensure adequate contraception is used as therapy may result in ovulation in some premenopausal anovulatory women with increased risk for pregnancy.

Dose: The management of antidiabetic therapy should be individualised. Periodic fasting blood glucose measurements should be performed to monitor therapeutic response prior to up-titrating dose. To be given with or without food.

Monotherapy: Start 4 mg as a single dose once daily or in divided doses twice daily; may be increased to 8 mg as a single dose once daily or in divided doses twice daily if FPG (fasting plasma

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glucose) shows inadequate response following 12 weeks of treatment.
Combination therapy with Metformin: Start 4 mg as a single dose once daily or in divided doses twice daily; may be increased to 8 mg/day following 12 weeks of therapy if there is insufficient reduction in FPG.
Combination therapy with Sulfonylurea: Start 4 mg as a single dose once daily or in divided doses twice daily; may be increased to 8 mg/day 8 to 12 weeks after initiation of therapy if there is insufficient reduction in FPG.
Combination therapy with Insulin: Start 4 mg as a single dose once daily or in divided doses twice daily; may reduce insulin dose by 10-25% if patient reports hypoglycaemia or if FPG concentrations decreased to less than 100 mg/dl. Futher adjustments should be individualised based on glucose-lowering response.
Oral triple combination therapy with Meformin and a Sulfonylurea: Start 4 mg as a single dose once daily or in divided doses twice daily; may cautiously adjust dose up to 8 mg/day 8 to 12 weeks after initiation of therapy if FPG is inadequately controlled.
Maximum recommended dose: 8 mg as a single dose once daily or in divided doses twice daily.

Note: No dosage adjustments are required in erderly, renal impairment (avoid combination with Metformin). Not recommended for children under 18 years.

POM **AVANDIA**® *(GSK)*
Tablet, Rosiglitazone 4 mg.

10.2 Thyroid hormones and antithyroid drugs

10.2.1 Thyroid hormones
10.2.2 Antithyroid drugs

10.2.1 Thyroid hormones

Thyroid agents are natural or synthetic agents containing **levothyroxine** (thyroxine) or **liothyronine** (tri-iodothyronine). The principal effect is to increase the metabolic rate. They also exert a cardiostimulatory effect which may be the result of a direct action on the heart.

Thyroid hormones are used in hypothyroidism (myxoedema) and also in diffuse non-toxic goitre, Hashimoto thyroiditis (lymphadenoid goitre) and thyroid carcinoma. Neonatal hypothyroidism requires prompt treatment for normal development.

Levothyroxine sodium (thyroxine sodium) is the treatment of choice for maintenance therapy. It is almost completely absorbed from the gastrointestinal tract but the full effects are not seen for up to 1 to 3 weeks after beginning therapy; there is a slow response to dose change and effects may persist for several weeks after withdrawal. Dosage of levothyroxine in infants and children for congenital hypothyroidism and juvenile myxoedema should be titrated according to clinical response, growth assessment and measurement of plasma thyroxine and thyroid-stimulating hormone.

LEVOTHYROXINE SODIUM

Synonym: Thyroxine sodium.
Indications: Hypothyroidism.
Contra-indications: Thyrotoxicosis
Precautions: Cardiovascular disorders (myocardial insufficiency or ECG evidence of myocardial infarction); hypopituitarism or predisposition to adrenal insufficiency (must be corrected by corticosteroid prior to initial levothyroxine); elderly; long-standing hypothyroidism, diabetes insipidus, diabetes mellitus (may need to increase dose of insulin or oral antidiabetic drug); pregnancy (Appendix 2), breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: (Usually with excessive dose) anginal pain, arrhythmias, palpitations, tachycardia, skeletal muscle cramps, diarrhoea, vomiting, tremors, restlessness, excitability, insomnia, headache, flushing, sweating, excessive loss of weight and muscular weakness.
Advice to patients: Do not change brands without physicians knowledge; report immediately to physician any chest pain, increased pulse, palpitations, heat intolerance, excessive sweating; do not discontinue without notifying your physician.
Nursing considerations: •Administer drug in the morning, as a single dose to reduce sleeplessness, and at the same time each day to maintain drug level in the blood.
•Assess vital signs of B.P. and pulse rate before giving each dose of drug.
•Tell patient to report immediately if chest pain, palpitations, sweating, nervousness, shortness of breath, or other signs of overdosage or aggravated cardio-

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vascular disease occur.

Dose: *Hypothyroidism*, by mouth, ADULT initially 50–100 micrograms daily (25–50 micrograms for those over 50 years) before breakfast, increased by 25–50 micrograms every 3–4 weeks until normal metabolism maintained (usual maintenance dose, 100–200 micrograms daily); where there is cardiac disease, initially 25 micrograms daily or 50 micrograms on alternate days, adjusted in steps of 25 micrograms every 4 weeks *Congenital hypothyroidism and juvenile myxoedema (see notes above)*, by mouth, CHILD up to 1 month, initially 5–10 micrograms/kg daily, CHILD over 1 month, initally 5 micrograms/kg daily, adjusted in steps of 25 micrograms every 2–4 weeks, until mild toxic symptoms appear, then reduce dose slightly.

POM **Levothyroxine sodium** *(WMF 18.8.1)*
Tablets, Levothyroxine sodium 25 micrograms, 50 micrograms, 100 micrograms [25-mg strength not included on WHO Model List].

POM **Levothyroxine sodium** *(EDL 19.9.1)*
Tablets, Levothyroxine sodium 0.05 mg, 0.1 mg.

POM **EUTHROX®** *(Biofem)*
Tablets, Levothyroxine sodium 25 ug, 50 ug, 150 ug; tabs marked 'EM/25', 'EM/50', 'EM/150' on one side respectively.
Pack - 100's.

10.2.2 Antithyroid drugs

Antithyroid drugs such as **propylthiouracil** and **carbimazole** are used in the management of thyrotoxicosis. They are also used to prepare the patient for thyroidectomy. They are usually well-tolerated, with mild leukopenia or rashes developing in a few percent of cases, usually during the first 6–8 weeks of therapy. During this time the blood count should be checked every 2 weeks or if a sore throat or other signs of infection develop. The drugs are generally given in a high dose in the first instance until the patient becomes euthyroid, the dose may then be gradually reduced to a maintenance dose which is continued for 12–18 months, followed by monitoring to identify relapse. There is a lag time of some 2 weeks between the achievement of biochemical euthyroidism and clinical euthyroidism. Beta-adrenoceptor antagonists (beta-blockers) (usually **propranolol**) may be used as a short-term adjunct to antithyroid drugs to control symptoms but their use in heart failure associated with thyrotoxicosis is controversial.

Treatment can be given, if necessary, in pregnancy but antithyroid drugs cross the placenta and in high doses may cause fetal goitre and hypothyroidism. The lowest dose that will control the hyperthyroid state should be used (requirements in Graves disease tend to fall during pregnancy). Propylthiouracil appears in breast milk but does not preclude breastfeeding as long as neonatal development is closely monitored and the lowest effective dose is used.

If surgery (partial thyroidectomy) is contemplated, it may be necessary to give **iodine** for 10 to 14 days in addition to antithyroid drugs to assist control and reduce vascularity of the thyroid. Iodine should not be used for long-term treatment since its antithyroid action tends to diminish. In patients in whom drug therapy fails to achieve long-term remissions definitive treatment with surgery or (increasingly) radioactive iodine is preferable.

CARBIMAZOLE

Pharmacology: Carbimazole, a thiourea derivative, is an antithyroid substance which depresses the formation of thyroid hormone.
Indications: Thyrotoxicosis.
Contra-indications: Tracheal obstruction, breast-feeding.
Precautions: Pregnancy; signs of blood disorder such as sore throat, fever or rashes.
Adverse effects: Rashes, nausea, headache, GI upset, blood disorders, arthralgia, alopecia, hepatitis, psychotic reactions.
Advice to patients: Notify physician immediately of symptoms of blood disorders viz sore throat, mouth ulcers, bruising, fever, malaise, or non-specific illness.
Dose: By mouth, usually 20-60 mg daily for 4-8 weeks; then reduced gradually to 5-15 mg daily for about 18 months.
Child: initially 15 mg daily, adjusted according to response.

POM **Carbimazole** *(EDL 19.9.2)*

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Tablet, Carbimazole 5 mg.

POM **CARBIROID®** *(Hovid)*
Tablet, Carbimazole 5 mg.
5 mg - 1000.

POTASSIUM IODIDE

Indications: Thyrotoxicosis (pre-operative treatment); sporotrichosis, subcutaneous phycomycosis (section 6.3).
Contra-indications: Breastfeeding (Appendix 3); long-term treatment.
Precautions: Pregnancy (Appendix 2), children.
Adverse effects: Hypersensitivity reactions including coryza-like symptoms, headache, lacrimation, conjunctivitis, pain in salivary glands, laryngitis, bronchitis, rashes; on prolonged treatment, depression, insomnia, impotence, goitre in infants of mothers taking iodides.
Dose: *Pre-operative management of thyrotoxicosis*, by mouth , ADULT 60–180 mg daily.

POM **Potassium iodide** *(WMF 18.8.2)*
Tablets, Potassium iodide 60 mg.

IODINE plus POTASSIUM IODIDE

Synonym: Lugol's Solution; Aqueous Iodine Oral Solution.
Indications: Pre-operative treatment of thyrotoxicosis.
Precautions: Pregnancy, breast-feeding, infants; not for long-term treatment.
Adverse effects: Mental depression, nervousness, insomnia, sexual impotence, myxoedema, headache, pain and swelling in the salivary glands, weakness, conjuctivitis, bronchitis, skin reactions.
Advice to patients: See Label 27 in Appendix 6. Take after meals with food or milk or dilute with a large quantity of water, fruit juice, milk, or both; take with a straw to prevent tooth discolouration; discontinue use if stomach pain, skin rash, metallic taste, or nausea and vomiting occur.
Nursing considerations: •Improve taste of drug (has very salty taste) by diluting with water, milk or juice; give with meals to minimize GI distress; give with a straw to prevent tooth discolouration; give at the same time each day to maintain blood level.
•Encourage patient to take adequate fluids.
•Advise patient not to discontinue drug abruptly to prevent thyroid crisis.
Dose: By mouth, 0.1-0.3 ml 3 times daily well diluted with water or milk.

POM **Iodine plus Potassium Iodide** *(EDL 19.9.2)*
Oral solution, Iodine 5%, potassium iodide 10%.

PROPYLTHIOURACIL

Propylthiouracil is a representative antithyroid drug. Various drugs can serve as alternatives.
Synonym: PTU.
Indications: Hyperthyroidism.
Precautions: Large goitre; pregnancy and breastfeeding (see also notes; Appendices 2 and 3); hepatic impairment (Appendix 5)—withdraw treatment if hepatic function deteriorates (fatal reactions reported); renal impairment—reduce dosage (Appendix 4).
Adverse effects: Nausea, rashes, pruritus, arthralgia, headache; rarely, alopecia, cutaneous vasculitis, thrombocytopenia, aplastic anaemia, lupus erythematosus-like syndrome, jaundice, hepatitis, hepatic necrosis, encephalopathy, nephritis.
Advice to patients: Do not exceed prescribed dosage; take at regular intervals around-the-clock; notify physician or pharmacist of symptoms of blood dyscrasias viz fever, sore throat, unusual bleeding or bruising, headache, or general malaise.
Nursing considerations: •Give drug with meals to reduce GI distress, and at the same time each day to maintain drug level in the blood.
•Advise patient to consult physician before taking OTC products for cough or any iodine containing products or iodized salt or sea foods such as shell fish.
•Instruct patient not to discontinue drug abruptly to prevent thyroid crisis.
•Stop drug if severe rash or cervical lymph nodes develop.
•Monitor CBC periodically to detect impending leukopenia, thrombocytopenia, and agranulocytodsis.
Dose: *Hyperthyroidism*, by mouth, ADULT 300–600 mg daily until patient becomes euthyroid; dose may then be gradually reduced to a maintenance dose of 50–150 mg daily.
PATIENT ADVICE: WARN PATIENT TO TELL DOCTOR IMMEDIATELY IF SORE THROAT, MOUTH ULCERS, BRUISING, FEVER, MALAISE, OR NON-SPECIFIC ILLNESS OCCURS.

POM **Propylthiouracil** *(WMF 18.8.2)*
Tablets, Propylthiouracil 50 mg.

POM **Propylthiouracil** *(EDL 19.9.2)*
Tablet, Propylthiouracil 50 mg.

10.3 Corticosteroids

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Corticosteroids (section 8.3) include hormones secreted by the adrenal cortex and synthetic analogues of these hormones. The adrenal cortex normally secretes **hydrocortisone** which has glucocorticoid activity and weak mineralocorticoid activity. It also secretes the mineralocorticoid aldosterone. Synthetic glucocorticoids include betamethasone, **dexamethasone** and **prednisolone**. Fludrocortisone [not included on WHO Model List] has glucocorticoid properties but it has potent mineralocorticoid properties and is used for its mineralocorticoid effects.

Pharmacology of the corticosteroids is complex and their actions are wide-ranging. In physiological (low) doses, they replace deficient endogenous hormones. In pharmacological (high) doses, glucocorticoids decrease inflammation and suppress the immune response.

In therapeutic doses glucocorticoids suppress release of corticotrophin (adrenocorticotrophic hormone, ACTH) from the pituitary thus the adrenal cortex ceases secretion of endogenous corticosteroids. If suppressive doses are given for prolonged periods, the adrenal cortex may atrophy and this leads to a deficiency on sudden withdrawal or dosage reduction or situations such as stress or trauma where corticosteroid requirements are increased. After high dosage or prolonged therapy, withdrawal should be gradual, the rate depending on various factors including patient response, corticosteroid dose, duration of treatment and disease state. The suppressive action of a corticosteroid on cortisol secretion is least when given in the morning. Corticosteroids should normally be given in a single morning dose to attempt to minimize pituitary-adrenal suppression. Because the therapeutic effects of corticosteroids are of longer duration than the metabolic effects, intermittent therapy may allow the body's normal metabolic rhythm and the therapeutic effects to be maintained. Alternate day dosing is, however, suitable only in certain disease states and with corticosteroids with small mineralocorticoid effects and a relatively short duration of action.

Hydrocortisone is used in adrenal replacement therapy and on a short-term basis by intravenous injection for the emergency management of some conditions. Its mineralocorticoid activity is too high for it to be used on a long-term basis for disease suppression. The mineralocorticoid activity of fludrocortisone is also high and its anti-inflammatory activity is of no clinical relevance. It is used together with glucocorticoids in adrenal insufficiency. **Prednisolone** has predominantly glucocorticoid activity and is the corticosteroid most commonly administered for long-term disease suppression. It is the active metabolite of prednisone, conversion of which is variable and prednisone should not be used interchangeably with prednisolone. **Dexamethasone** has very high glucocorticoid activity in conjunction with insignificant mineralocorticoid activity making it particularly suitable for high-dose therapy in conditions where water retention would be a disadvantage such as cerebral oedema. It also has a long duration of action and this, together with its lack of mineralocorticoid activity makes it particularly suitable for conditions requiring suppression of corticotrophin secretion such as congenital adrenal hyperplasia.

Disadvantages of corticosteroids

Overdosage or prolonged use may exaggerate some of the normal physiological actions of corticosteroids leading to mineralocorticoid and glucocorticoid adverse effects.

Mineralocorticoid adverse effects include hypertension, sodium and water retention and potassium loss. These effects are most marked with fludrocortisone but are significant with hydrocortisone, occur slightly with prednisolone and are negligible with dexamethasone.

Glucocorticoid adverse effects include diabetes mellitus and osteoporosis which is of particular importance in the elderly since it may result in osteoporotic fractures of the hip or vertebrae. High doses may also be associated with avascular necrosis of the femoral neck. Muscle wasting may also occur and there is a weak link with peptic ulceration. Mental disturbances can occur, including serious paranoid state or depression with risk of suicide, particularly in patients with a history of mental disorders; euphoria is also common. High doses may cause Cushing syndrome (typical moon face, striae and acne), which is usually reversible on withdrawal of

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treatment, but this should always be tapered gradually to avoid symptoms of acute adrenal insufficiency (see also Withdrawal). In children, corticosteroids may result in suppression of growth and corticosteroids administered during pregnancy can affect adrenal development in the fetus. Any adrenal suppression in the neonate following prenatal exposure usually resolves spontaneously after birth and is rarely clinically important. Healing of wounds may be impaired and infections and thinning of the skin may occur; spread of infections may result from modification of tissue reactions.

Adrenal suppression

Adrenal suppression occurs during prolonged therapy with corticosteroids, with development of adrenal atrophy which may persist for years after stopping. Abrupt withdrawal after a prolonged period may lead to acute adrenal insufficiency, hypotension or death (see Withdrawal of Systemic Corticosteroids, below). Withdrawal may also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and weight loss.

CORTICOSTEROID COVER DURING STRESS

To compensate for a diminished adrenocortical response caused by prolonged corticosteroid treatment, any significant intercurrent illness, trauma, or surgery requires a temporary increase in corticosteroid dose, or if already stopped, a temporary re-introduction of corticosteroid treatment. Anaesthetists **must** therefore know whether a patient is taking or has been taking a corticosteroid, to avoid a precipitous fall in blood pressure during anaesthesia or in the immediate postoperative period. A suitable regimen for corticosteroid replacement, in patients who have taken more than 10 mg prednisolone daily (or equivalent) within 3 months of surgery, is:

- *Minor surgery under general anaesthesia*—usual oral corticosteroid dose on the morning of surgery or hydrocortisone 25–50 mg intravenously at induction; the usual oral corticosteroid dose is recommenced after surgery
- *Moderate or major surgery*—usual oral corticosteroid dose on the morning of surgery and hydrocortisone 25–50 mg intravenously at induction, followed by hydrocortisone 25–50 mg 3 times a day by intravenous injection for 24 hours after moderate surgery or for 48–72 hours after major surgery; the usual preoperative oral corticosteroid dose is recommenced on stopping hydrocortisone injections

Infections

Prolonged courses of corticosteroids increase susceptibility to infections and increase their severity; clinical presentation of infections may also be atypical. Serious infections, for example septicaemia and tuberculosis, may reach an advanced stage before being recognised, and amoebiasis or strongyloidiasis may be activated or exacerbated (exclude before initiating a corticosteroid in those at risk or with suggestive symptoms). Fungal or viral ocular infections may also be exacerbated.

CHICKENPOX

Unless they have had chickenpox, patients receiving oral or parenteral corticosteroids for purposes other than replacement should be regarded as being at risk of severe chickenpox. Manifestations of fulminant illness include pneumonia, hepatitis and disseminated intravascular coagulation; rash is not necessarily a prominent feature.

Passive immunization with varicella–zoster immunoglobulin [not included on WHO Model List] is needed for exposed non-immune patients receiving systemic corticosteroids or for those who have used them within the previous 3 months; varicella–zoster immunoglobulin should preferably be given within 3 days of exposure and no later than 10 days. Confirmed chickenpox warrants specialist care and urgent treatment. Corticosteroids should not be stopped and dosage may need to be increased.

Topical, inhaled or rectal corticosteroids are less likely to be associated with an increased risk of severe chickenpox.

MEASLES

Patients taking corticosteroids should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin [not included on WHO Model List] may be needed.

Dosage and administration

Adverse effects of systemic glucocorticoids, including suppression of

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the HPA (hypothalamo-pituitary-adrenal) axis, are dose- and duration-dependent; thus patients should be given treatment for the shortest period at the lowest dose that is clinically necessary. Patient response is variable and doses should therefore be individualized. In life-threatening diseases, high doses may be needed because the complications of therapy are likely to be less serious than the disease. In long-term therapy in relatively benign chronic conditions such as rheumatoid arthritis, adverse effects often outweigh the advantages. In order to minimize the adverse effects, the maintenance dose should be kept as low as possible and if possible, single morning doses or alternate day therapy should be used. Glucocorticoids can improve the prognosis of serious conditions such as systemic lupus erythematosus, temporal arteritis and polyarteritis nodosa; in such disorders the effects of the disease process may be suppressed and symptoms relieved but the underlying condition is not cured.

Glucocorticoids are used both topically and systemically. In emergency situations, hydrocortisone may be given intravenously; in the treatment of asthma, inhalation therapy with beclometasone may be used (section 7.1.2). Whenever possible, local treatment with creams, intra-articular injections, inhalations, eye-drops or enemas should be used in preference to systemic therapy.

Withdrawal of systemic corticosteroids

The rate of withdrawal of systemic glucocorticoids is dependent upon several factors including size of dose, duration of treatment, individual patient's response and the likelihood of relapse of the underlying disease. If there is uncertainty about suppression of the HPA axis, withdrawal should be gradual to enable the adrenal gland to recover. Patients should be advised not to stop taking glucocorticoids abruptly unless permitted by their doctor.

Gradual withdrawal should be considered in those whose disease is unlikely to relapse and who have:

- recently received repeated courses (particularly if taken for longer than 3 weeks)
- taken a short course within 1 year of stopping long-term therapy
- other possible causes of adrenal suppression
- received more than 40 mg daily prednisolone (or equivalent)
- been given repeat doses in the evening
- received more than 3 weeks' treatment

Abrupt withdrawal may be considered in those whose disease is unlikely to relapse and who have received treatment for 3 weeks or less *and* who are not included in the patient groups described above.

During corticosteroid withdrawal the dose may be reduced rapidly down to the physiological dosage (equivalent to 7.5 mg prednisolone daily) and then reduced more slowly. Assessment of the disease may be needed during withdrawal to ensure that relapse does not occur.

DEXAMETHASONE

Therapeutic category: Corticosteroid; Glucocorticoid.

Indications: Suppression of inflammatory and allergic disorders (see also allergy and allergic disorders, section 8.3); shock; diagnosis of Cushing syndrome; congenital adrenal hyperplasia; cerebral oedema.

Contra-indications: See notes above; systemic infection (unless life-threatening or specific antimicrobial therapy given); avoid live virus vaccines in those receiving immunosuppressive doses (serum antibody response diminished).

Precautions: Adrenal suppression during prolonged treatment which persists for years after stopping treatment (see notes above); ensure patients understand importance of compliance with dosage and have guidance on precautions to reduce risks; monitor weight, blood pressure, fluid and electrolyte balance and blood glucose levels throughout prolonged treatment; infections (greater susceptibility, symptoms may be masked until advanced stage; clinical presentation may be atypical; risk of chickenpox and measles increased (see notes above); quiescent tuberculosis—chemoprophylactic therapy during prolonged corticosteroid treatment; elderly; children and adolescents (growth retardation possibly irreversible); hypertension, recent myocardial infarction (rupture reported), congestive heart failure, liver failure, renal impairment, diabetes mellitus including family history, osteoporosis (may be manifested as back pain, postmenopausal women at special

RETURN

risk), glaucoma including family history, severe affective disorder (particularly if history of steroid-induced psychosis), epilepsy, psoriasis, peptic ulcer, hypothyroidism, history of steroid myopathy; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Gastrointestinal effects including dyspepsia, peptic ulceration (with perforation), abdominal distension, acute pancreatitis, oesophageal ulceration and candidosis; musculoskeletal effects including proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture; endocrine effects including adrenal suppression, menstrual irregularities and amenorrhoea, Cushing syndrome (with high doses, usually reversible on withdrawal), hirsutism, weight gain, negative nitrogen and calcium balance, increased appetite, increased susceptibility to and severity of infection; neuropsychiatric effects including euphoria, psychological dependence, depression, insomnia, increased intracranial pressure with papilloedema in children (usually after withdrawal), psychosis and aggravation of schizophrenia, aggravation of epilepsy; ophthalmic effects including glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning and exacerbation of ophthalmic viral or fungal disease; also impaired healing, skin atrophy, bruising, striae, telangiectasia, acne, myocardial rupture following recent myocardial infarction, fluid and electrolyte disturbances, leukocytosis, hypersensitivity reactions (including anaphylaxis), thromboembolism, nausea, malaise and hiccups; perineal irritation may follow intravenous administration of phosphate ester.

Advice to patients: See label 10 in Appendix 6. Take with food to minimize GI upset; do not use longer than prescribed; report signs of infection or injury during therapy; let the physician or dentist know that you are on steroid before any surgery.

Nursing considerations: •Give with meals or milk to reduce GI upset.

•Give I.M. injection deep into the gluteal muscle; rotate sites; use 21G needle. S.C. injection may cause atrophy and sterile abscess and should be avoided.

•Not for alternate day therapy; once daily doses should be given in the morning for better results and less toxicity.

•Provide assistance with ambulation for the patient with bone tissue disease to prevent fractures.

•Patient should avoid abrupt withdrawal of medication to prevent adrenal crisis.

•May mask or exacerbate infections.

•Insulin dosage may need to be adjusted in diabetics; monitor blood glucose.

•Teach patient to report early signs of adrenal insufficiency namely fatigue, muscular weakness, joint pain, fever, anorexia, nausea, dyspnoea, dizziness and fainting.

Dose: *Suppression of inflammatory and allergic disorders*, by mouth, ADULT usual range 0.5–10 mg daily; by intramuscular injection or slow intravenous injection or intravenous infusion (as dexamethasone phosphate), ADULT initially 0.5–20 mg daily; CHILD 200–500 micrograms/kg daily

Cerebral oedema, by intravenous injection (as dexamethasone phosphate), ADULT 10 mg initially, then 4 mg by intramuscular injection (as dexamethasone phosphate) every 6 hours, as required for 2–10 days

Diagnosis of Cushing syndrome, see manufacturer's literature.

NOTE: DEXAMETHASONE 1 MG ≡ DEXAMETHASONE PHOSPHATE 1.2 MG ≡ DEXAMETHASONE SODIUM PHOSPHATE 1.3 MG

POM **Dexamethasone** *(WMF 18.1)*

Tablets, Dexamethasone 500 micrograms, 4 mg [4-mg strength not included on WHO Model List].

Injection (Solution for injection), Dexamethasone phosphate (as dexamethasone sodium phosphate) 4 mg/ml, 1-ml ampoule.

POM **Dexamethasone** *(EDL 19.1)*

Tablets, Dexamethasone. 0.5 mg, 4 mg.

POM **DECADRON®** *(Bolax/BPP)*

Tablet, Dexamethasone 0.5 mg; white scored tab. marked 'MSD 41'.

0.5 mg - 20; 100.

Injection, Dexamethasone sodium phosphate 4 mg per ml (equiv. to 3.33 mg dexamethasone per ml); clear, colourless solution in 2 ml vial.

POM **MESLON®** *(Beta Drugs)*

Injection, Dexamethasone USP 4 mg per ml; in 1-ml ampoule.

Pack – 25's x 1-ml; 10's x 1-ml.

FLUDROCORTISONE

RETURN

Therapeutic category: Corticosteroid; Mineralocorticoid.

Pharmacology: Fludrocortisone is a synthetic corticosteroid with both mineralocorticoid and glucocorticoid actions. But at the doses usually used for the mineralocorticoid activitiy, the glucocorticoid actions are not sufficient to be of clinical use.

Indications: Mineralocorticoid replacement in adrenocortical insufficiency.

Contra-indications, Precautions, etc.: See under Dexamethasone.

Advice to patients: See label 10 in Appendix 6. Notify physician if dizziness, severe or continuing headache, swelling of feet or lower legs or unusual weight gain occur.

Nursing considerations: •Administer drug with food or milk to minimise GI upset.

•Provide assistance with ambulation for the patient with bone tissue disease to prevent fractures.

•Diet low in sodium and high in potassium may be recommended.

•Advise patient to avoid discontinuing drug abruptly and to report signs of infection.

Dose: By mouth, *Adrenocortical insufficiency,*
Adult, 50-300 mcg daily.
Child: 5 mcg/kg daily.

POM **Fludrocortisone** *(EDL 19.1)*
Tablets, Fludrocortisone acetate 0.1 mg, 1 mg.

HYDROCORTISONE

Therapeutic category: Corticosteroid; Mineralocorticoid; Anti-inflammatory Agent.

Indications: Adrenocortical insufficiency; hypersensitivity reactions including anaphylactic shock (section 8.3); inflammatory bowel disease (section 4.7); skin (section 15.2); asthma (section 7.1.2).

Contra-indications: See notes above; systemic infection (unless life-threatening or specific antimicrobial therapy given); avoid live virus vaccines in those receiving immunosuppressive doses (serum antibody response diminished).

Precautions: Adrenal suppression during prolonged treatment which persists for years after stopping treatment (see notes above); ensure patients understand importance of compliance with dosage and have guidance on precautions to reduce risks; monitor weight, blood pressure, fluid and electrolyte balance and blood glucose levels throughout prolonged treatment; infections (greater susceptibility, symptoms may be masked until advanced stage; clinical presentation may be atypical; risks of chickenpox and measles increased (see notes above); quiescent tuberculosis—chemoprophylactic therapy during prolonged corticosteroid treatment; elderly; children and adolescents (growth retardation possibly irreversible); hypertension, recent myocardial infarction (rupture reported), congestive heart failure, liver failure, renal impairment, diabetes mellitus including family history, osteoporosis (may be manifested as back pain, postmenopausal women at special risk), glaucoma including family history, severe affective disorder (particularly if history of steroid-induced psychosis), epilepsy, psoriasis, peptic ulcer, hypothyroidism, history of steroid myopathy; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Gastrointestinal effects including dyspepsia, peptic ulceration (with perforation), abdominal distension, acute pancreatitis, oesophageal ulceration and candidosis; musculoskeletal effects including proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture; endocrine effects including adrenal suppression, menstrual irregularities and amenorrhoea, Cushing syndrome (with high doses, usually reversible on withdrawal), hirsutism, weight gain, negative nitrogen and calcium balance, increased appetite, increased susceptibility to and severity of infection; neuropsychiatric effects including euphoria, psychological dependence, depression, insomnia, increased intracranial pressure with papilloedema in children (usually after withdrawal), psychosis and aggravation of schizophrenia, aggravation of epilepsy; ophthalmic effects including glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning and exacerbation of ophthalmic viral or fungal disease; also impaired healing, skin atrophy, bruising, striae, telangiectasia, acne, myocardial rupture following recent myocardial infarction, fluid and electrolyte disturbances, leukocytosis, hypersensitivity reactions (including anaphylaxis), thromboembolism, nausea, malaise and hiccups.

Advice to patients: See label 10 in Appendix 6. See also under Prednisolone.

Nursing considerations: •Oral dose may be given with meals or milk to reduce GI upset.

RETURN

•Give IM injection deep in large muscle mass; rotate sites; avoid deltoid; use 21 G needle; SC injection may damage tissue, and should be avoided.
•Give once daily doses in the morning for better results and to prevent adrenal suppression.
•Provide assistance with ambulation in patients who have bone tissue disease to prevent fractures.
•Teach patient to report early signs of adrenal insufficiency viz fatigue, muscular weakness, joint pain, fever, nausea, dyspnoea, dizziness and fainting.
•May mask or exacerbate infections.
•Note that diabetics may require increased insulin; monitor blood sugar.
•Diet low in sodium and high in potassium and protein may be recommended.
•Tell patient to avoid OTC medications viz salicylates, alcohol in cough mixtures, and cold remedies unless otherwise instructed by doctor.
•Inspect patient's skin for petechiae; warn him that he may bruise easily.
•Observe for depression or psychotic episodes, especially when treatment involves high-dose.

Dose: *Replacement therapy in adrenocortical insufficiency*, by mouth, ADULT 20–30 mg daily in divided doses (usually 20 mg in the morning and 10 mg in early evening); CHILD 10–30 mg.
Acute adrenocortical insufficiency, by slow intravenous injection or by intravenous infusion, ADULT 100–500 mg, 3–4 times in 24 hours or as required; by slow intravenous injection, CHILD up to 1 year 25 mg, 1–5 years 50 mg, 6–12 years 100 mg.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Hydrocortisone** *(WMF 18.1)*
Tablets, Hydrocortisone 10 mg [not included on WHO Model List].
Injection (Powder for solution for injection), Hydrocortisone (as sodium succinate) 100-mg vial.

POM **Hydrocortisone** *(EDL 19.1)*
Injection, Hydrocortisone (as sodium succinate) 100 mg; powder for reconstitution in vial.

POM **CORTICAP®** *(Korlyns)*
Injection, Hydrocortisone (as Sodium succinate) 100 mg; white powder for injection in a 10 ml, clear glass vial plus clear, colourless solvent in ampoule.
Pack - Bottles of 10 vials and 10 ampoules.
Note: For reconstitution, each ampoule (2 ml) contains sterile water for injections and benzyl alcohol. After reconstitution, use immediately, and discard any remainder.

POM **STRICORT®** *(Strides Vital)*
Injection, Hydrocortisone 100 mg; in vials.
Pack – 100's.

METHYLPREDNISOLONE

Therapeutic category: Corticosteroid; Glucocorticoid; Anti-inflammatory Agent.
Pharmacology: Methylprednisolone is a synthetic glucocorticoid with potent anti-inflammatory effects in disorders of many organ systems; it has little mineralocorticoid effect.
Indications: Suppression of inflammatory and allergic disorders; cerebral oedema; rheumatic and dermatologic diseases.
Contra-indications, Precautions, etc: See under Prednisolone.
Advice to patients: See label 10 in Appendix 6. See also under Prednisolone.
Nursing considerations: •Oral dose may be given with meals to reduce GI upset.
•Give IM injection deep in large muscle mass; rotate sites; avoid deltoid; use 21G needle; after shaking parenteral suspension; SC injection may damage tissue, and should be avoided.
•Give I.V. dose slowly over 1 minute. Acetate salt is not for I.V. use; it should not be used when fast onset of action is needed.
•Give once daily doses in the morning for better results and to prevent adrenal suppression.
•Teach patient to report early signs of adrenal insufficiency viz fatigue, muscular weakness, joint pain, fever, nausea, dyspnoea, dizziness and fainting.
•Monitor body weight, serum electrolytes, vital signs, and report abnormal weight gain or any chest pain to the doctor.
•Monitor intake and urinary output, noting especially decrease in output.
•May mask or exacerbate infections.
•Note that diabetics may require increased insulin; monitor blood sugar.
•Provide assistance with ambulation in patients who have bone tissue disease to prevent fractures.
•Monitor sleep pattern of the patient since euphoria may interfere with sleep initially. Reassure patient that he will adjust within 1-3 weeks.
•Diet low in sodium and high in potassuim and protein may be recommended.
•May be used for alternate-day therapy.
•Observe patient for depression or psychotic symptoms, especially when high doses are used.

Dose: *By IM injection or slow IV injection or infusion*, initially 10–500 mg; graft rejection, up to 1 g daily *by intravenous infusion* for up to 3 days.

POM **Methylprednisolone** *(EDL 19.1)*
Injection, Methylprednisolone acetate 40 mg per ml; aqueous suspension in 1 ml, 2 ml, 5 ml vials.

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POM **METHYSOL**® *(Korlyns)*

Injection (125 mg), Methylprednisolone (as Sodium succinate) 125 mg; white crystalline powder in a 10 ml glass vial

125 mg - 10 vials + 10 diluent Amps (2.0 ml).

Dose: *Acute allergic reactions, status asthmaticus, cerebral oedema,* Adult, initially 10-40 mg depending on the condition being treated; may be repeated 2-3 times in 24 hours.

Child: By IV injection (over a period of one to several minutes), not less than 0.5 mg per kg every 24 hours; to be reduced gradually once the patient's condition is under control. Dosage should depend more on the severity of the condition and response of the patient than on the age and size.

Injection (500 mg), Methylprednisolone (as Sodium succinate) 500 mg; white crystalline powder in a 20 ml glass vial

500 mg - 5 vials + 5 diluent Vials (7.8 ml).

Dose: *Suppression of graft injection reaction,* by IV injection, 0.5-2.0 g every 24-48 hours (30 mg/kg/day). Because of the risk of arrhythmias, it should be given by infusion in cases of myocardial damage.

PREDNISOLONE

Prednisolone is a representative corticosteroid. Various drugs can serve as alternatives.

Therapeutic category: Adrenal corticosteroid; Glucocorticoid; Anti-inflammatory Agent.

Indications: Suppression of inflammatory and allergic reactions (see also section 8.3); with antineoplastic drugs for acute leukaemias and lymphomas (section 12.2.2); eye (section 13.2); asthma (section 7.1.2)

Contra-indications: See notes above; systemic infection (unless life-threatening or specific antimicrobial therapy given); avoid live virus vaccines in those receiving immunosuppressive doses (serum antibody response diminished).

Precautions: Adrenal suppression during prolonged treatment which persists for years after stopping treatment (see notes above); ensure patients understand importance of compliance with dosage and have guidance on precautions to reduce risks; monitor weight, blood pressure, fluid and electrolyte balance and blood glucose levels throughout prolonged treatment; infections (greater susceptibility, symptoms may be masked until advanced stage; clinical presentation may be atypical; risk of chickenpox and measles increased (see notes above); quiescent tuberculosis—chemoprophylactic therapy during prolonged corticosteroid treatment; elderly; children and adolescents (growth retardation possibly irreversible); hypertension, recent myocardial infarction (rupture reported), congestive heart failure, renal impairment, hepatic impairment (Appendix 5); diabetes mellitus including family history, osteoporosis (may be manifested as back pain, postmenopausal women at special risk), glaucoma including family history, severe affective disorder (particularly if history of steroid-induced psychosis), epilepsy, psoriasis, peptic ulcer, hypothyroidism, history of steroid myopathy; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Gastrointestinal effects including dyspepsia, peptic ulceration (with perforation), abdominal distension, acute pancreatitis, oesophageal ulceration and candidosis; musculoskeletal effects including proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture; endocrine effects including adrenal suppression, menstrual irregularities and amenorrhoea, Cushing syndrome (with high doses, usually reversible on withdrawal), hirsutism, weight gain, negative nitrogen and calcium balance, increased appetite, increased susceptibility to and severity of infection; neuropsychiatric effects including euphoria, psychological dependence, depression, insomnia, increased intracranial pressure with papilloedema in children (usually after withdrawal), psychosis and aggravation of schizophrenia, aggravation of epilepsy; ophthalmic effects including glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning and exacerbation of ophthalmic viral or fungal disease; also impaired healing, skin atrophy, bruising, striae, telangiectasia, acne, myocardial rupture following recent myocardial infarction, fluid and electrolyte disturbances, leukocytosis, hypersensitivity reactions (including anaphylaxis), thromboembolism, nausea, malaise and hiccups.

Advice to patients: See label 10 in Appendix 6. Notify surgeon or dentist before surgical repairs; may cause GI upset; take oral

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formulation with food or milk to decrease GI effects.

Nursing considerations: •Oral dose may be given with meals to minimize GI upset.
•Tell patient not to discontinue drug abruptly or without doctor's consent.
•This drug may mask or exacerbate infections, instruct patient to report slow healing of wound.
•Teach patient the early signs of adrenal insufficiency which may include fatigue, muscular weakness, joint pain, fever, anorexia, nausea, dizziness and fainting.
•Watch for depression or psychotic episodes; diabetic patient may require increased insulin, ensure blood glucose is monitored.
•Don't confuse with prednisone.
•May be used for alternate-day therapy
•Diet low in sodium and high in potassium and protein may be recommended.

Dose: *Suppression of inflammatory and allergic disorders*, by mouth, ADULT initially up to 10–20 mg daily (severe disease, up to 60 mg daily), preferably taken in the morning after breakfast; dose can often be reduced within a few days, but may need to be continued for several weeks or months; CHILD fractions of adult dose may be used (for example, at 1 year 25% of adult dose, at 7 years 50%, and at 12 years 75%) but clinical factors must be given due weight.
Maintenance, by mouth, ADULT 2.5–15 mg daily or higher; cushingoid features are increasingly likely with doses above 7.5 mg daily; CHILD fractions of adult dose may be used (for example, at 1 year 25% of adult dose, at 7 years 50%, and at 12 years 75%) but clinical factors must be given due weight.
Myasthenia gravis, initially 10 mg on alternate days, increased in steps of 10 mg on alternate days to 1–1.5 mg/kg (maximum 100 mg) on alternate days or initially 5 mg daily increased in steps of 5 mg daily to usual dose of 60–80 mg daily (0.75–1 mg/kg daily).

Note: **Alternate-Day Therapy (ADT)** should be considered for long-term therapy; ADT is a corticosteroid dosing regimen in which twice the usual daily dose of corticoid is administered every other morning. The purpose of this mode of therapy is to provide the patient requiring long-term, pharmacologic-dose treatment with the beneficial effects of corticoids while minimising certain undesirable effects, including pituitary-adrenal suppression, the cushingoid state, corticoid withdrawal symptoms, and growth suppression in children. The rationale for this treatment schedule is based on two major premises: (a) the anti-inflammatory or therapeutic effect of corticoids persists longer than their physical presence and metabolic effects, and (b) administration of corticosteroid every other morning allows for reestablishment of more nearly normal hypothalamic-pituitary-adrenal (HPA) activity on the off-steroid day.

POM **Prednisolone** *(WMF 18.1)*
Tablets, Prednisolone 5 mg, 25 mg.

POM **Prednisolone** *(EDL 19.1)*
Tablets, Prednisolone 1 mg, 5 mg.

POM **DELTACORTRIL®** *(Neimeth)*
Tablet, Prednisolone 5 mg.
5 mg - 100; 1000.

POM **PERILON®** *(Hovid)*
Tablet, Prednisolone 5 mg.
5 mg - 10 x 10 (blister)

POM **PRECORTISYL®** *(NGC)*
Tablets, Prednisolone 5 mg; white scored tab.
5 mg - 500; 1000.

POM **PREDNISAM®** *(Sam)*
Tablet, Prednisolone 5 mg.
5 mg - 100; 1000.

PREDNISONE

Therapeutic category: Corticosteroid; Glucocorticoid; Anti-inflammatory Agent.
Pharmacology: Prednisone is inactive and must be metabolised to prednisolone which may be impaired in patients with impaired liver function. See under prednisolone.
Indications: Adrenocortical insufficiency, hypercalcaemia, rheumatic and collagen disorders; dermatologic, ocular, respiratory, GI, and neoplastic diseases; organ transplantation and a variety of diseases including those of haematologic, allergic, inflammatory, and autoimmune in origin.
Contra-indications: Serious infections, except septic shock or tuberculous meningitis; systemic fungal infections, hypersensitivity to prednisone or any component; varicella.
Precautions: See under Prednisolone.
Interactions: See under Prednisolone
Adverse effects: See under Prednisolone
Advice to patients: See under Prednisolone
Nursing considerations: *See under Prednisolone*.

RETURN

Dose: By mouth, initially 5-60 mg/day depending on the nature and severity of the disease, and patient's response. See also under prednisolone.

POM **APO-PREDNISONE**® *(Lahams)*
Tablet, Prednisone 5mg; white scored tab marked 'APO 5'.
5 mg - 1000.

10.4 Sex Hormones

10.4.1 Estrogens (Female sex hormones)
10.4.2 Progestogens (Female sex hormones)
10.4.3 Androgens (Male sex hormones)

10.4.1 Estrogens (Female sex hormones)

Estrogens are necessary for the development of female secondary sexual characteristics; they also stimulate myometrial hypertrophy with endometrial hyperplasia. They affect bone by increasing calcium deposition. They are secreted at varying rates during the menstrual cycle throughout the period of activity of the ovaries. During pregnancy, the placenta becomes the main source of estrogens. At the menopause, ovarian secretion declines at varying rates.

Estrogen therapy is given cyclically or continuously principally for contraception and for the alleviation of menopausal symptoms. If long-term therapy is required for menopausal hormone therapy a progestogen should be added to prevent cystic hyperplasia of the endometrium (or of endometrial foci in women who have had a hysterectomy) and possible transformation to cancer.

The palliative care of advanced inoperable, metastatic carcinoma of the breast in both men and postmenopausal women is another indication for estrogen therapy.

HORMONE REPLACEMENT THERAPY (HRT)

Estrogens are used for replacement therapy in perimenopausal and menopausal women for the treatment of vasomotor instability, vulvar and vaginal atrophy associated with the menopause and for the prevention of osteoporosis. HRT should **not** be prescribed with the aim of reducing the incidence of heart disease. Hormone replacement therapy may be used for menopausal women whose lives are unduly inconvenienced by vaginal atrophy or vasomotor instability. Vaginal atrophy may respond to a short course of a vaginal estrogen preparation. Systemic treatment is needed for vasomotor and other symptoms of estrogen deficiency and can be given for up to 2–3 years; in women with a uterus (or endometrial foci), a progestogen should be added to reduce the risk of endometrial cancer. Medroxyprogesterone acetate (see also section 18.5) may be given in a dose of 10 mg daily for the last 12–14 days of each estrogen HRT cycle. Alternatively, norethisterone 1 mg daily may be given on the last 12–14 days of each 28-day estrogen cycle.

HRT should be considered for women with early natural or surgical menopause (before age 45 years) because they have a high risk of osteoporosis. Small doses of estrogen given systemically in the perimenopausal and postmenopausal period also diminish osteoporosis, but the slight increased risk of breast cancer needs to be taken into account. For early menopause, HRT can be given until the approximate age of natural menopause (until age 50 years).

For longer-term use of HRT in postmenopausal women (with a uterus or without a uterus), women must be made aware of the increased incidence of breast cancer and other adverse effects. Each decision to start HRT should be made on an individual basis, and treatment should be regularly reappraised (at least once a year). Factors such as corticosteroid therapy, family history of osteoporosis, thinness, lack of exercise, alcoholism or smoking, early menopause, fractures to the hip or forearm before age 65 years should be taken into account when considering the use of HRT; women of African origin appear to be less susceptible to osteoporosis than those who are white or of Asian origin.

There is an increased risk of deep-vein thrombosis and of pulmonary embolism in women taking HRT. In women who have predisposing factors such as a personal or family history of deep venous thrombosis or pulmonary embolism, severe varicose veins, obesity, surgery, trauma or prolonged bed-rest, the overall risk may outweigh the benefit.

Using HRT increases the risk of breast

cancer slightly. The increased risk is related to the duration of HRT use and this excess risk disappears within about 5 years of stopping. The risk of breast cancer is greater with combined HRT (an estrogen and a progestogen) than with estrogen-only HRT (but estrogen alone may not be suitable for women with intact uterus, see above).

Epidemological studies indicate that in women aged between 50 and 65 years not using HRT , about 32 cases of breast cancer will be diagnosed in every 1000 women. In those using HRT, the risk of breast cancer is increased as follows:

- Women using combined HRT with an estrogen and a progestogen for 5 years, about 6 additional cases in 1000; in those using combined HRT for 10 years, about 19 additional cases in 1000
- Women using estrogen-only HRT for 5 years, about 2 additional cases in 1000; in those using estrogen-only HRT for 10 years, about 5 additional cases in 1000.

HRT does not provide contraception. If a potentially fertile woman needs to use HRT, non-hormonal contraceptive measures are necessary.

Precautions for patients on HRT undergoing surgery and reasons to stop HRT are the same as those for hormonal contraceptives (see notes in section 11.3.1).

ETHINYLESTRADIOL

Ethinylestradiol is a representative estrogen. Various drugs can serve as alternatives.

Indications: Hormone replacement for menopausal symptoms; osteoporosis prophylaxis; palliation in breast cancer in men and postmenopausal women; contraception in combination with a progestogen (section 11.3.1).

Contra-indications: Pregnancy; estrogen-dependent cancer; active thrombophlebitis or thromboembolic disorders or history of recent venous thromboembolism (unless already on anticoagulant therapy); undiagnosed vaginal bleeding; breastfeeding (Appendix 3); liver disease (where liver function tests have failed to return to normal), Dubin-Johnson and Rotor syndromes (or monitor closely).

Precautions: Progestogen may need to be added to regimen to reduce risk of endometrial cancer due to unopposed estrogen (see notes above); migraine (or migraine-like headache); history of breast nodules of fibrocystic disease—closely monitor breast status (risk of breast cancer, see notes above); uterine fibroids may increase in size; symptoms of endometriosis may be exacerbated; predisposition to thromboembolism (see notes above); presence of antiphospholipid antibodies; increased risk of gallbladder disease; hypophyseal tumours; porphyria; **interactions**: Appendix 1.

Adverse effects: Nausea and vomiting, abdominal cramps and bloating, weight increase; breast enlargement and tenderness; premenstrual-like syndrome; sodium and fluid retention; thromboembolism (see notes above); altered blood lipids; cholestatic jaundice; rashes and chloasma; changes in libido; depression, headache, migraine, dizziness, leg cramps (rule out venous thrombosis); contact lenses may irritate.

Advice to patients: Photosensitivity may occur. Women should inform their physicians if signs or symptoms of any of the following occur: Thromboembolic or thrombotic disorders including sudden severe headache or vomiting, disturbance of vision or speech, loss of vision, numbness or weakness in an extremity, sharp or crushing chest pain, calf pain, shortness of breath, severe abdominal pain or mass, mental depression or unusual bleeding. Women should discontinue taking the medication if they suspect they are pregnant or become pregnant.

Nursing considerations: •Give at bedtime to minimise occurrence of adverse effects; teach patient self-examination of the breasts.

•Explain to patient on cyclic therapy for postmenopausal symptoms that, although withdrawal bleeding may occur during week off drug, fertility has not been restored. Pregnancy cannot occur since she has not ovulated.

Dose: *Hormone replacement*, by mouth, ADULT (female) 10–20 micrograms daily.
Palliation in breast cancer in postmenopausal women, by mouth, ADULT 0.1–1 mg 3 times daily.

POM **Ethinylestradiol** *(WMF 18.4)*
Tablets, Ethinylestradiol 10 micrograms, 50 micrograms.

POM **Ethinylestradiol** *(EDL 19.3)*
Tablets, Ethinylestradiol 0.01 mg, 0.05 mg.

ESTRADIOL

Indications: Intramuscular estrogen indicated in primary and secondary amenorrhoea, deficiency symptoms in young women after oophorectomy or radiological castration for non-carcinomatosis disease, gynaeoclogical operations, dysfunctional bleeding..

Contra-indications: Pregnancy; existing or suspected hormone dependent tumours of the uterus or mammae; previous or existing liver tumours; endometriosis; thromboembolic processes.

Precautions: Regular general medical and gynaecological examination before starting treatment and at 6-monthly intervals.; exclude pregnancy. Risk of thromboembolic diseases appears to increase especially in patients with history of thromboembolic diseases or in the presence of severe diabetes with vascular changes or sickle-cell anaemia. Rarely, malignant liver tumours leading to threatening intraabdominal haemorrhage may occur; patient should report any unusual upper abdominal complaints. Monitor patient with diabetes (need for oral antidiabetics or insulin can change).

Adverse effects: Rarely, feeling of tension in the breasts; liver tumours.

Dose: By slow I.M. injection only, *Primary and secondary amenorrhoea*, initially 20 mg on 1st day; 10 mg on 14th day with 5 mg Oral Norethisterone 2-3 times daily from the 19th to the 26th day of treatment (withdrawal bleeding starts about 28th day). In place of Norethisterone, 250 mg I.M. Hydroxyprogesterone may be given on the 14th day.

Continuation of therapy (over minimum 2-3 cycles), 10 mg on the 6th and 16th day of the artificial cycle; then, by mouth, 5 mg Norethisterone 2 times daily from the 19th to the 26th day of the cycle. In place of Norethisterone, 250 mg I.M. Hydroxyprogesterone may be given on the 16th day together with the 10 mg Estradiol.

Note: Give injection very slowly to avoid transient urge to cough, coughing fits, respiratory distress that may occur during or immediately after the injection of oily solutions

POM **PRIMOGYN DEPOT®** *(CHI/Schering)*
Injection (Depot), Estradiol valerate 10 mg per ml; oily injection.
Pack - 1 x 1 ml amp.

ESTROGENS, CONJUGATED

Oral Hormonal Replacement Therapy (HRT)

Indications: Menopausal and postmenopausal estrogen replacement therapy for vasomotor symptoms and allied disorders such as oesteoporosis, atrophic vaginitis, kraurosis vulvae, and postmenopausal atrophic urethritis.

Contra-indications: Cancer of the breast and other estrogen-dependent neoplasia; undiagnosed abnormal genital bleeding; thrombophlebitis, thrombosis or thromboembolic disorders; acute or chronic liver disease; severe cardiac or renal disease; pregnancy (for estrogen-progestogen combination only).

Precautions: Not recommended for use as oral contraceptive. The estrogen-progestogen preparation is unsuitable for use with oral contraceptive and is not necessary for women who have had a hysterectomy (for whom oestrogen alone is recommended). The estrogen-only preparation is unsuitable for long-term use alone in women with an intact uterus (for whom estrogen-progestogen combination is recommended).

Adverse effects: Nausea, vomiting, anorexia, bloating, breast enlargement and tenderness, peripheral oedema, headache, increased libido, migraine, dizziness, cholestatic jaundice, rash, depression.

Advice to patients: See under Ethinylestradiol

Nursing considerations: •*See under Ethinyloestradiol*.

Dose: See under preparations below.

Conjungated Estrogen-only

POM **PREMARIN®** *(Wyeth/Delpitano)*
Tablets, Conjugated estrogen 0.625 mg (maroon), 1.25 mg (yellow), 2.4 mg (purple); all 's-c' tabs.

Dose: *Menopausal symptoms*, 0.625-1.25 mg daily for 21 days from 5th day of cycle; repeated after 7 days if necessary.

In women with intact uterus, the addition of a progestogen for 10-12 days per cycle is essential.

Conjugated Estrogen + Norgestrel (Progestogen)

POM **PREMPAK-C®** *(Wyeth/Delpitano)*
Tablets, (0.625 calendar pack), Conjugated estrogens 0.625 mg (28 maroon tabs), norgestrel 150 mcg (12 light brown tabs); all s-c tabs.

Dose: *Menopausal symptoms (including oesteoporosis prophylaxis)*, if uterus intact, 1 maroon tab daily continously, and 1 brown tab. daily on days 17-28 of each 28-day estrogen treatment cycle.

Treatment should start on 1st day of menstruation or at any time if cycles have ceased or are infrequent. Subsequent courses are repeated without interval.

Tablets (1.25 calendar pack), Conjugated estrogens 1.25 mg (28 yellow tabs), norgestrel 100 mg (12 light brown tabs); all s-c tabs.

Dose: As above but taking 1 yellow tab daily continously instead of 1 maroon tab. To be used only when symptoms are not fully controlled with the 0.625 mg tablets.

DIETHYLSTILBESTROL

Synonym: Stilboestrol; DES

Therapeutic category: Estrogen

Pharmacology: Diethylstilbestrol is a synthetic estrogen which is not a steroid but has actions and uses similar to estradiol like the ethinylestradiol. It is used mainly in neoplastic conditions.

Indications: Menopausal symptoms; secondary amenorrhoea due to ovarian insufficiency; breast cancer, prostatic cancer.

Contra-indications, Precautions, etc: See Ethinylestradiol.

Advice to patients: See under Ethinylestradiol

Dose: See Diethylstilbestrol in section 12.3

POM **Diethylstilbestrol** *(EDL 19.3)*

Tablets, Diethylstilbestrol 0.5 mg, 1 mg, 5 mg, 25 mg

10.4.2 Progestogens (Female sex hormones)

Progesterone is a hormone secreted by the corpus luteum whose actions include induction of secretory changes in the endometrium, relaxation of uterine smooth muscle and production of changes in the vaginal epithelium. Progesterone is relatively inactive following oral administration and produces local reactions at site of injection. This has led to the development of synthetic progestogens including **levonorgestrel**, **norethisterone** and **medroxyprogesterone**. Where endometriosis requires drug treatment, it may respond to synthetic progestogens on a continuous basis. They may also be used for the treatment of severe dysmenorrhoea. In postmenopausal women receiving long-term estrogen therapy for hormone replacement, a progestogen needs to be added for women with an intact uterus to prevent hyperplasia of the endometrium (section 10.4.1).

Progestogens are also used in combined oral contraceptives and progestogen-only contraceptives (section 11.3.1).

ALLYLOESTRENOL

Therapeutic category: Progestogen

Indications: Threatened or habitual abortion; threatened premature labour.

Contra-indications: History of thrombo-embolic disorders, mammary or genital carcinoma; liver dysfunction; undiagnosed vaginal bleeding.

Precautions: Diabetes, epilepsy, migraine.

Adverse effects: Occasional GI complaints.

Dose: By mouth, *threatened abortion*, 1-3 tabs daily for 5-7 days.
Habitual abortion: 1-2 tabs daily as soon as pregnancy is diagnosed.
See lit for details.

POM **Allyloestrenol** *(EDL 19.4)*

Tablets, Allyloestrenol 5 mg.

DYDROGESTERONE

Indications: Dydrogesterone is indicated in cases where there is established or suspected deficiency in endogenous progesterone such as in infertility; threatened abortion; habitual abortion; dysmenorrhoea; endometriosis; irregular cycles; in combination with oestrogens, it can be used in secondary amenorrhoea, functional bleeding.

Contra-indications: Pregnancy, undiagnosed vaginal bleeding, hepatic impairment or active liver disease, severe arterial disease, breast or genital tract carcinoma; porphyria.

Precautions: Diabetes, hypertension, cardiac or renal disease.

Adverse effects: Acne, urticaria, fluid retention, weight changes, GI disturbances, changes in libido, breast discomfort, premenstrual symptoms, irregular menstrual cycles; also depression, insomnia, somnolence, alopecia, hirsutism, anaphylactoid-like reaction; rarely jaundice.

Dose: *Endometriosis*, 10 mg 2-3 times daily from 5th to 25th day of cycle or continuously.
Infertility, irregular cycles, 10 mg twice daily from 11th to 25th day for at least 6 cycles.
Habitual abortion, 10 mg twice daily from day 11 to day 25 of cycle until conception, then continuously until 20th week of pregnancy and gradually reduced.

RETURN

Dysfunctional uterine bleeding, 10 mg twice daily (together with an estrogen) for 5-7 days to arrest bleeding; 10 mg twice daily (together with an oestrogen) from 11th to 25th day of cycle to prevent bleeding.
Severe dysmenorrhoea, 10 mg twice daily from 5th to 25th day of cycle. Combined oral contraceptive is best in younger women where contraception is also required.
Amenorrhoea, 10 mg twice daily from 11th to 25th day of cycle with estrgen therapy from 1st to 25th day of cycle. See lit. for more details.

POM **DUPHASTON®** *(NGC)*
Tablet, Dydrogesterone 10 mg.

HYDROXYPROGESTERONE

Therapeutic category: Parenteral progestogen.
Indications: Habitual and threatened abortion, infertility due to corpus-luteum insufficiency, primary and secondary amenorrhoea, uterine hypoplasia.
Contra-indications: A history of herpes of pregnancy, history of or existing liver tumours.
Precautions: General medical and gynaecological examination (including the breasts) to exclude herpes of pregnancy, liver tumours, diabetic women.
Interactions: •Insulin and antidiabetic requirements may change.
Advice to patients: Take this medicine only as directed; do not exceed recommended dosage nor take it for a longer period of time; if you suspect you may have become pregnant, stop taking this medicine; take with food; notify physician of pain in the calves along with swelling and warmth, severe headache, visual disturbance.
Nursing considerations: •Administer oily solution deep into the gluteal muscle; rotate the sites.
•Advise patient never to use drug to induce withdrawal bleeding or test for pregnancy, because drug may cause defects in the newborn or masculinisation of the female foetus.
•Instruct patient to report breast pain or tenderness, vaginal discharge or bleeding, swelling of hand or feet, visual disturbances or migraine.
•Teach patient self-examination of the breasts.
•Inform patient that normal menstruation may not resume for 2-3 months after drug therapy.
Dose: By I.M. injection, *Habitual abortion*, as soon as pregnancy is diagnosed 250-500 mg at weekly intervals during the initial months or as needed.
Threatened abortion, initially 500 mg 2-3 times weekly until the bleeding ceases; then 250 mg twice weekly until patient remains free from complaints.
Infertility due to corpus luteum insufficiency, 250 mg about 3 days after the rise in basal body temperature; then, 5-10 mg I.M. Estradiol may be added due to a likely coexisting oestrogen deficiency.
Primary and secondary amenorrhoea, See under Estradiol in Section 10.4.1.

POM **Hydroxyprogesterone** *(EDL 19.4)*
Injection, Hydroxyprogesterone hexanoate 250mg per ml; in 1ml, 2ml amps.

POM **PRIMOLUT DEPOT®** *(CHI/Schering)*
Injection (Depot), Hydroxyprogesterone hexanoate 250 mg per ml.
Pack - 250 mg/ml amp.

MEDROXYPROGESTERONE

Medroxyprogesterone acetate is a complementary progestogenic drug.
Indications: Endometriosis; dysfunctional uterine bleeding; secondary amenorrhoea; contraception (section 11.3.1); adjunct in HRT (section 10.4.1).
Contra-indications: Pregnancy (Appendix 2); hormone-dependent breast or genital neoplasms; undiagnosed vaginal bleeding; hepatic impairment or active liver disease (Appendix 5); severe arterial disease; porphyria.
Precautions: Small increase in possible risk of breast cancer; migraine; depression; thromboembolic or coronary vascular disease; diabetes mellitus; trophoblastic disease; hypertension; renal disease; breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Acne, urticaria, fluid retention, weight gain, gastrointestinal disturbances, changes in libido, breast discomfort, premenstrual symptoms, irregular menstrual cycles; depression, insomnia, somnolence, headache, alopecia, hirsutism; anaphylactoid reactions; rarely jaundice.
Dose: *Mild to moderate endometriosis*, by mouth, adult 10 mg 3 times daily for 90 consecutive days, beginning on day 1 of cycle.
Dysfunctional uterine bleeding, by mouth, adult 2.5–10 mg daily for 5 to 10 days beginning on day 16 to 21 of cycle for 2 cycles.

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Secondary amenorrhoea, by mouth, adult 2.5–10 mg daily for 5–10 days beginning on day 16 to 21 of cycle for 3 cycles.

POM **Medroxyprogesterone** *(WMF 18.5)*
Tablets, Medroxyprogesterone acetate 5 mg.

NORETHISTERONE

Therapeutic category: Oral progestogen
Indications: Endometriosis; menorrhagia; severe dysmenorrhoea; contraception (section 11.3.1); HRT (section 10.4.1).
Contra-indications: Pregnancy (Appendix 2); undiagnosed vaginal bleeding; hepatic impairment or active liver disease (Appendix 5); severe arterial disease; breast or genital tract cancer; porphyria; history in pregnancy of idiopathic jaundice, severe pruritus or pemphigoid gestationis.
Precautions: Epilepsy; migraine; diabetes mellitus; hypertension; cardiac or renal disease and those susceptible to thromboembolism; depression; breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Acne, urticaria, fluid retention, weight increase, gastrointestinal disturbances, changes in libido, breast discomfort, premenstrual symptoms, irregular menstrual cycles, depression, insomnia, somnolence, headache, dizziness, alopecia, hirsutism, anaphylactoid-like reactions; exacerbation of epilepsy and migraine; rarely jaundice.
Dose: *Endometriosis*, by mouth, ADULT (female) 10 mg daily starting on fifth day of cycle (increased if spotting occurs to 20–25 mg daily, reduced once bleeding has stopped).
Menorrhagia, by mouth, ADULT (female) 5 mg three times daily for 10 days to stop bleeding; to prevent bleeding 5 mg twice daily from day 19 to 26 of cycle.
Dysmenorrhoea, by mouth, ADULT (female) 5 mg 2–3 times daily from day 5 to 24 for 3 to 4 cycles.

POM **Norethisterone** *(WMF 18.5)*
Tablets, Norethisterone 5 mg.

POM **Norethisterone** *(EDL 19.4)*
Tablet, Norethisterone 5 mg,
Injection, Norethisterone 200mg per ml.

POM **NORELUT®** *(Hovid)*
Tablet, Norethisterone 5 mg.
5 mg - 500; 1000.

POM **NORISTERAT®** *(SFH)*
Injection, Norethisterone enanthate 200 mg; oily solution in 1 ml amp.

POM **PRIMOLUT N®** *(CHI/Schering)*
Tablet, Norethisterone 5 mg, white tab. marked 'AN' in a hexagon.
5 mg - 30.

10.4.3 Androgens (Male sex hormones)

Androgens are secreted by the testes and weaker androgens by the adrenal cortex and ovaries. In the male, they are responsible for the development and maintenance of the sex organs and the secondary sexual characteristics, normal reproductive function, and sexual performance ability in addition to stimulating the growth and development of the skeleton and skeletal muscle during puberty. At high doses in the normal male androgens inhibit pituitary gonadotrophin secretion and depress spermatogenesis.
Testosterone is used as replacement therapy in those who are hypogonadal due to either pituitary (secondary hypogonadism) or testicular disease (primary hypogonadism). Androgens are useless as a treatment of impotence and impaired spermatogenesis unless there is associated hypogonadism; they should not be given until the hypogonadism has been properly investigated and treatment should always be under expert supervision. When given to patients with hypopituitarism they can lead to normal sexual development and potency but not fertility. If fertility is desired, the usual treatment is with gonadotrophins or pulsatile gonadotrophin-releasing hormone which will stimulate spermatogenesis as well as androgen production. Androgens cannot induce fertility in men with primary hypogonadism. Caution should be used in treating boys with delayed puberty with excessive doses of testosterone since the fusion of epiphyses is hastened and may result in short stature. Androgens, including testosterone have also been used in postmenopausal women for the palliative treatment of androgen-responsive, advanced, metastatic breast cancer; care is required to prevent masculinizing effects.

TESTOSTERONE

Testosterone enantate is a complementary androgenic drug.

Indications: Hypogonadism; palliative treatment of advanced breast cancer in women.

Contra-indications: Breast cancer in men, prostate cancer, hypercalcaemia, pregnancy (Appendix 2), breastfeeding (Appendix 3), nephrosis, history of primary liver tumours.

Precautions: Cardiac, renal or hepatic impairment (Appendix 5), elderly, ischaemic heart disease, hypertension, epilepsy, migraine, diabetes mellitus, skeletal metastases (risk of hypercalcaemia); regular examination of prostate during treatment; prepubertal boys; **interactions**: Appendix 1.

Adverse effects: Prostate abnormalities and prostate cancer, headache, depression, gastrointestinal bleeding, nausea, polycythaemia, cholestatic jaundice, changes in libido, gynaecomastia, anxiety, asthenia, generalized paraesthesia, electrolyte disturbances including sodium retention with oedema and hypercalcaemia; increased bone growth; androgenic effects such as hirsutism, male-pattern baldness, seborrhoea, acne, priapism, precocious sexual development and premature closure of epiphyses in pre-pubertal males, virilism in females, and suppression of spermatogenesis in men.

Advice to patients: See Labels 21 and 25 in Appendix 6. Virilization may occur in female patients; report menstrual irregularities; male patient should report persistent penile erections; all patients should report persistent GI distress, diarrhoea, or jaundice.

Nursing considerations: •Store I.M. preparation at room temperature; warming injection to room temperature and shaking vial will help redissolve crystals that may have formed after storage.

•Administer by deep I.M. injection into the upper outer quadrant of the gluteus maximus; report soreness at injection site.

•Monitor for signs of hypoglycaemia; advise patient to report such signs immediately they occur.

•Provide diet with increased calories and protein; reduce sodium if oedema occurs.

•For therapeutic response in breast cancer, 1 to 3 months course is necessary; report if the disease progresses.

•Periodic liver function tests should be performed.

Dose: *Hypogonadism*, by slow intramuscular injection; ADULT (males), initially 200–250 mg every 2–3 weeks; maintenance 200–250 mg every 3–6 weeks.

Breast cancer, by slow intramuscular injection, ADULT (females) 250 mg every 2–3 weeks.

POM **Testosterone** *(WMF 18.2)*

Oily injection (Solution for injection), Testosterone enantate 200 mg/ml, 1-ml ampoule; 250 mg/ml, 1-ml ampoule [250 mg/ml not included on WHO Model List].

POM **Testosterone** *(EDL 19.2)*

Capsule, Testosterone (as undecanoate) 40 mg

Injection, Testosterone 25 mg (as propionate), 200 mg (as enanthate) per ml; oily in 1 ml amp.

Injection (250), Testosterone propionate 30 mg, testosterone phenylpropionate 60 mg, testosterone caproate 60 mg, testosterone decanoate 100 mg.

POM **PRIMOTESTON®** *(CHI/Schering)*

Injection, Testosterone propionate 25 mg per ml; oily in 1ml amp.

Dose: By I.M. injection, *Androgen deficiency*, 50 mg 2-3 times weekly.

Delayed puberty, 50 mg weekly.

Breast cancer, 100 mg 2-3 times weekly.

POM **PRIMOTESTON DEPOT®** *(CHI/Schering)*

Injection (Depot), Testosterone enanthate 250 mg per ml.

Pack - 250 mg/ml amp.

Dose: By slow I.M. injection, *Male hypogonadism*, initially 250 mg every 2-3 weeks; maintenance, 250 mg every 3-6 weeks.

Potency disorders, initially 100 mg, followed by another 100 mg after 1 week; then 100 mg every 2-4 weeks.

Male climacteric, 100 mg every 2-3 weeks.

Aplastic anaemia, 250 mg every 2-3 weeks.

MESTEROLONE

Therapeutic category: Oral Androgen.

Indications: Orally active androgen indicated in hypogonadism, infertility, potency disturbance, reduced efficiency in middle and advanced age.

Contra-indications, Precautions: See under Testosterone.

Adverse effects: Rarely benign and malignant liver tumours. Frequent or persistent erections

RETURN

may occur (reduce dose or discontinue).

Dose: By mouth, Adult, *Androgen deficiency and male infertility associated with hypogonadism*, 25 mg 3-4 times daily for several months.
Maintenance: 50-75 mg daily in divided doses
Potency disturbances and diminishing efficiency, initially 25 mg 3 times daily; may be reduced according to patient's need. Maintenance: 25 mg 1-2 times daily for several months.
Not recommended for children.

POM **PROVIRON**® *(CHI/Schering)*
Tablet, Mesterolone 25 mg.
25 mg - 20.

10.5 Drugs acting on pituitary ovarian axis

10.5.1 Anti-estrogens (Ovulation inducers)
10.5.2 Anterior pituitary hormones (Gonadotrophins)
10.5.3 Posterior pituitary hormones

10.5.1 Anti-estrogens (Ovulation inducers)

The anti-estrogen, **clomifene** is used in the treatment of female infertility due to disturbances in ovulation. It induces gonadotrophin release by occupying estrogen receptors in the hypothalamus, thereby interfering with feedback mechanisms. Patients should be carefully counselled and should be fully aware of the potential adverse effects, including a risk of multiple pregnancy (rarely more than twins), of this treatment. Most patients who are going to respond will do so to the first course; 3 courses should be adequate; long-term cyclical therapy (more than 6 cycles) is not recommended as it may increase risk of ovarian cancer.

CLOMIFENE

Clomifene citrate is a complementary drug for fertility treatment.

Synonym: Clomiphene
Therapeutic category: Ovulation stimulator
Indications: Anovulatory infertility.
Contra-indications: Hepatic disease; ovarian cysts; hormone dependent tumours or uterine bleeding of undetermined cause; pregnancy (exclude before treatment, Appendix 2).
Precautions: Visual disturbances (discontinue and initiate eye examination) and ovarian hyperstimulation syndrome (discontinue treatment immediately); polycystic ovary syndrome (cysts may enlarge during treatment); uterine fibroids, ectopic pregnancy, incidence of multiple births increased (consider ultrasound monitoring); breastfeeding (Appendix 3).
Adverse effects: Visual disturbances, ovarian hyperstimulation, hot flushes, abdominal discomfort, occasional nausea and vomiting, depression, insomnia, breast tenderness, headache, intermenstrual spotting, menorrhagia, endometriosis, convulsions, weight gain, rashes, dizziness and hair loss.
Advice to patients: May cause visual disturbances, dizziness, lightheadedness; if possibility of pregnancy, stop the drug and consult your physician.
Nursing considerations: •Ovulation is assessed by basal body temperature or serum progesterone 2 weeks after last clomifene dose; teach patient how ovulation can be determined (there is a slight decrease in temperature, then a sharp increase for ovulation); reassure patient that generally ovulation occurs after first course of therapy but if pregnancy does not occur, course of therapy may be repeated twice.
•Advise patient to attempt coitus 3 days before and every other day after ovulation.
•Caution patient not to perform hazardous task because drug may cause dizziness or visual disturbances.
•Advise patient to stop drug and inform physician if pregnancy is suspected.
•Tell patient that multiple births are common and that risk increases with high doses of drug.
•Advise patient to stop drug and report immediately if abdominal symptoms or pain occurs; may indicate ovarian enlargement or ovarian cyst.

Dose: *Anovulatory infertility*, by mouth, ADULT (female) 50 mg daily for 5 days, starting within 5 days of onset of menstruation, preferably on the second day, or at any time if cycles have ceased; a second course of 100 mg daily for 5 days may be given in the absence of ovulation.

POM **Clomifene** *(WMF 18.6)*
Tablets, Clomifene citrate 50 mg

POM **Clomifene** *(EDL 19.6)*
Tablet, Clomifene citrate 50 mg.

POM **CLIFEN**® *(Pharmabox)*
Tablet, Clomifene citrate 50 mg; light-yellow f-c oval tab.

RETURN

50 mg - 10's.

POM **IKACLOMIN**® *(Dizpharm)*
Tablet, Clomifene citrate 50 mg
50 mg - 10's.

10.5.2 Anterior Pituitary Hormones (Gonadotrophins)

The Gonadotrophins, Luteinizing hormone (LH) and Follicle-stimulating hormone (FSH), are secreted by the anterior pituitary in response to hypothalamic gonadotrophin-releasing hormone (GNRH).

Human gonadotrophins are available as

(a) **Human menopausal gonadotrophin (HMG)**, or menotrophin which is an extract of the urine of postmenopausal women containing primarily follicle-stimulating hormone (with luteinising hormone), and

(b) **Human chorionic gonadotrophin (HCG)**
or chorionic gonadotrophin which is a preparation of a glycol-protein fraction secreted by the placenta and obtained from the urine of pregnant women having the action of the pituitary luteinizing hormone.

In both male and female, HMG or menotrophin (i.e., FSH plus LH) must be used in conjunction with a LH, i.e., HCG, to permit ovulation and implantation in women and testosterone production and full masculinisation in men. HMG or menotrophin is given to stimulate follicular growth and maturation and bring oestrogen levels into the optimum range for ovulation. HCG is then given to stimulate ovulation. There is a risk of multiple pregnancy and the abortion rate may be higher than with pregnancy following spontaneous ovulation. Hyperstimulation of the ovaries causes ovarian enlargement and if severe, ascites, pleural effusion, electrolyte imbalance and hypovolaemia.

The gonadotrophins are also occasionally used in the treatment of oligospermia associated with hypopituitarism. Their use in primary gonadal failure is not justified. HCG has also been used in delayed puberty in the male to stimulate endogenous testosterone production, but has little advantage over testosterone.

HCG is well absorbed after I.M. administration and has a biologic half-life of 8 hours, compared to 30 minutes for LH.

HUMAN CHORIONIC GONADOTROPHIN

Synonym: Chorionic Gonadotrophin, CG; HCG.

Therapeutic category: Ovulation Stimulator.

Indications: In women, primary amenorrhoea, secondary amenorrhoea over about 6 months, post partum amenorrhoea, infertility due to a shortened corpus luteum phase.

In boys and men, cryptorchidism in boys of six years and older, secondary hypogonadism, delayed puberty, impotentia coeundi.

Contra-indications: Carcinoma of the prostate.

Precautions: In male, latent or overt cardiac failure, renal dysfunction, hypertension, epilepsy or migraine (or a history of these conditions). In female, pregnancies occuring after ovulation induction may increase the risk of miscariage and multiplets.

Adverse effects: Oedema, headache, tiredness, mood changes, local reactions; sexual precocity.

Advice to patients: Discontinue immediately if pregnancy is suspected.

Nursing considerations: •Administer I.M., and rotate injection site to prevent muscle atrophy.
•Administer usually after failure of clomifene in anovulatory patients; in infertility, encourage patients to have sexual intercourse from the day before HCG therapy until ovulation occurs; inform patient that when used with menotrophins to induce ovulation, multiple pregnancy/births are possible;
•Instruct patient to report facial, axillary and pubic hair changes, change in voice, penile enlargement, acne, abdominal pain, distension and vaginal bleeding in female patient, bloating, nausea, vomiting and diarrhoea; be alert for symptoms of ectopic pregnancy.

Dose: By I.M. or S.C. injection, according to patient's response.

POM **Human Chlorionic Gonadotrophin** (*EDL 19.6)*
Injection, Chronic gonadotrophin 500 units, 1000 units; in amps.

POM **CHORIGON**® (*Dizpharm)*
Injection, Chronic gonadotrophin 2500 I.U., 5000 I.U.

POM **PRIMOGONYL**® *(NGC)*
Injection, Human Chorionic gonadotrophin 1000 I.U.; dried substance plus solvent in separate amps.

FOLLICLE-STIMULATING HORMONE plus LUTEINISING HORMONE

Synonym: Human Menopausal Gonadotrophins; Menotropin (i.e., the 1:1

ratio).

Therapeutic category: Gonadotrophin; Ovulation Stimulator.

Indications: Sequentially with HCG to induce ovulation and pregnancy in the infertile woman with functional anovulation; used with HCG in men to stimulate spermatogenesis in those with primary hypogonadotrophic hypogonadism.

Contra-indications: Primary ovarian failure, overt thyroid and adrenal dysfunction, abnormal bleeding, pregnancy, men with normal urine gonadotrophin concentrations, elevated gonadotrophin levels indicating primary testicular failure.

Precautions: Ovarian enlargement (use the lowest possible dose); multiple pregnancy (advise patient on the frequency and potential hazards).

Adverse effects: Gynaecomastia, ovarian enlargement, abdominal distension, pain/rash at injection site, multiple pregnancy.

Advice to patients: Multiple ovulations resulting in plural gestations have been reported.

Nursing considerations: •Administer by deep I.M. after reconstituting with 1-2 ml of normal saline injection, use immediately; rotate injection site to prevent muscle atrophy.

•Inform patient of the frequency and potential hazards of multiple pregnancy; in the treatment of infertility, encourage patient to have daily intercourse from the day before drug is given until ovulation occurs (pregnancy usually occurs 4-6 weeks after therapy).

•Instruct patient to report severe abdominal pain, bloating, swelling of hands or feet, nausea, vomiting, diarrhoea, substantial weight gain or shortness of breath.

Dose: By deep I.M. injection, according to patient's response.

POM **Follicle-stimulating Hormone plus Luteinising Hormone** *(EDL 19.6)*

Injection, Human FSH 75 units, human LH 75 units; powder for reconstitution.

POM **PERGONAL®** *(Dizpharm)*

Injection, Menotropin (equiv. to human FSH 75 I.U. plus human LH 75 I.U.); powder in amp. plus 1 ml solvent.

Pack - 5.

UROFOLLITROPIN (FSH)

Synonym: Urofollitrophin.

Pharmacology: Urofollitropin is obtained from human menopausal urine, with only FSH activity. Human menopausal gonadotrophin (HMG) exerts FSH and LH activities. For this reason, HMG is indicated in hypogonatropic hypopituitarism (WHO Group I patients), where both gonadotrophin secretions are needed. In patients showing normal or high LH levels (WHO Group II), selective FSH deficiencies require availability of preparations without LH activity; this characteristic belongs to FSH. FSH stimulates both the growth and maturation of follicles; it induces the secretion of oestrogens and a proliferation of the endometrium.

Indications: Stimulation of follicular growth in infertile women. A course of Urofollitropin is usually followed by human chorionic gonadotrophin (hCG) to induce ovulation. It is used:

(a) For single follicular development in cases such as hypothalamic pituitary dysfunction (WHO Group II classification), including patients with polycystic ovarian disease.

(b) For multiple follicular development (assisted conception techniques); incases such as tubal occlusion, unexplained infertility and male factor infertility.

Contra-indications: For safety reasons, avoid in cases of prior hypersensitivity to menotrophins; pregnancy; ovarian enlargement or cyst not due to polycystic ovarian syndrome; gynaecological haemorrhages of unknown aetiology; ovarian, uterine or mammary carcinoma. Also avoid use when an effective response cannot be obtained such as in primary ovarian failure (ovarian dysgenesis, premature menopause); malformations of sexual organs incompartible with pregnancy; fibroid tumours of the uterus incompartible with pregnancy.

Precautions: Adhere to the recommended dosage and monitor patient closely to avoid ovarian hyperstimulation syndrome which occurs usually 1 to 2 weeks following hCG administration and ovulation. In case of symptoms such as pelvic pain, abdominal distension or ovarian enlargement or if oestrogen assays or ultrasound examination suggest an excessive oestrogen response, urofollitropin administration should be discontinued and hCG should not be administered and intercourse avoided in order to prevent ovarian hyperstimulation. Symptoms such as ascites, pericardial effusion, hydrothorax, haemo-concentration, secondary hyperaldosteronism or hypercoagulability should be controlled through appropriate measures, including avoidance of unnecessary pelvic examination.

Interactions:

•Co-administration with clomiphene citrate may potentiate the follicular response, whereas concurrent use of GnRH agonist-induced

pituitary desensitisation may increase the dosage of urofollitropin needed to elicit an adequate ovarian response.

•Avoid mixing with other drugs in the same syringe.

Adverse effects: Local reactions at the injection site, fever and arthralgias; GI symptoms, bloating of the stomach, pelvic pain or sore breasts; mild to moderate ovarian enlargement, ovarian cysts; rarely severe hyperstimulation syndrome, arterial thrombo-embolisms; few incidence of multiple births; pregnancy wastage by miscarriage or abortion especially in women with other fertility problems; ectopic pregnancy especially in women with history of prior tubal disease.

Dose: By S.C. or I.M. injection, Adult, *Women with hypothalamic-pituitary dysfunction who present with either oligomenorrhoea or amenorrhoea (WHO Group II),* usually 75-150 IU daily (commencing within the first 7 days of the menstrual cycle for menstruating patients); increased or decreased by up to 75 IU/day at 7 or 14 day intervals if necessary to obtain an adequate, but not excessive, response. If no adequate response after 4 weeks of treatment, that cycle should be abandoned. An optimal response is followed by a single I.M. injection of up to 10,000 IU hCG 24-48 hours after the last urofollitropin injection. Patient is encouraged to have coitus on the day of and that following hCG administration. If excessive response is obtained, stop treatment and withhold hCG; treatment should recommence in the next cycle at a dosage lower than that of the previous cycle. *Women undergoing superovulation for in-vitro fertilisation and other assisted conception techniques,*usually 150-225 IU daily (commencing on day 2 or 3 of the cycle); doage may be adjusted according to the patient's response up to a maximum of 450 IU daily. Treatment should be continued until adequate follicular development is achieved. A single injection of up to 10,000 IU hCG is given 24-48 hours after the last urofollitropin injection to induce follicular maturation.

Note: The powder should be reconstituted immediately prior to use with the solvent provided. In order to avoid the injection of large volumes, up to 5 ampoules of urofollitropin may be dissolved in 1 ml of solvent.

POM **METRODIN HP** ®*(Dizpharm)*
Injection, Urofollitropin 75 IU, 150 IU; powder for reconstitution in amps. plus 1 ml solvent. Pack - 1; 10.

10.5.3 Posterior Pituitary Hormones

The hormones secreted by the posterior pituitary are **vasopressin** (antidiuretic hormone, ADH) and **Oxytocin**. Oxytocin is used in obstetrics (see section 11.1).

Diabetes Insipidus: Underproduction of ADH causes pituitary (cranial) diabetes insipidus, which is characterized by the passage of large volumes of urine of low osmolality, and polydipsia. Treatment is by hormone replacement, although mild cases of cranial diabetes insipidus may respond to **chlorpropamide** 250 mg daily or **carbamazepine** 200-400 mg daily. These drugs sensitize the renal tubule to the action of remaining endogenous vasopressin.

In nephrogenic diabetes insipidus the symptoms of polyuria and polydipsia are due to a refractoriness of the kidney to respond to the action of vasopressin. In the absence of a correctable cause such as hypokalaemia or hypercalcaemia, patient may benefit from the paradoxical antidiuretic effect of thiazides, e.g., **bendrofluazide** 5-10 mg daily; chlorthalidone 100 mg twice daily reduced to maintenance dose of 50 mg daily.

Vasopressin, an octapeptide hormone, has a direct anti-diuretic action on the kidneys. It is the treatment of choice for pituitary diabetes insipidus. It also constricts peripheral vessels and causes contraction of the intestine, gall-bladder, and urinary bladder. It is devoid of oxytocic activity and is ineffective in nephrogenic diabetes insipidus. When other methods of treatment fail, bleeding oesophageal varices may respond to ADH. Here vasopressin (20 units) is infused over about 5 minutes i.v. and may stop the bleeding by causing constriction of splanchnic arterioles and a reduction in portal venous pressure.

Vasopressin is well absorbed from buccal and nasal mucosa and may also be given s.c., i.m., or i.v. Its plasma half-life is about 15 minutes and it is rapidly inactivated by the liver and kidneys. Circulating ADH is largely unbound.

Desmopressin is a synthetic Vasopressin analogue with greater antidiuretic activity, a more prolonged action and no significant pressor activity. It is given intranasally for maintenance therapy, and by injection in the postoperative period or in unconscious patients; the injection is also used for the diagnosis of diabetes

insipidus.

Interactions: Drugs known to potentiate the effects of Vasopressin include chlorpropamide, clofibrate, and carbamazepine. Inhalation of vasopressin may be ineffective when nasal congestion is present.

VASOPRESSIN

Synonym: Antidiuretic hormone (ADH).

Therapeutic category: Anti-diuretic.

Indications: Diabetes insipidus due to a deficiency in antidiuretic hormone; bleeding from oesophageal varices.

Contra-indications: Vascular disease, chronic nephritis with nitrogen retention.

Precautions: Asthma, epilepsy, migraine, heart failure; adjust fluid intake to avoid hyponatraemia and water intoxication; children, elderly, pregnancy.

Interactions:

•Drugs known to potentiate the effects of Vasopressin include chlorpropamide, clofibrate, and carbamazepine.

•Inhalation of vasopressin may be ineffective when nasal congestion is present.

Adverse effects: Hypersensitivity reactions including bronchial constriction; in large doses pallor, nausea, eructation, desire to defaecate, uterine cramps; constriction of coronary arteries, which may cause chest pain, myocardial ischaemia and infarction.

Advice to patients: Side effects such as abdominal cramps and nausea may be reduced by drinking a glass of water with each dose.

Nursing considerations: •Assess patient's B.P. and pulse when giving I.M.; weigh patient daily.

•Observe for signs of I.V. infiltration and gangrene.

•Warn elderly patients not to increase their normal fluid intake to avoid water intoxication and hyponatraemia; watch patient for signs of water intoxication viz lethargy, behavioural changes, disorientation, and neuromuscular excitability.

•Check for oedema in extremeties. If water retention is severe, a diuretic may be prescribed by the doctor.

Dose: By S.C. or I.M. injection, *Diabetes insipidus*, 5-20 units 4 hourly.
See lit for details.

POM **Vasopressin** *(EDL 19.8)*
Injection, Vasopressin 20 units per ml, in 1 ml amp.

DESMOPRESSIN

Therapeutic category: Synthetic Vasopressin Analogue; Antihaemophilic Agent; Haemostatic Agent.

Indications: Treatment of diabetes insipidus and controlling bleeding in mild to moderate haemophilia; also in nocturnal enuresis.

Contra-indications: Hypersensitivity to desmopressin or any component; cardiac insufficiency and related conditions.

Precautions: Avoid overhydration; renal impairment, Cardiovascular disease, hypertension, elderly, cystic fibrosis.

Interactions: •Demeclocycline, lithium (decreased ADH effects).

•Chlorpropamide, fludrocortisone (increased ADH effects).

Adverse effects: Nausea, abdominal cramps, headache, dizziness, pain at injection site, increase in B.P., water intoxication and hyponatraemia.

Advice to patients: Avoid overhydration; notify physician if headache, shortness of breath, heartburn, nausea, abdominal cramps, or vulval pain occur.

Nursing considerations: •Advise patient to drink only enough water to satisfy thirst; if water retention is severe, diuretic may be prescribed.

•Adjust fluid intake to reduce risk of water intoxication and sodium depletion especially in children and elderly, shown by lethargy, behavioural change, disorientation, neuromuscular excitability.

•Nasal congestion, allergic rhinitis, or upper respiratory tract infections may impair drug absorption, therefore, advise patient to report such conditions to the physician.

•Advise patient not to take OTC products for cough since these preparations may contain epinephrine which can decrease drug response; do not use with alcohol.

•Teach patient using S.C. desmopression to rotate injection sites to prevent tissue damage.

Dose: Intranasally, *Diagnosis of Diabetes Insipidus*, Adult and child, 20 mcg; limit fluid intake to 500 ml from 1 hour before to 8 hours after administration.
Treatment of Diabetes Insipidus, Adult, 10-40 mcg daily in 1-2 divided doses; Child: 5-20 mcg; infants may require lower doses.
Primary Nocturnal Enuresis Adult (under 65 years) and child (over 5 years), initially 20 mcg at bedtime; may be increased to 40 mcg if lower dose is not effective. Withdraw for at least 1 week for reassessment after 3 months.
By S.C. or I.M. injection, *Diagnosis of Diabetes Insipidus*, Adult and Child, 2 mcg.
Treatment of Diabetes Insipidus, Adult, 1-4 mcg daily;
Child: 400 nanograms.
See lit for details.

POM **Desmopressin** *(EDL 19.8)*
Injection, Desmopressin 4 mcg per ml

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Nasal spray, Desmopressin 10 mcg per metered spray.
Intranasal solution, Desmopressin 100 mcg per ml

10.6 Other Endocrine Drugs

Bromocriptine
Bromocriptine acts as a partial dopamine receptor agonist. It inhibits the secretion of the anterior pituitary hormone prolactin without affecting normal levels of other pituitary hormones. However, bromocriptine can reduce elevated levels of growth hormone (GH) in patients with acromegaly. It does not have the undesirable effects of oestrogens. It normalises the ovarian function, and can be used to prevent or inhibit physiological lactation and to treat pathological prolactin-related conditions.

Danazol
Danazol is a synthetic derivative of ethisterone. It suppresses the pituitary-gonadal axis by inhibiting the output of pituitary gonadotrophins in both male and female. It has neither oestrogenic nor progestational activity but possesses mild androgenic activity. The action is reversible; ovulation and cyclic bleeding usually return within 60 to 90 days of discontinuation of therapy.
Danazol is slowly metabolised in human, having a half-life of over 15 hours. This results in stable circulating levels when the drug is administered twice daily. It is highly concentrated in the liver, adrenals, and kidneys and is excreted in both faeces and urine.

BROMOCRIPTINE

Therapeutic category: Prolactin inhibitor
Indications: Prolactin-dependent menstrual cycle disorders such as amenorrhoea, female infertility, premenstrual symptoms, hyperprolactinaemia in men, prolactinomas, acromegaly, inhibition of lactation such as after abortion, benign breast disease; Parkinson's disease.
Contra-indications: Hypersensitivity to bromocriptine or other ergot alkaloids, toxaemia of pregnancy, hypertension postpartum and in the puerperium.
Precautions: Pregnancy; history of psychic or severe cardiovascular disorders, patients on drugs that can alter B.P. should be monitored; acromegalic patients with history or evidence of peptic ulceration.
Interactions: Alcohol, erythromycin, CNS depressants.
Adverse effects: Orthostatic hypotension, nasal congestion, nausea, vomiting, somnolence; very rarely constipation, dyspepsia, psychomotor agitation, cold-induced vasospasm; at high doses, psychic disturbances, fatigue, bladder trouble.
Advice to patients: See Label 21 in Appendix A. Take with food or milk; drowsiness commonly occurs upon initiation of therapy; limit use of alcohol; avoid exposure to cold; incidence of side effects is high with nausea the most common; hypotension occurs commonly with initiation of therapy, usually upon rising after prolonged sitting or lying; discontinue immediately if pregnant; may restore fertility; women desiring not to become pregnant should use mechanical contraceptive means.
Nursing considerations: •Give with meals to minimize GI upset.
•Raise bed rails and institute safety measures; aid patient with ambulation, may cause postural hypotension and drowsiness.
•Advise patient to avoid dizziness and fainting by getting up slowly.
•Since early postpartumm pregnancy can occur, test for pregnancy every 4 weeks.
•Inform patient that it may take between 6-8 weeks for menstruation to be reinstated and galactorrhoea to be suppressed.
•In parkinsonism, bromocriptine is usually given together with either levodopa alone or levodopa-carbidopa combination.
Dose: By mouth, *Menstrual Cycle disorder and female infertility*, 1.25 mg 2-3 times daily; increased to 2.5 mg 2-3 times daily, if necessary.
Premenstrual symptoms, 1-2.5 mg daily starting on the 14th day of the cycle; increased in steps of 1.25 mg daily up to 2.5 mg twice daily until menstruation sets in.
Hyperprolactinaemia in men, 1.25 mg 2-3 times daily; increased gradually to 5-10 mg per day.
Prolactinomas, 1.25 mg 2-3 times daily; increased gradually as required to keep plasma prolactin adequately suppressed (occasionally up to 30 mg daily).
Acromegaly, 1.25 mg 2-3times daily; increased gradually to 10-20 mg daily depending on response and side effects.
Inhibition of lactation, 1.25 mg with food in the morning and evening on the 1st day; followed by 2.5 mg twice daily for 14 days. To prevent the onset of lactation, treatment should be instituted within a few hours of parturition or abortion, but not before vital signs have stabilized.

Puerperal breast engorgement, 2.5 mg as a single dose; may be repeated after 6-12 hours.
Incipient puerperal mastitis, as for inhibition of lactation plus an antibiotic.
Benign breast disease, 1.25 mg 2-3 times daily; increased gradually to 5-7.5 mg per day.
Parkinsons disease, see Bromocriptine in section 1.6.1.

POM **Bromocriptine** *(EDL 19.6)*
Tablet or Capsule, Bromocriptine 1 mg, 2.5 mg (as mesylate)

POM **APO-BROMOCRIPTINE®** *(Lahams)*
Tablet, Bromocriptine mesylate 2.5 mg; white, oval tab. marked 'APO 2.5'.
2.5 mg - 100.

POM **BROMERGON®** *(Taylek)*
Tablet, Bromocriptine(as methane-sulphonate) 2.5 mg.
2.5 mg - 30; 100.

POM **PARILAC®** *(Dizpharm)*
Tablet, Bromocriptine (as mesylate) 2.5 mg
2.5 mg - 30

POM **PARLODEL®** *(Novartis)*
Tablets, Bromocriptine (as mesylate) 1 mg, 2.5 mg; white scored tab. marked tab. name and strength.
1 mg - 100
2.5 mg - 30.

DANAZOL

Therapeutic category: Gonadotrophin release inhibitor; Androgen.

Indications: Endometriosis, associated infertility; benign breast disease (chronic cystic mastitis, virginal breast hyperplasia, mazoplasia, mastodynia); severe cyclical mastalgia with or without nodularity unresponsive to counseling or simple analgesics to reduce pain, tenderness and nodularity; dysfunctional uterine bleeding presenting as menorrhagia and associated dysmenorrhoea; preparation for hysteroscopic endometrial ablation to thin the endometrium and facilitate surgery; severe symptomatic gynaecomastia, both idiopathic and drug induced, to reduce the size of the breast and to control associated pain and tenderness.

Contra-indications: Pregnancy, breast-feeding; markedly impaired hepatic, renal or cardiac function; porphyria; andrgen-dependent tumour; undiagnosed abnormal genital bleeding; thromboembolic disease.

Precautions: Discontinue therapy if virilisation (may be irreversible on continued use), papilledema, headache, visual disturbances or raised intracranial pressure, jaundice or significant hepatic disturbance, thrombosis or thromboembolism occurs; hepatic, renal or cardiovascular disease (avoid if severe); diabetes mellitus, polycythemia, epilepsy, lipoprotein disorder, migraine; exclude carcinoma before initiation of therapy; nonhormonal method of contraception should be used.

Interactions: •May increase plasma level of carbamazepine, phenytoin, phenobarbitone, cyclosporin.
•Can cause insulin resistance to antidiabetic drugs.
•Can potentiate the action of warfarin (inhibits metabolism).
•Can reduce the effectiveness of antihypertensive agents.

Adverse effects: Acne, oedema, mild hirsuitism, decrease in breast size, deepening of the voice, oily skin or hair, weight gain and rarely clitorial hypertrophy are androgenic effects associated with danazol. Also hyperoestrogenic effects such as sweating vaginitis including itching, dryness, burning and vaginal bleeding, nervousness, and emotional liability have been reported. Allergic effects such as skin rashes and CNS effects such as dizziness, headache, nervousness and nausea have also been reported. Others include back-ache and hair loss.

Advice to patients: Notify physician if masculinity effects occur; virilisation may occur in female patients; report menstrual irregularities; male patients report persistent penile erections; all patients should report persistent GI distress, diarrhoea or jaundice.

Nursing considerations: •Administer with food or milk to minimise GI symptoms.
•Avoid use in women of child-bearing age until pregnancy is ruled out.
•Advise patient to have a wash after sexual intercourse to decrease the signs of vaginitis, and to wear cotton pants.
•Advise patient to have routine self-examination of the breasts.
•Evaluate signs of virilisation, deepening of voice, decreased libido, facial hair (may not be reversible); advise patient not to discontinue drug abruptly.

Dose: Adult females: *Endometriosis*, 200-800 mg daily in '4' divided doses. Duration: 3-6 months uninterrupted but may be extended to 9 months.
Benign breast disese, 300 mg daily in

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divided doses. Duration: 3-6 months.

Menorrhagia, usually 200 mg daily for 12 weeks.

Severe cyclical mastalgia, 100-400 mg daily usually for 3-6 months.

Note: For the above conditions, treatment should start during menstruation preferably on day 1 otherwise appropriate tests should be performed to ascertain that the patient is not pregnant while on danazol therapy.

Young girls: *Precocious puberty*, 100-400 mg daily, according to patient's age and weight.

Gynaecomastia, 400 mg daily in up to 4 divided doses for 6 months (adolescents 200 mg daily, increased to 400 mg daily if no response after 2 months).

For pre-operative thinning of endometrium, 400-800 mg daily in up to 4 divided doses for 3-6 weeks.

POM **Danazol** *(EDL 19.6)*

Capsules, Danazol 100 mg, 200 mg.

POM **DANOL®** *(Sanofi)*

Capsules, Danazol 200 mg; white opaque cap. 200 mg - 50.

11. Drugs used in obstetrics, gynaecology and urinary-tract disorders

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11.1 Drugs used in obstetrics
11.2 Genital antifungal drugs
11.3 Contraceptives
11.3.1 Hormonal contraceptives
11.3.2 Intrauterine contraceptive devices
11.3.3 Barrier methods
11.4 Drugs for genito-urinary disorders
11.4.1 Drugs for urinary retention
11.4.2 Drugs used in urological pain
11.4.3 Drugs used in erectile dysfunction

11.1 Drugs used in obstetricts

Drugs may be used to modify uterine contractions. These include oxytocic drugs used to stimulate uterine contractions both in induction of labour and to control postpartum haemorrhage and beta$_2$-adrenoceptor agonists used to relax the uterus and prevent premature labour.

POSTPARTUM HAEMORRHAGE

Ergometrine and **oxytocin** differ in their actions on the uterus. In moderate doses oxytocin produces slow generalized contractions with full relaxation in between; ergometrine produces faster contractions superimposed on a tonic contraction. High doses of both substances produce sustained tonic contractions. Oxytocin is now recommended for routine use in postpartum and post-abortion haemorrhage since it is more stable than ergometrine. However, ergometrine may be used if oxytocin is not available or in emergency situations.

PREMATURE LABOUR

Salbutamol is a beta$_2$-adrenoceptor agonist which relaxes the uterus and can be used to prevent premature labour in uncomplicated cases between 24 and 33 weeks of gestation. Its main purpose is to permit a delay in delivery of at least 48 hours. The greatest benefit is obtained by using this delay to administer corticosteroid therapy or to implement other measures known to improve perinatal health. Prolonged therapy should be avoided since the risks to the mother increase after 48 hours and the response of the myometrium is reduced.

ECLAMPSIA AND PRE-ECLAMPSIA

Magnesium sulfate has a major role in eclampsia for the prevention of recurrent seizures. Monitoring of blood pressure, respiratory rate and urinary output is

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carried out, as is monitoring for clinical signs of overdosage (loss of patellar reflexes, weakness, nausea, sensation of warmth, flushing, double vision and slurred speech—calcium gluconate injection (section 6.8) is used for the management of magnesium toxicity).

Magnesium sulfate is also used in women with pre-eclampsia who are at risk of developing eclampsia; careful monitoring of the patient (as described above) is necessary.

ERGOMETRINE

ERGOMETRINE IS SUBJECT TO INTERNATIONAL CONTROL UNDER THE UNITED NATIONS CONVENTION AGAINST ILLICIT TRAFFIC IN NARCOTIC DRUGS AND PSYCHOTROPIC SUBSTANCES (1988).

Ergometrine is a representative oxytocic drug. Various drugs can serve as alternatives.

Synonym: Ergonovine

Therapeutic category: Oxytocic

Indications: Prevention and treatment of postpartum and post-abortion haemorrhage in emergency situations and where oxytocin not available.

Contra-indications: Induction of labour, first and second stages of labour; vascular disease, severe cardiac disease especially angina pectoris; severe hypertension; severe renal and hepatic impairment; sepsis; eclampsia.

Precautions: Cardiac disease, hypertension, hepatic impairment (Appendix 5) and renal failure (Appendix 4), multiple pregnancy, porphyria; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, headache, dizziness, tinnitus, abdominal pain, chest pain, palpitations, dyspnoea, bradycardia, transient hypertension, vasoconstriction; stroke, myocardial infarction and pulmonary oedema also reported.

Advice to patients: May cause nausea, vomiting, dizziness, increased B.P., headache, ringing in the ears, chest pain, or shortness of breath.

Nursing considerations: •Administer I.M. deep into large muscle mass and rotate site of injection if repeat doses are required; I.V. use should be limited to patients with severe uterine bleeding or other life threatening emergency situations.

•Monitor B.P., pulse rate and uterine response; report sudden changes in vital signs and uterine hypotonia as well as the type and amount of vaginal blood loss.

•Contractions begin 5-15 minutes after oral dose; 2-5 minutes after I.M. dose; immediately after I.V. dose. The uterine effects persists for 3 hours or more with oral or I.M. administration; 45 minutes after I.V. injection.

Dose: *Prevention and treatment of postpartum haemorrhage, when oxytocin is not available*, by intramuscular injection, ADULT and adolescent 200 micrograms when the anterior shoulder is delivered or immediately after birth.
Excessive uterine bleeding, by slow intravenous injection, ADULT and adolescent 250–500 micrograms when the anterior shoulder is delivered or immediately after birth.
Secondary postpartum haemorrhage, by mouth, ADULT and adolescent 400 micrograms 3 times daily for 3 days.

POM **Ergometrine** *(WMF 22.1)*
Tablets, Ergometrine maleate 200 micrograms.
Injection (Solution for injection), Ergometrine maleate 200 micrograms/ml, 1-ml ampoule.
NOTE: INJECTION REQUIRES TRANSPORT BY 'COLD CHAIN' AND REFRIGERATED STORAGE.

POM **Ergometrine** *(EDL 22)*
Tablet, Ergometrine maleate 0.5 mg
Injection, Ergometrine maleate 0.5 mg per ml

POM **LEKERGIN®** *(Taylek)*
Tablet, Ergometrine maleate 0.5 mg; capsule shaped tab.
0.5 mg - 20; 100; 500.
Injection, Ergometrine maleate 0.5 mg per ml; in 1 ml amp.
Pack - 50.

MAGNESIUM SULFATE

Indications: Prevention of recurrent seizures in eclampsia; prevention of seizures in pre-eclampsia.

Precautions: Hepatic impairment (Appendix 5); renal failure (Appendix 4); in severe hypomagnesaemia administer initially via a controlled infusion device; **interactions**: Appendix 1.

Adverse effects: Generally associated with hypermagnesaemia (see also notes above), nausea, vomiting, thirst, flushing of skin, hypotension, arrhythmias, coma, respiratory depression, drowsiness, confusion, loss of tendon reflexes, muscle weakness; see also Appendix 2.

Dose: *Prevention of recurrent seizures in*

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eclampsia, by intravenous injection, ADULT and adolescent initially 4 g over 5–15 minutes followed either by intravenous infusion, 1 g/hour for at least 24 hours after the last seizure or by deep intramuscular injection 5 g into each buttock then 5 g every 4 hours into alternate buttocks for at least 24 hours after the last seizure; recurrence of seizures may require additional intravenous injection of 2 g.

Prevention of seizures in pre-eclampsia, by intravenous infusion, adult and adolescent initally 4 g over 5–15 minutes followed either by intravenous infusion , 1 g/hour for 24 hours or by deep intramuscular injection 5 g into each buttock then 5 g every 4 hours into alternate buttocks for 24 hours; if seizure occurs, additional dose by intravenous injection of 2 g.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

FOR *INTRAVENOUS INJECTION* CONCENTRATION OF MAGNESIUM SULFATE SHOULD NOT EXCEED 20% (DILUTE 1 PART OF MAGNESIUM SULFATE INJECTION 50% WITH AT LEAST 1.5 PARTS OF WATER FOR INJECTION); FOR INTRAMUSCULAR INJECTION , MIX MAGNESIUM SULFATE INJECTION 50% WITH 1 ML LIDOCAINE INJECTION 2%.

POM **Magnesium sulfate** *(WMF 22.1)*
Injection (Solution for injection), Magnesium sulfate 500 mg/ml, 2-ml ampoule, 10-ml ampoule.

OXYTOCIN

Therapeutic category: Oxytocic

Indications: Routine prevention and treatment of postpartum and post-abortion haemorrhage; induction of labour.

Contra-indications: Hypertonic uterine contractions, mechanical obstruction to delivery, fetal distress; any condition where spontaneous labour or vaginal delivery inadvisable; avoid prolonged administration in oxytocin-resistant uterine inertia, in severe pre-eclamptic toxaemia or in severe cardiovascular disease.

Precautions: Induction or enhancement of labour in presence of borderline cephalopelvic disproportion (avoid if significant); mild to moderate pregnancy-associated hypertension or cardiac disease; age over 35 years; history of low-uterine segment caesarean section; avoid tumultuous labour if fetal death or meconium-stained amniotic fluid (risk of amniotic fluid embolism); water intoxication and hyponatraemia (avoid large volume infusions and restrict fluid intake); caudal block anaesthesia (risk of severe hypertension due to enhanced vasopressor effect of sympathomimetics); **interactions**: Appendix 1.

Adverse effects: Uterine spasm, uterine hyperstimulation (usually with excessive doses—may cause fetal distress, asphyxia and death, or may lead to hypertonicity, tetanic contractions, soft-tissue damage or uterine rupture); water intoxication and hyponatraemia associated with high doses and large-volume infusions; nausea, vomiting, arrhythmias, rashes and anaphylactoid reactions also reported.

Nursing considerations: •Administer by I.V. infusion and in hospital where critical care facilities and doctor are available.

•Do not give by bolus I.V. injection; rapid I.V. injection may cause short-lasting drop in B.P.

•Used for induction and enhancement of labour only when pelvis is adequate, and fetal maturity and position are assured and favourable.

•Monitor and record uterine contractions, heart rate, fetal heart rate and character of vaginal blood loss ¼-hourly.

•Observe for fetal distress indicated by deceleration, bradycardia, tachycardia and notify the physician.

•Larges doses may cause excessive fluid retention which can lead to seizures and coma; monitor fluid I&O.

•Not recommended for routine I.M. use; it may be given I.M. after delivery of placenta to prevent post-partum haemorrhage.

Dose: *Induction of labour*, by intravenous infusion, ADULT and adolescent, initially 0.001–0.002 units/minute increased in 0.001–0.002 units/minute increments at intervals of 30 minutes until a maximum of 3–4 contractions occur every 10 minutes; maximum recommended rate 0.02 units/minute; no more than 5 units should be administered in 24 hours.

NOTE: THE DOSE SHOWN ABOVE IS SUITABLE FOR USE IN HOSPITAL WHERE EQUIPMENT TO CONTROL THE INFUSION RATE IS AVAILABLE; ALTERNATIVE RECOMMENDATIONS MAY BE SUITABLE FOR OTHER SETTINGS (CONSULT *MANAGING COMPLICATIONS IN PREGNANCY AND CHILDBIRTH: A GUIDE FOR MIDWIVES AND DOCTORS* 2003 . GENEVA: WHO).

IMPORTANT: CAREFUL MONITORING OF FETAL HEART RATE AND UTERINE MOTILITY ESSENTIAL FOR DOSE TITRATION (NEVER GIVE INTRAVENOUS BOLUS INJECTION DURING LABOUR); DISCONTINUE IMMEDIATELY IN UTERINE HYPERACTIVITY OR FETAL DISTRESS.

Prevention of postpartum haemorrhage, by slow intravenous injection, ADULT and adolescent 5 units when the anterior shoulder is

delivered or immediately after birth. *Prevention of postpartum haemorrhage*, by intramuscular injection, adult and adolescent 10 units when the anterior shoulder is delivered or immediately after birth. *Treatment of postpartum haemorrhage*, by slow intravenous injection, adult and adolescent 5–10 units or by intramuscular injection , 10 units, followed in severe cases by intravenous infusion , a total of 40 units should be infused at a rate of 0.02–0.04 units/minute; this should be started after the placenta is delivered.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. PROLONGED INTRAVENOUS ADMINISTRATION AT HIGH DOSES WITH LARGE VOLUME OF FLUID (FOR EXAMPLE IN INEVITABLE OR MISSED ABORTION OR POSTPARTUM HAEMORRHAGE) MAY CAUSE WATER INTOXICATION WITH HYPONATRAEMIA. TO AVOID: USE ELECTROLYTE-CONTAINING DILUENT (NOT GLUCOSE), INCREASE OXYTOCIN CONCENTRATION TO REDUCE FLUID, RESTRICT FLUID INTAKE BY MOUTH; MONITOR FLUID AND ELECTROLYTES.

POM **Oxytocin** *(WMF 22.1)*
Injection (Solution for injection), Oxytocin 10 units/ml, 1-ml ampoule.

POM **Oxytocin** *(EDL 22)*
Injection, Oxytocin 5 units, 10 units per ml; in amps.

POM **SYNTOCINON®** *(Novartis)*
Injections, Synthetic Oxytocin 5 units, 10 units per ml.

SALBUTAMOL

Salbutamol is a representative myometrial relaxant. Various drugs can serve as alternatives.

Indications: Uncomplicated premature labour between 24–33 weeks gestation; asthma (section 7.1.1).

Contra-indications: First and second trimester of pregnancy; cardiac disease, eclampsia and pre-eclampsia, intra-uterine infection, intra-uterine fetal death, antepartum haemorrhage, placenta praevia, cord compression, ruptured membranes

Precautions: Monitor pulse and blood pressure and avoid over-hydration; suspected cardiac disease, hypertension, hyperthyroidism, hypokalaemia, diabetes mellitus; if pulmonary oedema suspected, discontinue immediately and institute diuretic therapy; **interactions**: Appendix 1.

Adverse effects: Nausea, vomiting, flushing, sweating, tremor; hypokalaemia, tachycardia, palpitations, and hypotension, increased tendency to uterine bleeding; pulmonary oedema; chest pain or tightness and arrhythmias; hypersensitivity reactions including bronchospasm, urticaria and angioedema reported.

Nursing considerations: •Monitor maternal B.P. and pulse rate closely; it should not exceed 135-140 beats/minute.

Dose: *Premature labour*, by intravenous infusion, ADULT initially 10 micrograms/minute, rate gradually increased according to response at 10-minute intervals until contractions diminish then increase rate (maximum of 45 micrograms/minute) until contractions have ceased, maintain rate for 1 hour then gradually reduce; or by intravenous or intramuscular injection, ADULT 100–250 micrograms repeated according to response, then by mouth, 4 mg every 6–8 hours (use for more than 48 hours not recommended).

POM **Salbutamol** *(WMF 22.1)*
Tablets, Salbutamol (as sulfate) 4 mg.
Injection (Solution for injection), Salbutamol (as sulfate) 50 micrograms/ml, 5-ml ampoule.

See Salbutamol in section 7.1.1 for the proprietary preparations.

11.2 Genital antifungal drugs

Imidazole drugs **(Clotrimazole**, **Tioconazole**, **Econazole**, Fenticonazole, **Isoconazole** and **Miconazole)** are effective in short courses of 3 to 14 days according to the preparation used; single dose preparations offer an advantage when compliance is a problem.

Nystatin is a well established treatment (but stains clothing yellow). Recurrence is common if the full course of treatment is not completed and is also particularly likely if there are predisposing factors such as antibiotic therapy, oral contraceptive use, pregnancy, or diabetes mellitus. Possible reservoirs of infection may also lead to recontamination and should be treated. These include other skin sites such as the digits, nail beds, and umbilicus as well as the GIT, and the bladder. The partner may also be the source of the re-infection and should be treated with cream at the same time.

CLOTRIMAZOLE

Therapeutic category: Imidazole antifungal
Indications: Candidal and trichomonal vaginitis, leucorrhoea.
Precautions: Avoid use during menstruation.
Adverse effects: Local mild burning or irritation.
Advice to patients: May cause irritation to the skin; avoid contact with eyes.
Nursing considerations: •Clean area with soap and water before applying.
•Advise patient to use nonstop for the prescribed period; if condition persists or worsens, or if irritation, burning, itching, redness or stinging occur, discontinue use and report to physician.
•Advise patient to abstain from sexual intercourse during vaginal or vulval treatment.
•Advise patient to continue using during menstruation and to wash hands before and after each application.
Dose: Vaginal tablets, 200 mg inserted nightly for 3 nights or 100 mg nightly for 6 nights.

POM **Clotrimazole** *(EDL 14.6)*
Vaginal tablet, clotrimazole 100 mg, 200 mg.

POM **CLOMAZ®** *(L.B.S.)*
Vaginal tablet, Clotrimazole 100 mg; white oblong tab. marked with marker's name.
100 mg - 6 with applicator.

POM **MYCORON®** *(Justeen)*
Cream, Clotrimazole 1% w/w.
Pack – 30 g.

POM **MYCOTEN®** *(Drugfield)*
Vaginal tablet, Clotrimazole 100 mg.
Vaginal cream, Clotrimazole 1%.

POM **SABRESTEN®** *(Gemini)*
Vaginal cream, Clotrimazole 0.35 g per 35 g.
Pack - 35 g with applicator.
Dose: 1 filled applicator (approx. 5 g) should be inserted daily into the vagina as deeply as possible, preferably at night, for 6 consecutive days. A six day treatment is generally sufficient for vaginitis caused by fungi.
Note: Best result is achieved when lying back with the legs slightly drawn up. If necessary, a second six-day treatment may be carried out. Treatment should be timed so as to avoid the menstrual period and be finished before the onset of menstruation. In cases of concomitant vulvitis or *Candida balanitis* of the sexual partner and in order to prevent reinfection, both partners should also undergo local treatment with Sabresten cream. Sabresten vaginal cream is odourless and can be washed off.

ECONAZOLE

Therapeutic category: Imidazole antifungal
Indications: Vulvovaginal candidiasis
Nursing considerations: •*See under Clotrimazole.*
Dose: Depot ovules, 150 mg inserted as a single dose; may be repeated on day 5.
Ovules, 150 mg inserted nightly for 3 nights
Vaginal cream, one applicatorful inserted once daily for 7-10 days.

POM **Econazole** *(EDL 14.6)*
Vaginal cream, Econazole 1%.

ISOCONAZOLE

Indications: One shot antimycotic for fungal infections of the vagina including mixed infections with gram-positive bacteria.
Dose: Insert 1 ovule as single dose deep into vagina at bedtime.
Not to be used during menstruation.

POM **GYNO-TRAVOGEN®** *(CHI/Schering)*
Vaginal Ovule, Isoconazole nitrate 600 mg.
Pack - 1 Ovule plus applicator.

MICONAZOLE

Therapeutic category: Imidazole antifungal.
Pharmacology: Miconazole possesses not only a potent fungicidal action against dermatophytes and candida species but also a bactericidal activity against gram-positive bacteria. It has a soothing effect on the symptoms that frequently accompany candida infections, e.g. pruritis, leukorrhoea and burning sensation.
Indications: Vulvovaginitis caused by candida and/or grampositive bacteria; leukorrhoea; itching, burning sensation of the vulva.
Advice to patients: Avoid contact with the eyes; for vaginal product, insert high into vagina and complete full course of therapy; notify physician if itching or burning occur; refrain from intercourse to prevent reinfection.
Nursing considerations: *See under Clotrimazole.*
Dose: Cream, 1 applicatorful (5 g) once daily for 7 days, even after the pruritus leukorrhoea have disappeared.
Ovules, 200 mg every night for 7 days or 400 mg every night for 3 consecutive days.

POM **Miconazole** *(EDL 14.6)*
Ovules, Miconazole nitrate 200 mg, 400 mg.

Vaginal cream, Miconazole nitrate.

POM **GYNO-DAKTARIN®** *(Janssen-Cilag)*
Cream, Miconazole nitrate 2%
Pack - 40 g plus applicator
Ovules, Miconazole nitrate 200 mg, 400 mg.
200 mg - 7
400 mg - 3.

POM **MYCOHEAL®** *(Supreme)*
Ovules, Miconazole nitrate 200 mg, 400 mg.
200 mg - 7
400 mg - 3.

NYSTATIN

Therapeutic category: Antifungal antibiotic.
Indications: Vaginal candidiasis
Adverse effects: Transient local discomfort may be experienced.
Advice to patients: See under Miconazole.
Nursing considerations: *See under Clotrimazole.*
Dose: Adult, 1 or 2 pessaries intravaginally for at least 14 days; not to be interrupted during menstrual period.
Vaginal cream, 1 or 2 applications (of 4 g each) high into the vagina for 14 consecutive nights, or longer, regardless of any intervening menstrual period.
Reinfection from the candidal content of the intestinal tract may be prevented by concomitant therapy with oral nystatin.
Nystatin cream, gel or ointment should be applied to the perineal region 2-4 times daily, if necessary.
Note: To prevent reinfection with *Candida*, the male consort should be treated concurrently with nystatin cream or gel applied to the external genital area 2-4 times daily during the treatment period.

POM **Nystatin** *(EDL 6.11)*
Pessary, Nystatin 100,000 units.

TIOCONAZOLE

Therapeutic category: Imidazole Antifungal.
Pharmacology A broad spectrum antifungal agent which also has antibacterial activity against certain Gram-positive organisms.
Indications: Local treatment of vaginal yeast infections.
Contra-indications: Hypersensitivity to imidazole antifungal agents.
Precautions: Pregnancy
Adverse effects: Local irritation.
Dose: 300 mg intravaginally at night as a one-day single dose treatment; may be repeated one week later if necessary.
Note: To be inserted deep in the vagina preferably before retiring for the night; avoid use during menstruation.

POM **Tioconazole** *(EDL 14.6)*
Ovules, Tioconazole 300 mg.

POM **GYNO-TROSYD®** *(Pfizer)*
Vaginal ovule, Tioconazole 300 mg.
300 mg - 1

11.3 Contraceptives

11.3.1 Hormonal contraceptives
11.3.2 Intrauterine contraceptive devices
11.3.3 Barrier methods

11.3.1 Hormonal contraceptives

Hormonal contraception is one of the most effective methods of reversible fertility control.

COMBINED ORAL CONTRACEPTIVES
Estrogen plus progestogen combinations are the most widely used hormonal contraceptives. They produce a contraceptive effect mainly by suppressing the hypothalamic-pituitary system resulting in prevention of ovulation; in addition, changes in the endometrium make it unreceptive to implantation.

Endometrial proliferation is usually followed by thinning or regression of the endometrium resulting in reduced menstrual flow. Ovulation usually resumes within three menstrual cycles after oral contraception has been discontinued; anovulation and amenorrhoea persisting for six months or longer requires investigation and appropriate treatment if necessary.

Potential non-contraceptive benefits of combined oral contraceptives include improved regularity of the menstrual cycle, decreased blood loss, less iron-deficiency anaemia and significant decrease in dysmenorrhoea. Long-term use is associated with reduced risk of endometrial and ovarian cancer and of some pelvic infections.

An association between the amount of estrogen and progestogen in oral contraceptives and an increased risk of adverse cardiovascular effects has been observed. The use of oral contraceptive combinations containing the progestogens,

desogestrel or gestodene are associated with a slightly increased risk of venous thromboembolism compared with oral contraceptives containing the progestogens, levonorgestrel or norethisterone.

RISK FACTORS FOR VENOUS THROMBOEMBOLISM OR ARTERIAL DISEASE

Risk factors for *venous thromboembolism* include family history of venous thromboembolism in first-degree relative aged under 45 years, obesity, long-term immobilization and varicose veins.

Risk factors for *arterial disease* include family history of arterial disease in first-degree relative aged under 45 years, diabetes mellitus, hypertension, smoking, age over 35 years (avoid if over 50 years), obesity and migraine.

If any one of the factors is present, combined oral contraceptives should be used with caution; if 2 or more factors for either venous thromboembolism or arterial disease are present, combined oral contraceptives should be avoided. Combined oral contraceptives are contraindicated in migraine with aura, in severe migraine without aura regularly lasting over 72 hours despite treatment and in migraine treated with ergot derivatives.

SURGERY

Estrogen-containing oral contraceptives should preferably be discontinued (and adequate alternative contraceptive arrangements made) 4 weeks before major elective surgery and all surgery to the legs or surgery which involves prolonged immobilization of a lower limb. They should normally be restarted at the first menses occuring at least 2 weeks after full mobilization. When discontinuation is not possible thromboprophylaxis (with heparin and graduated compression hosiery) is advised.

REASONS TO STOP COMBINED ORAL CONTRACEPTIVES IMMEDIATELY

Combined estrogen-containing oral contraceptives should be stopped immediately if any of the following symptoms occur and resumed only after consultation with a health care provider:

- Sudden severe chest pain (even if not radiating to left arm);
- Sudden breathlessness (or cough with blood-stained sputum);
- Severe pain in calf of one leg;
- Severe stomach pain;
- Serious neurological effects including unusual, severe, prolonged headache especially if first time or getting progressively worse or sudden partial or complete loss of vision or sudden disturbance of hearing or other perceptual disorders or dysphagia or bad fainting attack or collapse or first unexplained epileptic seizure or weakness, motor disturbances, very marked numbness suddenly affecting one side or one part of body;
- Hepatitis, jaundice, liver enlargement;
- Blood pressure above systolic 160 mmHg and diastolic100 mmHg;
- Detection of 2 or more risk factors for venous thromboembolism or arterial disease, see notes above

PROGESTOGEN-ONLY CONTRACEPTIVES

Progestogen-only contraceptives, such as oral **levonorgestrel** may offer a suitable alternative when estrogens are contraindicated but the oral progestogen-only preparations do not prevent ovulation in all cycles and have a higher failure rate than combined estrogen-containing preparations. Progestogen-only contraceptives carry less risk of thromboembolic and cardiovascular disease than combined oral contraceptives and are preferable for women at increased risk of such complications, for example smokers over 35 years. They can be used as an alternative to estrogen-containing combined preparations prior to major surgery. Oral progestogen-only contraceptives may be started 3 weeks after birth; breastfeeding women should preferably start at least 6 weeks after birth. Menstrual irregularities (oligomenorrhoea, menorrhagia, amenorrhoea) are common. Injectable preparations of **medroxyprogesterone acetate** or **norethisterone enantate** may be given intramuscularly. They have prolonged action and should only be given with full counselling and manufacturer's information leaflet.

EMERGENCY CONTRACEPTION

Levonorgestrel is used for emergency contraception. Levonorgestrel 1.5 mg should be taken as a single dose within 120 hours of unprotected intercourse; alternatively, levonorgestrel 750 micrograms can be taken within 72 hours of unprotected intercourse followed 12

hours later by another 750 micrograms. Under these circumstances levonorgestrel prevents about 86% of pregnancies that would have occurred if no treatment had been given. Adverse effects include nausea, vomiting, headache, dizziness, breast discomfort, and menstrual irregularities. If vomiting occurs within 2–3 hours of taking the tablets, replacement tablets can be given with an antiemetic.

It should be explained to the woman that her next period may be early or late; that she needs to use a barrier contraceptive method until her next period, and that she should return promptly if she has any lower abdominal pain or if the subsequent menstrual bleed is abnormally light, heavy, brief or absent. There is no evidence of harmful effects to the fetus if pregnancy should occur.

Advice To Oral Contraceptive Users

Users of oral contraceptives should be guided on the selection of a suitable product and should also be advised before and while taking such product. The following is a guide to the health care personnel and some of them are excerpts from the literature on Wyeth's oral contraceptives (*courtesy*: Wyeth/Delpitano Nigeria).

1. Selection Of An Oral Contraceptive:
   Combined oestrogen and progestogen oral contraceptives are most effective and generally used. Higher concentrations of the oestrogen and progestogen provide increased protection but with possibility of increased side-effects. Generally, a preparation with the lowest oestrogen and progestogen content which gives good cycle control and minimal side-effects in the individual patient is chosen. The oestrogen content usually ranges from 20 to 50 micrograms; the upper range may be suitable in conditions of reduced bioavailability such as in those using antiepileptics.
   Progestogen-only pills are less effective than the combined pills and may berecommended only when oestrogen are contraindicated and in heavy smokers.
   When changing from combined to progestogen-only pill treatment should start on the day following completion of the combined contraceptives course; there is no break in tablet taking.
2. Before Starting Oral Contraceptive:
   Tell your doctor or pharmacist if you are taking any drug or medication and if you have had a serious health problem. After starting, if you need any kind of medicine (whether prescribed by a doctor or obtained without a prescription) be sure to tell your doctor or pharmacist.
   This is important because some drugs may interfere with the action of the contraceptive. Also whenever you visit a doctor or health clinic for any reason, mention that you are taking oral contraceptive.
   If while taking oral contraceptive you develop an illness with vomiting and diarrhoea that lasts over 24 hours, your protection may be reduced. In such a case, continue taking your pills, and also use a supplementary birth control method such as the barrier method until the end of that cycle.
3. Your First Package:
   If you are a new oral contraceptive user, wait until your next menstrual period begins. Then, counting the first day of bleeding as DAY 1, (whether bleeding starts makes no difference), take your first tablet on DAY 5, whether bleeding has stopped or not. If you have been taking contraceptive, start your new oral contraceptive on the day you would have started a new package of the tablets.
   Take one tablet daily for 21 days, followed by a 7-day interval during which menstrual bleeding occurs. Everyday (ED) pills contain seven inactive pills corresponding with the 7-day interval. Take your tablets at the same time each day, preferably at the evening meal or at bedtime.
   If the first course is started on the 5th day of the cycle, ovulation may not be inhibited during that cycle and additional contraceptive precaution should therefore be taken during the first 7 days or when changing from a high to low oestrogen preparation. Additional contraceptive precautions are unnecessary in the first separate cycle if the tablets are started on the first day of the cycle as is now usually recommended.
4. How To Continue:
   When you finish your first pack, take no tablets for 7 days (your period usually begins about 3 days after the last tablets). Start the next pack 8 days after the tablet, even if you are still bleeding. A new pack is always started on the same day of the week as the day you started taking your present pack. As stated above, everyday (ED) pills contain seven inactive pills corresponding with the 7-day interval and hence, no interval is necessary in between packs.
5. Omitted Tablets:
   If you forget to take 1 or more pills; or if you start a package late, your body may not have enough of the substances needed to prevent pregnancy. In such cases, use a supplementary birth control method (other than oral contraceptive tablets, for example, mechanical) until you have taken a tablet daily for 7 days or until you finish the package if less than 7 days tablets daily remain.
   Suppose you forget to take a day's pill, take the missed pill when you remember, and the pill for that day at the regular time.
   In this case, you take 2 pills for the day you remember. Continue your schedule until the package is finished. Remember to use a supplementary contraceptive method as described above.
   Suppose you forget 2 tablets in a row. Take the 2 missed pills when you remember, and the pill for that day at regular time. In this case you take 3 pills on the day you remember.

Continue your schedule until the package is finished. Remember to use a supplementary contraceptive method as described above. If you forget 3 tablets in row do not take them when you remember and do not finish the package. Wait 4 more days. This makes 1 week without tablets. Then, begin a new package 8 days after the last tablet you took even if you are still bleeding. During the 7 days without tablet and until you have taken a tablet daily for 7 days from the new package use a supplementary birth control method for example, mechanical.

6. If You Miss A Period:
A missed period rarely means pregnancy provided you have followed the schedule. Failure to menstruate occurs occasionally with all oral contraceptives. Even if you have taken your tablets regularly, should you miss a period, consult your doctor before starting your next package. If you omitted any pill or started a package later, and do not menstruate during the tablet-free days, see your doctor. Take no more tablets until he says you can resume. Use an alternative method of contraceptive, not oral contraceptive tablets, for example, mechanical until pregnancy is ruled out.
7. Adjusting To Oral Contraceptives:
Most side effects of the pill are serious and usually occur during the first few months while your body adjusts. The most common side effects are nausea, vomiting, bleeding between menstrual periods, weight gain and breast tenderness.
8. When To Consult Your Doctor:
Stop taking tablets and see your doctor immediately if you have persistent leg, chest or abdominal pain, breathing difficulties, severe headache or vomiting, dizziness or fainting, difficulty in seeing or talking, numb or weak feeling in an arm or leg, if you cough up blood, if you notice unexpected vaginal bleeding or changes in your menstrual period, if you become very sad or irritable, or have other unusual symptoms.
9. Cigarette Smoking:
Cigarette smoking increases the risk of serious side effects on the heart and blood vessels from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarette per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should not smoke.
10. Childbirth:
Following childbirth oral contraceptives can be started at any time after 3 to 4 weeks postpartum (not earlier because of the increased risk of thrombosis in relation to the combined pill, and of breakthrough bleeding in relation to the progestogen-only pill). If they are started later than 4 weeks postpartum extra contraceptive precautions sholud be taken for 7 days.

COMBINED ORAL CONTRACEPTIVES

Ethinylestradiol with levonorgestrel and ethinylestradiol with norethisterone are representative combined oral contraceptive preparations. Various combinations can serve as alternatives.

Indications: Contraception; menstrual symptoms; endometriosis (see also progestogens, section 10.4.2).

Contra-indications: Use within 3 weeks of birth; breastfeeding until weaning or for first 6 months after birth (Appendix 3); personal history of or 2 or more risk factors for venous or arterial thrombosis (see notes above); heart disease associated with pulmonary hypertension or risk of embolism; migraine (see below); history of sub-acute bacterial endocarditis; ischaemic cerebrovascular disease; liver disease, including disorders of hepatic secretion such as Dubin-Johnson or Rotor syndromes, infectious hepatitis (until liver function normal); porphyria; systemic lupus erythematosus; liver adenoma; history of cholestasis with oral contraceptives; gallstones; estrogen-dependent neoplasms; neoplasms of breast or genital tract; undiagnosed vaginal bleeding; history during pregnancy of pruritus, chorea, herpes, deteriorating otosclerosis, cholestatic jaundice; pemphigoid gestationis; diabetes mellitus (if either retinopathy, neuropathy or if more than 20 years duration); after evacuation of hydatidiform mole (until return to normal of urine and plasma gonadotrophin values).

Precautions: Risk factors for venous thromboembolism and arterial disease (see notes above); migraine (see below); hyperprolactinaemia (seek specialist advice); some types of hyperlipidaemia; gallbladder disease; severe depression; long-term immobilization (see also Travel below); sickle-cell disease; inflammatory bowel disease including Crohn disease; **interactions**: Appendix 1.

MIGRAINE: PATIENTS SHOULD REPORT ANY INCREASE IN HEADACHE FREQUENCY OR ONSET OF FOCAL SYMPTOMS (DISCONTINUE IMMEDIATELY AND REFER URGENTLY TO NEUROLOGY EXPERT IF FOCAL NEUROLOGICAL SYMPTOMS NOT TYPICAL OF AURA PERSIST FOR MORE THAN ONE HOUR); **CONTRAINDICATIONS**: MIGRAINE WITH TYPICAL FOCAL AURA; MIGRAINE WITHOUT AURA REGULARLY LASTING OVER 72 HOURS DURATION DESPITE TREATMENT; MIGRAINE TREATED WITH ERGOT DERIVATIVES; **PRECAUTIONS**: MIGRAINE WITHOUT FOCAL AURA OR CONTROLLED WITH 5HT1 AGONIST.

TRAVEL: WOMEN TAKING ORAL CONTRACEPTIVES MAY BE AT INCREASED RISK OF DEEP-VEIN THROMBOSIS DURING TRAVEL INVOLVING LONG PERIODS OF IMMOBILITY (OVER 5 HOURS). THE RISK MAY BE REDUCED BY APPROPRIATE EXERCISE DURING THE JOURNEY AND POSSIBLY BY WEARING ELASTIC HOSIERY.

Adverse effects: Nausea, vomiting, headache, breast tenderness, increase in body weight, thrombosis, changes in libido, depression, chorea, skin reactions, chloasma, hypertension, impairment of liver function, 'spotting' in early cycles, absence of withdrawal bleeding, irritation of contact lenses; rarely, photosensitivity and hepatic tumours; breast cancer (small increase in risk of breast cancer during use which reduces during the 10 years after stopping; risk factor seems related to age at which contraceptive is stopped rather than total duration of use; small increase in risk of breast cancer should be weighed against the protective effect against cancers of the ovary and endometrium which persists after stopping).

Dose: *Contraception (21-day combined (monophasic) preparations)*, by mouth, ADULT (female), 1 tablet ('pill') daily for 21 days; subsequent courses repeated after 7-day pill-free interval (during which withdrawal bleeding occurs).

ADMINISTRATION: EACH TABLET ('PILL') SHOULD BE TAKEN AT APPROXIMATELY THE SAME TIME EACH DAY; IF DELAYED BY LONGER THAN 24 HOURS CONTRACEPTIVE PROTECTION MAY BE LOST. IT IS IMPORTANT TO BEAR IN MIND THAT THE CRITICAL TIME FOR LOSS OF PROTECTION IS WHEN A PILL IS OMITTED AT THE BEGINNING OR END OF A CYCLE (WHICH LENGTHENS THE PILL-FREE INTERVAL).

MISSED PILL: IF A PILL IS NOT TAKEN ON TIME, IT SHOULD BE TAKEN AS SOON AS POSSIBLE, AND THE NEXT ONE TAKEN AT THE USUAL TIME. IF ADMINISTRATION IS DELAYED BY MORE THAN 12 HOURS, THE WOMAN SHOULD RESUME TAKING THE PILL AT THE USUAL TIME AS SOON AS POSSIBLE; FURTHERMORE, BECAUSE CONTRACEPTIVE EFFICACY IS REDUCED, AN ADDITIONAL METHOD OF CONTRACEPTION SUCH AS THE CONDOM IS REQUIRED FOR 7 DAYS—IF THE 7 DAYS EXTEND BEYOND THE END OF THE PACKET, A NEW PACKET IS STARTED WITHOUT LEAVING A GAP BETWEEN PACKETS. EMERGENCY CONTRACEPTION IS RECOMMENDED IF EITHER 2 OR MORE PILLS ARE MISSED FROM THE FIRST 7 PILLS IN A PACKET OR 4 OR MORE CONSECUTIVE PILLS ARE MISSED MID-PACKET

DIARRHOEA AND VOMITING: VOMITING UP TO 3 HOURS AFTER TAKING AN ORAL CONTRACEPTIVE OR VERY SEVERE DIARRHOEA CAN INTERFERE WITH THE ABSORPTION OF THE PILL. ADDITIONAL PRECAUTIONS SHOULD BE USED DURING AND FOR 7 DAYS AFTER RECOVERY. IF VOMITING AND DIARRHOEA OCCUR DURING THE LAST 7 PILLS, THE NEXT PILL-FREE PERIOD SHOULD BE OMITTED.

POM **Combined oral contraceptives** *(WMF 18.3.1)*

Tablets, Ethinylestradiol 30 micrograms, levonorgestrel 150 micrograms.

Tablets, Ethinylestradiol 35 micrograms, norethisterone 1 mg.

ETHINYLESTRADIOL plus LEVONORGESTREL

Indications, **Contra-indications**, **Precautions**, etc: See under Combined oral contraceptives above.

POM **Levonorgestrel plus Ethinylestradiol** *(EDL 19.5.1)*

Tablet, Levonorgestrel 0.15 mg, ethinylestradiol 0.03 mg.

POM **LOGYNON ®** *(CHI/Schering)*

Tablets, Levonorgestrel 0.05 mg, ethinylestradiol 0.03 mg (6 tabs);
Levonorgestrel 0.075 mg, ethinylestradiol 0.04 mg (5 tabs);
Levonorgestrel 0.125 mg, ethinylestradiol 0.03 mg (10 tabs).
Pack - 21.

POM **MICROGYNON 30®** *(CHI/Schering)*

Tablet, Levonorgestrel 0.15 mg, ethinylestradiol 0.03 mg.
Pack - 21.

POM **NEOGYNON®** *(CHI/Schering)*

Tablet, Levonorgestrel 0.15 mg, ethinylestradiol 0.05 mg.
Pack - 21.

POM **NORDETEE®** *(Wyeth/Delpitano)*

Tablet, Ethinylestradiol 0.03 mg, laevonorgestrel 0.15 mg.
Pack - 21.

POM **NORDIOL®** *(Wyeth/Delpitano)*

Tablet, Ethinylestradiol 0.05 mg, laevonorgestrel 0.25 mg.
Pack - 21.

POM **OVRAL®** *(Wyeth/Delpitano)*

Tablet, Ethinylestradiol 0.05 mg, norgestrel 0.5 mg (equiv. to levonorgestrel 0.25 mg).

With ferrous fumarate

POM **DUOFEM®** *(SFH)*

Tablet, Norgestrel 0.3 mg, ethinylestradiol 0.03 mg (white tab.) PLUS Ferrous fumarate 75 mg (brown tab.) in a 28 day pack containing 21 "active" white pills (with hormones) and 7 brown "reminder" pills (with iron).

Dose: 1 tab. daily for 28 consecutive days starting from 1st day of cycle and continuing non-stop until the pack is empty.

Advice to patients: Take each pill at the same time every day. Do not skip pills even if you

RETURN

are spotting or bleeding between monthly periods or feel sick to your stomach (nausea). Do not skip pills even if you do not have sex very often. Start the next pack on the day after your last "reminder" (brown) pill. Do not wait any day between the packs.

DESOGESTREL plus ETHINYLESTRADIOL

Indications, **Contra-indications**, **Precautions**, etc: See under Combined oral contraceptives above.

POM **Desogestrel plus Ethinylestradiol** *(EDL 19.5.1)*
Tablet, Desogestrel 0.15 mg, ethinylestradiol 0.03 mg.

NORETHISTERONE plus ETHINYLESTRADIOL

Indications, **Contra-indications**, **Precautions**, etc: See under Combined oral contraceptives above.

POM **Norethisterone plus Ethinylestradiol** *(EDL 19.5.1)*
Tablet, Norethisterone 1 mg, ethinyloestradiol 0.05 mg.

POM **MINOVLAR®** *(NGC)*
Tablet, Ethinylestradiol 0.05 mg, norethisterone 1 mg.
Pack - 21

LEVONORGESTREL

Indications: Contraception (particularly when estrogens are contraindicated); emergency hormonal contraception.
Contra-indications: Progestogen-only oral contraceptives: undiagnosed vaginal bleeding; severe arterial disease; liver tumours; breast cancer; thromboembolic disorders; sickle-cell anaemia; porphyria; after evacuation of hydatidiform mole (until return to normal of urine and plasma gonadotrophin values); progestogen-only emergency hormonal contraceptives: severe liver disease; porphyria.
Precautions: Possible small increase in risk of breast cancer; cardiac disease; sex-steroid dependent cancer; past ectopic pregnancy; malabsorption syndrome; ovarian cysts; active liver disease, recurrent cholestatic jaundice, history of jaundice in pregnancy (Appendix 5); increase in frequency or severity of headache (discontinue pending investigation); breastfeeding (Appendix 3); **interactions**: Appendix 1.
Dose: *Contraception*, by mouth, ADULT (female), 1 tablet ('pill') (30 micrograms) daily, starting on the first day of the cycle and then continuously.

ADMINISTRATION: EACH TABLET ('PILL') SHOULD BE TAKEN AT APPROXIMATELY THE SAME TIME EACH DAY. IF DELAYED FOR LONGER THAN 3 HOURS CONTRACEPTIVE PROTECTION MAY BE LOST.
MISSED PILL: IF A PILL IS NOT TAKEN ON TIME, IT SHOULD BE TAKEN AS SOON AS POSSIBLE, AND THE NEXT ONE TAKEN AT THE USUAL TIME. IF ADMINISTRATION IS DELAYED BY MORE THAN 3 HOURS, THE WOMAN SHOULD RESUME TAKING THE PILL AT THE USUAL TIME AS SOON AS POSSIBLE; FURTHERMORE, BECAUSE CONTRACEPTIVE EFFICACY IS REDUCED, AN ADDITIONAL METHOD OF CONTRACEPTION SUCH AS THE CONDOM IS REQUIRED FOR 2 DAYS. EMERGENCY CONTRACEPTION MAY BE CONSIDERED IF 1 OR MORE PROGESTOGEN-ONLY CONTRACEPTIVE PILLS ARE MISSED OR TAKEN MORE THAN 3 HOURS LATE.
DIARRHOEA AND VOMITING: VOMITING UP TO 3 HOURS AFTER TAKING AN ORAL CONTRACEPTIVE OR VERY SEVERE DIARRHOEA CAN INTERFERE WITH THE ABSORPTION OF THE PILL. ADDITIONAL PRECAUTIONS SHOULD BE USED DURING AND FOR 7 DAYS AFTER RECOVERY.

Emergency (post-coital) contraception, by mouth, ADULT (female), 1.5 mg as a single dose (taken within 120 hours (5 days) of unprotected intercourse); alternatively 750 micrograms (taken within 72 hours of unprotected intercourse) followed by a second dose of 750 micrograms 12 hours later.

ADMINISTRATION: TAKING AS SOON AS POSSIBLE AFTER UNPROTECTED INTERCOURSE INCREASES EFFICACY; SHOULD NOT BE ADMINISTERED IF MENSTRUAL BLEEDING OVERDUE.

Adverse effects: Menstrual irregularities but tend to resolve on long-term treatment (including oligomenorrhoea and menorrhagia); nausea, vomiting, headache, dizziness, breast discomfort, depression, skin disorders, disturbances of appetite, weight increase, change in libido.

MEDROXYPROGESTERONE

Medroxyprogesterone acetate is a complementary drug.
Indications: Parenteral progestogen-only contraception (short-term or long-term); menstrual symptoms and endometriosis (section 10.4.2).
Contra-indications: Pregnancy (Appendix 2); hormone-dependent breast or genital

neoplasms; undiagnosed vaginal bleeding; hepatic impairment or active liver disease (Appendix 5); severe arterial disease; porphyria.

Precautions: Small increase in possible risk of breast cancer; migraine; liver disease; thromboembolic or coronary vascular disease; diabetes mellitus; trophoblastic disease; hypertension; renal disease; **interactions**: Appendix 1.

Adverse effects: Menstrual irregularities; delayed return to fertility; reduction in bone mineral density; weight gain; depression; rarely, anaphylaxis.

Dose: *Contraception (short-term)*, by deep intramuscular injection, ADULT (female) 150 mg within first 5 days of cycle or within first 5 days after parturition (delay until 6 weeks after parturition if breastfeeding).
Contraception (long-term), by deep intramuscular injection, ADULT (female) as for short-term, repeated every 3 months.

ADMINISTRATION: IF INTERVAL BETWEEN INJECTIONS IS GREATER THAN 3 MONTHS AND 14 DAYS, EXCLUDE PREGNANCY BEFORE NEXT INJECTION AND ADVISE PATIENT TO USE ADDITIONAL CONTRACEPTIVE MEASURES (FOR EXAMPLE BARRIER) FOR 7 DAYS AFTER THE INJECTION.
PATIENT ADVICE: WOMEN MUST RECEIVE FULL COUNSELLING (BACKED BY MANUFACTURER'S APPROVED LEAFLET) BEFORE TREATMENT, CONCERNING MENSTRUAL IRREGULARITIES AND BECAUSE OF PROLONGED ACTIVITY AND THE POTENTIAL FOR A DELAY IN RETURN TO FULL FERTILITY.

Note: Injection vial should be vigorously shaken just before use to ensure that the dose being administered represents a uniform suspension. I.M. injection is in the gluteal or deltoid muscle. To increase assurance that the patient is not pregnant at the time of the first administration, it is recommended that this injection be given only during the first 5 days after the onset of a normal menstrual period; within 5-days postpartum if not breast-feeding; or if breast-feeding, at 6-weeks postpartum. If the period between injections is greater than 14-weeks, patient should be examined to rule out pregnancy before administering the drug.

POM **Medroxyprogesterone** *(WMF 18.3.1)*
Injection (Suspension for injection), Medroxyprogesterone acetate 150 mg/ml, 1-ml vial.

POM **Medroxyprogesterone** *(EDL 19.5.2)*
Injection, Medroxyprogesterone acetate 150 mg per ml; in 1 ml vial.

NORETHISTERONE ENANTATE

Indications: Parenteral progestogen-only contraception (short-term).

Contra-indications: Pregnancy (Appendix 2); breast or endometrial cancer; severe liver disease (Dubin-Johnson or Rotor syndromes) (Appendix 5); history during pregnancy of jaundice, pruritus, herpes or of deteriorating otosclerosis; severe diabetes mellitus with vascular changes; hypertension; 12 weeks before planned surgery and during immobilization; thromboembolic disease; disturbances of lipid metabolism; undiagnosed vaginal bleeding; porphyria.

Precautions: Possible small increase in risk of breast cancer; migraine; liver dysfunction; depression; diabetes mellitus; previous ectopic pregnancy; cardiac and renal disease; **interactions**: Appendix 1.

Adverse effects: Bloating, breast discomfort, headache, dizziness, depression, nausea, menstrual irregularities; rarely, weight gain.

Dose: *Short-term contraception*, by deep intramuscular injection into gluteal muscle, ADULT (female) 200 mg within 5 days of cycle or immediately after parturition; repeated after 2 months.

ADMINISTRATION: IF INTERVAL BETWEEN INJECTIONS IS GREATER THAN 2 MONTHS AND 14 DAYS, EXCLUDE PREGNANCY BEFORE NEXT INJECTION AND ADVISE PATIENT TO USE ADDITIONAL CONTRACEPTIVE MEASURES (FOR EXAMPLE BARRIER) FOR 7 DAYS AFTER THE INJECTION.
PATIENT ADVICE: WOMEN MUST RECEIVE FULL COUNSELLING (BACKED BY MANUFACTURER'S APPROVED LEAFLET) BEFORE TREATMENT, CONCERNING POSSIBLE MENSTRUAL IRREGULARITIES AND BECAUSE OF PROLONGED ACTIVITY.

Note: It should be administered as a deep i.m. injection (preferably intragluteal, alternatively into the upper arm). It is advised to place a plaster over the injection site to prevent any reflux of the drug solution. The short-lasting reactions (urge to cough, coughing fits, respiratory distress) which occur in rare cases during or immediately after the injection of oil solutions can be avoided by injecting the solution extremely slowly. Following discontinuation, normal ability to conceive usually returns about 4-5 months after the last injection.

POM **Norethisterone enantate** *(WMF 18.3.1)*

Oily injection (Solution for injection), Norethisterone enantate 200 mg/ml, 1-ml ampoule.

POM **Norethisteron enantate** *(EDL 19.5.2)*
Injection, Norethisterone enantate 200 mg per ml; in 1 ml amp.

NORETHISTERONE plus ESTRADIOL

Pharmacology: The progesterone-estrogen combination acts primarily by inhibiting ovulation and altering the cervical mucus. In addition, it causes morphological and enzymatic changes in the endometrium which have the effect of rendering nidation difficult.
Indications: Hormonal contraception.
Contra-indications: Pregnancy; severe disturbances of liver function; jaundice or persistent itching during a previous pregnancy; Dubin-Johnson syndrome; Rotor syndrome; past or present liver tumours; past or present thromboembolic processes in arteries or veins and conditions which predispose to such diseases (e.g. disturbances of the clotting system with a tendency towards thrombosis, certain heart diseases); sickle-cell anaemia; present or treated cancer of the breast or the endometrium; severe diabetes with vascular changes; disturbances of lipometabolism; a history of herpes of pregnancy; otosclerosis with deterioration during pregnancy.
Precautions: Regular general medical and gynaecological examination (including the breasts and a cytological smear of the cervix) before starting treatment and at 6-monthly intervals; rule out disturbances of the clotting system; exclude pregnancy. Risk of venous and arterial thromboembolic diseases (e.g. stroke, myocardial infarction) appears to increase further when heavy smoking, increasing age and the use of combined hormonal contraceptives coincide. Rarely, malignant liver tumours leading to threatening intraabdominal haemorrhage may occur; patient should report any unusual upper abdominal complaints. Monitor patient closely for diabetes mellitus, hypertension, varicose veins, a history of phlebitis, otosclerosis, multiple sclerosis, epilepsy, porphyria, tetany, chorea minor. Breast-feeding must be stopped if the newborn is suffering from severe or persistent jaundice.
Discontinue medication if:

- Risk factors for thrombolism are present namely first time migrainous headache or frequent and unusually severe headache; sudden perceptual disorders (e.g. disturbances of vision or hearing); first signs of thrombophlebitis or thrombo-embolic symptoms (e.g. unusual pain in or swelling of the legs, stabbing pain on breathing or coughing for no apparent reason); pain and tightness in the chest; impending operations (six weeks before hand); immobilization (for instance, after accidents).
- Onset of jaundice, hepatitis, itching over the whole body, increase in frequency of epileptic seizures, significant rise in blood pressure, pregnancy.

Interactions: See Appendix 1.
Adverse effects: Rarely, headache, gastric upsets, nausea, a feeling of tension in the breasts, changes in body weight and libido or depressive moods; Break-through bleeding and amenorrhea.
Dose: *Contraception*, by deep slow IM injection (preferably intragluteal, alternatively into the upper arm), 1 ml on 1st day of a cycle; repeat doses are given regardless of the cycle pattern at intervals of 30 ± 3 days (i.e. minimum 27, maximum 33 days).
Note: Administer the IM injection slowly to avoid short lasting reactions (urge to cough, coughing fits, respiratory distress) which may occur during or immediately after the injection of oily solutions. Place a plaster over the injection site after the injection to prevent any reflux of the solution.
If the injection is extended beyound the maximum of 33 days, no adequate contraceptive cover will be available from that time onwards. If no withdrawal bleeding occurs within 30 days after an injection, pregnancy must be ruled out by means of a suitable test.
A vaginal bleeding episode will occur 1-2 weeks after the first injection. This is normal and if the treatment is continued, bleeding episodes will usually occur at 30 day intervals. The time of the monthly injection will normally be during the bleeding free interval. Ability to conceive is usually resumed within 60 days after the last injection, otherwise appropriate treatment is indicated in women who wish to become pregnant.

POM **NORIGYNON®** *(CHI/Schering)*
Injection, Norethisterone enanthate 50 mg, estradiol valerate 5 mg; oily solution in 1 ml ampoule.

11.3.2 Intrauterine contraceptive devices

Copper-bearing intrauterine contraceptive devices consist of a plastic carrier wound with copper wire or fitted with copper bands; some also have a central core of silver to prevent fragmentation of copper. Smaller devices have been introduced to

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minimize adverse effects and the replacement time for these devices is normally between 3 and 8 years. Fertility declines with age and therefore a copper intrauterine device fitted in a woman over 40 years of age, may remain in the uterus until menopause.

The intrauterine device is appropriate for women who expect to use it for continuous long-term contraception. It is suitable for older parous women; intrauterine devices should be used with caution in young nulliparous women because of the increased risk of expulsion. Young women at risk of sexually transmitted infections are also at risk of pelvic inflammatory disease.

The timing and technique of fitting an intrauterine device play a critical part in its subsequent performance and call for proper training and experience. Patients should receive full counselling backed by the manufacturer's approved leaflet. For routine contraception the device can be inserted between 4 and 12 days after the start of menstruation; for emergency contraception the device can be inserted at any time in the menstrual cycle within 5 days of unprotected intercourse. There is an increased risk of infection for 20 days after insertion and this may be related to existing lower genital tract infection. Pre-screening (at least for chlamydia and gonorrhoea) should if possible be performed. If sustained pelvic or lower abdominal pain occur during the following 20 days after insertion of the device, the woman should be treated as having acute pelvic inflammatory disease. An intrauterine device should not be removed in mid-cycle unless an additional contraceptive was used for the previous 7 days. If removal is essential (for example to treat severe pelvic infection) post-coital contraception should be considered. If the woman becomes pregnant, the device should be removed in the first trimester and the possibility of ectopic pregnancy considered; if the threads of the intrauterine device are already missing on presentation, the pregnancy is at risk of second trimester abortion, haemorrhage, pre-term delivery and infection.

EMERGENCY CONTRACEPTION

Insertion of a copper intrauterine contraceptive device is a highly effective method of emergency contraception and is more effective than hormonal methods of emergency contraception. Sexually transmitted diseases should be tested for and insertion of the device should usually be covered by antibacterial prophylaxis.

Advice To Users Of Copper T

1. How The Copper T Is Inserted And Removed

   Before insertion, your doctor will examine your pelvis to determine the size, shape and position of the uterus. An instrument called a speculum will hold your vagina open so that the cervix (the entrance to the uterus) can be seen. The cervix is then cleaned with an antiseptic solution and an instrument call a tenaculum is attached to it. This instrument assists in holding the uterus steady during insertion. The doctor will then guide a narrow instrument called a sound through the opening of the cervix into the uterus. The sound measures the depth and position of the uterus. Then your doctor will guide the copper T (with the cross arms of the T folded down) through the vagina and the cervix into the uterus. As the copper T. is inserted, the arm of the T will unfold. After the inserter is removed, the threads attached to the end of the copper T will be clipped. The threads will extend into the vaginal from the cervical opening. The tenaculum and speculum will then be removed. At various stages during this procedure, you may feel some pain, cramping, nauseated, weak or faint. At the end, you should remain lying down for a while and rise slowly to prevent fainting.

   When it is time to remove the copper T, your doctor must remove it. Its removal may cause pain or cramping. The arms of the copper T should fold upwards as it is withdrawn from the uterus.

2. Checking Your Copper T

   The Copper T can come out of the uterus (womb) without your knowing it, especially during or right after menstrual period. Therefore, at least after each menstrual period, you should check to make sure the threads can be felt at the cervix as follows:

   a) Wash your hands
   b) Squat down or seat yourself on the toilet
   c) Insert the index or middle finger into your vagina and locate your cervix. The cervix is the mouth of the uterus. It feels firm, like the tip of your nose.
   d) Feel for the threads of the copper T. The threads should extend from the cervix and be high in your vagina. The threads may be difficult to feel.
   e) If you can feel the threads, the copper T is probably, but not always, in place. You should not pull on the threads. Doing so many displace the copper T.
   f) If you cannot feel the copper T itself, it has probably been displaced from the uterus. Also if you or your partner can feel the copper T during intercourse, it is displaced. And until you can be examined by a doctor, use an alternative birth control method.

3. When To Consult Your Doctor

   Copper T is intended to prevent pregnancy. It does not protect against transmission of HIV (AIDS) and other sexually transmitted diseases such as chlamydia, genital herpes, genital warts, gonorrhoea, hepatitis B and symphillis. If you have the copper T inserted, contact your doctor immediately for any of the following reasons:

   a) A missed period may indicate pregnancy and copper T

should be removed.

b) Abnormal vaginal bleeding or discharge; a delayed period followed by scanty or irregular bleeding; pelvic or lower abdominal pain or cramps or unexplained fever; genital sores or lesion, or fever with vaginal discharge. These are symptoms of infection or ectopic pregnancy (i.e. pregnancy outside of the uterus) and require immediate treatment.

c) Tail or thread disappearance or pain during sex indicate that the copper T may have expelled or displaced, or may have perforated the uterus.

COPPER-CONTAINING IUD

Indications: Contraception; emergency contraception.

Contra-indications: Pregnancy; severe anaemia; 48 hours–4 weeks post partum; puerperal sepsis; postseptic abortion; cervical or endometrial cancer; pelvic inflammatory disease; recent sexually transmitted disease (if not fully investigated and treated); pelvic tuberculosis; unexplained uterine bleeding; malignant gestational trophoblastic disease; distorted or small uterine cavity; copper allergy; Wilson disease; medical diathermy.

Precautions: Anaemia; heavy menstrual bleeding, endometriosis, severe primary dysmenorrhoea, history of pelvic inflammatory disease, history of ectopic pregnancy or tubal surgery, fertility problems, nulliparity and young age, severely scarred uterus or severe cervical stenosis, valvular heart disease (requires antibacterial cover)—avoid if prosthetic valve or history of endocarditis; HIV infection or immunosuppressive therapy (risk of infection—avoid if marked immunosuppression); joint and other prostheses; increased risk of expulsion if inserted before uterine involution; gynaecological examination before insertion and 4–6 weeks afterwards—counsel women to see doctor promptly if significant symptoms such as pain; anticoagulant therapy; remove if pregnancy occurs (consider possibility of ectopic pregnancy).

Adverse effects: Uterine or cervical perforation, displacement, expulsion; pelvic infection exacerbated; heavy menstrual bleeding; dysmenorrhoea; pain and bleeding and occasionally epileptic seizure or vasovagal attack on insertion.

ADMINISTRATION: *Contraception* (see also notes above), the device can be inserted at any time between day 4 and day 12 after the start of menstrual bleeding; not to be fitted during heavy menstrual bleeding

Emergency contraception (see also notes above), the device may be inserted up to 120 hours (5 days) after unprotected intercourse, at any time of menstrual cycle; if intercourse has occurred more than 5 days previously, device can still be inserted up to 5 days after the earliest likely calculated day of ovulation; device can be removed at the beginning of menstruation if no longer required.

Note: Copper T must be replaced every 5 to 8 years, to maintain its contraceptive effectiveness.

POM **Copper** *(EDL 19.5.3)*
Intra-uterine device, various copper containing devices.

11.3.3 Barrier methods

BARRIER METHODS

NOTE: BARRIER METHODS ARE NOT AS EFFECTIVE IN PREVENTING CONCEPTION AS HORMONAL CONTRACEPTION AND COPPER INTRAUTERINE DEVICES. SPERMICIDAL METHODS WHEN USED ALONE ARE GENERALLY CONSIDERED RELATIVELY INEFFECTIVE AND SUCH USE IS NOT RECOMMENDED.

Indications: Contraception; for condoms, also to decrease risk of transmission of HIV and other sexually transmitted diseases.

Precautions: Oil-based products including baby oil, massage oil, lipstick, petroleum jelly, sun-tan oil can damage latex condoms and render them less effective as barrier method of contraception and as a protection from sexually transmitted infections (including HIV); if a lubricant required, use one that is water-based; male condom must be put on before the penis touches the vaginal area and the penis must not touch the vaginal area after the condom has been taken off; spermicides or diaphragm not suitable for women at high risk of HIV infection or with HIV infection.

Adverse effects: Vaginal and cervical irritation (spermicides), toxic shock syndrome (diaphragm, cap).

OTC **Barrier methods** *(WMF 18.3.3)*
Barriers, Male latex condoms, male non-latex condoms or female non-latex condoms; diaphragm or cervical caps.

OTC **VIVA® Condoms** *(Korlyns)*
Male latex condoms.

SPERMICIDES

Recommended for use together with barrier methods such as condoms and IUDs. They do not give adequate security when used alone.

11.4 Drugs for genito-urinary disorders

11.4.1 Drugs for urinary retention
11.4.2 Drugs used in urological pain
11.4.3 Drugs used in erectile dysfunction

11.4.1 Drugs for urinary retention

DOXAZOSIN

THERA.CAT: Alpha -adrenergic blocker/ vasodilator

Pharmacology: Benign prostatic hyperplasia (BPH) is a common cause of urinary outflow obstruction in aging males, and in severe cases may lead to urinary retention and renal damage. The obstructive symptoms and reduced urinary flow rate are associated with an increase in smooth muscle tone in the prostate and bladder neck, mediated by the $alpha_1$ adrenoceptor. The selective alpha-blockers such as doxazosin and prazosin decrease urethral resistance and may relieve the obstruction and BPH symptoms. Doxazosin acts within 1-2 weeks to decrease the severity of BPH symptoms and improve urinary flow rate.

Indications: Treatment of both the urinary outflow obstruction and obstructive and irritative symptoms associated with BPH. Obstructive symptoms such as hesitation, intermittency, dribbling. weak urinary stream, incomplete emptying of the bladder. Irritative symptoms include nocturia, daytime frequency, urgency, burning.

Contra-indications, Precautions, etc: See Doxazosin in Section 5.3.3.

Dose: Benign prostatic hyperplasia, initially 1 mg once daily in the a.m. or p.m.; increased if necessary at intervals of 1-2 weeks to 2 mg, 4 mg and max. 8 mg once daily.
Maintenance, usually 2-4 mg daily.

Note: Routine check on B.P. is recommended.

POM **CARDURA®** (*Pfizer*)
Tablets, Doxazosin mesylate 2 mg, 4 mg.
2 mg - 10 (blister)
4 mg - 10 (blister)

11.4.2 Drugs used in urological pain

POTASSIUM CITRATE

Indications: Relief of discomfort in mild urinary-tract infections; alkalinisation of urine.

Precautions: Renal impairment, cardiac disease, elderly.

Interactions: See Potassium salts in Appendix 1.

POM **Moko Mist Potassium Citrate** *(New Healthway)*
Solution, Potassium citrate 3 g, citric acid 0.5 g per 10 ml.
Pack - 200 ml

11.4.3 Drugs used in erectile dysfunction

SILDENAFIL

Pharmacology: Sexual stimulation produces erection of the penis via the release of nitric oxide (NO) in the corpus cavernosum. NO then activates the enzyme guanylate cyclase, which results in increased levels of cyclic guanosine monophosphate (cGMP), producing smooth muscle relaxation in the corpus cavernosum and allowing inflow of blood. Sildenafil enhances the effect of nitric oxide (NO) by inhibiting phosphodiesterase type 5 (PDE5), which is responsible for degradation of cGMP in the corpus cavernosum. Sildenafil has no direct relaxant effect on isolated human corpus cavernosum. It has no effect also in the absence of sexual stimulation.

Sildenafil is rapidly absorbed after oral administration, with absolute bioavailability of about 40%.

Time for maximum plasma concentration (Tmax) is within 30 to 120 minutes (median 60 minutes) of oral dosing in the fasted state. High fat meal will reduce the rate of absorption. Elimination is mainly by hepatic metabolism, with an active metabolite similar in properties to the parent compound. Sildenafil and its major metabolite are both approximately 96% bound to plasma proteins. Metabolites are excreted mainly in the faeces and to a lesser extent in the urine.

Indications: Treatment of erectile dysfunction.

Contra-indications: Hypersensitivity to any component of the drug. It potentiates the hypotensive effects of nitrates and concurrent administration with organic nitrates in any form should be avoided. Avoid use in newborns,

children, or women.

Precautions: Thorough medical history and physical examination are needed for proper diagnosis of erectile dysfunction (ED), determination of underlying causes and selection of appropriate treatment. Establishment of cardiovascular status of the patient is recommended before initiating any treatment for ED. Avoid co-administration with other agents used for the treatment of ED. Anatomical deformation of the penis, sickle cell anaemia, multiple myeloma, leukaemia (monitor closely). Lower doses are recommended in hepatic impairment, elderly, severe renal impairment and during concomitant use of potent cytochrome P450, 3A4 inhibitors.

Interactions: • Sildenafil metabolism is principally mediated by the cytochrome P450 3A4. Inhibitors of these isoenzymes (such as Ketoconazole, erythromycin or cimetidine) may reduce sildenafil clearance while inducers of the enzymes, such as rifampicin, will decrease plasma levels of sildenafil.

Adverse effects: Headaches, flusing, dyspepsia, nasal congestion, urinary tract infection, abnormal vision, diarrhoea, dizziness, rash. Other less common adverse events include chest pain, abdominal pain, asthenia, cardiovascular disturbances, GIT disturbances, metabolic and nutritional disorders; others are disturbances of the musculoskeletal, CNS, respiratory tract, skin, special senses and urogenital tract.

Advice to patients: Sildenafil offers no protection against sexually transmitted diseases and protective measures are necessary to guard against such including HIV.

Dose: By mouth, usually 50 mg once daily to be taken approx. 1 hour before sexual activity; may be increased to 100 mg or reduced to 25 mg once daily depending on effectiveness and tolerance. In conditions associated with increased plasma levels of sildenafil such as elderly, hepatic impairment, severe renal impairment and concomitant use of potent cytochrome P450 3A4 inhibitors, a starting dose of 25 mg once daily is recommended.

Sildenafil may be taken anywhere from 4 hours to 0.5 hour before sexual activity.

POM **VIAGRA®** *(Pfizer)*

Tablet, Sildenafil citrate 50 mg; blue, f-c, rounded-diamond-shaped tab.

50 mg - 4 (blister pack).

VARDENAFIL

Indications: Treatment of erectile dysfunction.

Contra-indications: Hypersensitivity to any of the drug's components; avoid co-administration with nitrates or nitric oxide donors (may potentiate the hypotensive effects of nitrates); avoid co-administration with HIV Protease inhibitors such as indinavir or ritonavir (which are potent inhibitors of CYP 3A4).

Precautions: Assess the cardiovascular status of patients prior to therapy (has vasodilator effects which may result in mild and transient decreases in blood pressure); patients with anatomical deformation of the penis (such as angulation, cavernosal fibrosis or Peyronie's disease) or in patients who have conditions which may predispose them to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia); avoid co-administration with other treatments for erectile dysfunction. Avoid use in severe hepatic impairment, endstage renal disease requiring dialysis, hypotension (resting systolic blood pressure of <90 mmHg), recent history of stroke or myocardial infarction (within 6 months), unstable angina, and known hereditary degenerative retinal disorders such as retinitis pigmentosa. Patients with bleeding disorders or significant active peptic ulceration. Not indicated for use in newborns, children or women.

Interactions: Vardenafil is metabolized predominantly by hepatic via cytochrome P450 (CYP) isoform 3A4, with some contribution from CYP 3A5 and CYP2C isoforms. Therefore, inhibitors of these enzymes may reduce Vardenafil clearance.

Concomitant use of potent cytochrome P450 3A4 (CYP 3A4) inhibitors viz ketoconazole, itraconazole, indinavir, or ritonavir may produce markedly increased Vardenafil plasma levels (max. dose of 5 mg Vardenafil should not be exceeded when used in combination with erythromycin, ketoconazole and itraconazole). Avoid use with dosages of ketoconazole and itraconazole higher than 200 mg.

Adverse reactions: Vardenafil was generally very well tolerated. Adverse events were generally transient and mild to moderate in nature. When Vardenafil was taken as recommended, the following adverse drug reactions were reported in placebo controlled clinical trials; headache, dizziness, flushing, erythema, nasal congestion, oedema mucosal, rhinitis, dyspepsia, nausea.

Post marketing, myocardial infarction (MI) has been reported in temporal association with the use of Vardenafil and sexual activity, but it is

not possible to determine whether MI is related to Vardenafil, or to sexual activity, to the patient's underlying cardiovascular disease, or to a combination of these factors.

Advice to patients: May take with or without food; do not drive or operate machinery until the effect of drug is established; efficacious when taken up to 4-5 hours before sexual activity.

Dose: By mouth, Usually 5-10 mg once daily approximately 25-60 minutes before sexual activity; may be increased up to a max. 20 mg once daily.

Elderly (above 65 years): Start 5 mg once daily; may be increased up to max. 20 mg once daily based on efficacy and tolerability. Renal clearance may be reduced in elderly.

Children (from birth to 16 years): Not recommended.

Hepatic impairment: Use normal dose in mild hepatic impairment and start 5 mg once daily in moderate hepatic impairment; may be increased to a max. 10 mg based on tolerability and efficacy. Not recommended in severe hepatic impairment.

Renal impairment: No dosage adjustment is needed.

POM **LEVITRA®** *(GSK)*

Tablets, Vardenafil (as monohydrochloride trihydrate) 5 mg, 10 mg, 20 mg.
5 mg - 1's; 2's; 4's; 8's; 12's.
10 mg - 1's; 2's; 4's; 8's; 12's.
20 mg - 1's; 2's; 4's; 8's; 12's.

12. Antineoplastic and immunosuppressive drugs and drugs used in palliative care

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12.1 Cytotoxic (antineoplastic) drugs
12.1.1 Alkylating drugs
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12.2 Immunosuppressive drugs
12.2.1 Cytotoxic immunosuppressants
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12.2.3 Interferons
12.3 Sex hormones and antagonists used in malignant diseases
12.4 Drugs used in palliative care

Management of Cancer involves three lines of attack: Surgery; Radiation therapy and Chemotherapy.
Chemotherapy is used as palliative measure and to prolong life. It involves the use of

1. Cytotoxic drugs
2. Steroid hormones, and
3. Immunotherapy.

The study of the cell-cycle provides a rational basis for the design of cancer treatment protocols. There are cell-cycle specific (CCS) and cell-cycle non-specific (CCNS) drugs.
CCS drugs: Asparaginase, Azathioprine, Bleomycin, MTX, Vinblastine, Vinscritine, Cytarabine.
CCNS drugs: Actinomycin D, Bleomycin, Busulfan, Carmustin, Chlorambucil, Cyclophosphamide, Daunorubicin.
Agents may be selected which exert their effects primarily in different phases of the cycle. Sequencing of drug combinations can be done to provide maximal benefits. Drug combinations provide maximal cell kill within the range of toxicity tolerated by the host for each drug and prevent or slow the development of new resistant cells. Essentially, all classes of anticancer drugs select and allow overgrowth of specifically drug–resistant neoplastic cells. This is a major cause of chemotherapeutic failure.

2.1 Cytotoxic (antineoplastic) drugs

12.1.1 Alkylating drugs
12.1.2 Cytotoxic antibiotics
12.1.3. Antimetabolites and related therapy
12.1.4 Vinca alkaloids and etoposide
12.1.5 Other antineoplastic drugs

NOTE: WHO ADVISES THAT ADEQUATE RESOURCES AND SPECIALIST SUPERVISION ARE A PREREQUISITE FOR THE INTRODUCTION OF THIS CLASS OF DRUGS. SPECIFIC EXPERTISE, DIAGNOSTIC PRECISION, INDIVIDUALIZATION OF DOSAGE OR SPECIAL EQUIPMENT ARE REQUIRED FOR THEIR PROPER USE.

The treatment of cancer with drugs, radiotherapy and surgery is complex and should only be undertaken by an oncologist. For this reason, the following information is provided merely as a guide. Chemotherapy may be curative or used to alleviate symptoms or to prolong life. Where the condition can no longer be managed with cytotoxic therapy, alternative palliative treatment (section 12.4) should be considered.

For some tumours, single-drug chemotherapy may be adequate, but for many malignancies a combination of drugs

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provides the best response. Examples of combination therapy include:

- 'CHOP' (cyclophosphamide, doxorubicin, vincristine, prednisolone) for non-Hodgkin disease;
- 'ABVD' (doxorubicin, bleomycin, vinblastine, dacarbazine) for Hodgkin disease;
- 'MOPP' (chlormethine, vincristine, procarbazine, prednisolone) for Hodgkin disease.

Cytotoxic drugs are often combined with other classes of drugs (section 12.3) in the treatment of malignant conditions. Such drugs include hormone agonists and antagonists, corticosteroids and immunostimulant drugs. Combinations are, however, more toxic than single drugs.

The following information covers drugs that have specific anti-tumour activity. However, they are toxic drugs which should be used with great care and monitoring. The specific doses and details of contraindications, precautions and adverse effects for cytotoxic drugs have been omitted from this section since treatment should be **undertaken by specialists** using agreed regimens. Health authorities may wish to formulate their own regimens on the basis of expert advice.

PRECAUTIONS AND CONTRA-INDICATIONS

Treatment with cytotoxic drugs should be initiated only after baseline tests of liver and kidney function have been performed and baseline blood counts established. It may be necessary to modify or delay treatment in certain circumstances. The patient should also be monitored regularly during chemotherapy and cytotoxic drugs withheld if there is significant deterioration in bone-marrow, liver or kidney function.

Many cytotoxic drugs are teratogenic and should not be administered during pregnancy especially in the first trimester. Contraceptive measures are required during therapy and possibly for a period after therapy has ended. Cytotoxic drugs are also contraindicated during breastfeeding.

Cytotoxic drugs should be administered with care to avoid undue toxicity to the patient or exposure during handling by the health care provider. Local policies for the handling and reconstitution of cytotoxic drugs should be strictly adhered to; also all waste, including patient's body fluids and excreta (and any material contaminated by them) should be treated as hazardous.

Extravasation of intravenously administered cytotoxic drugs can result in severe pain and necrosis of surrounding tissue. If extravasation occurs, aspiration of the drug should first be attempted, then the affected limb is elevated and warm compresses applied to speed and dilute the infusion or it is localized by applying cold compresses until the inflammation subsides; in severe cases, hydrocortisone cream may be applied topically to the site of inflammation. The manufacturer's literature should also be consulted for more specific information.

ADVERSE EFFECTS

Cytotoxic drugs have a considerable potential to damage normal tissue. Specific adverse effects apply, but a number of effects are common to all cytotoxics such as bone-marrow and immunological suppression. Furthermore, the concomitant use of immunosuppressive drugs will enhance susceptibility to infections. Fever associated with neutropenia or immunosuppression requires immediate treatment with antibiotics.

Nausea and vomiting. Nausea and vomiting following administration of cytotoxic drugs and abdominal radiotherapy are often distressing and may compromise further treatment. Symptoms may be acute (occurring within 24 hours of treatment), delayed (first occurring more than 24 hours after treatment), or anticipatory (occurring before subsequent doses). Delayed and anticipatory symptoms are more difficult to control than acute symptoms and require different management.

Cytotoxic drugs associated with a low risk of emesis include etoposide, fluorouracil, low-dose methotrexate, and the vinca alkaloids; those with an intermediate risk include low-dose cyclophosphamide, doxorubicin, and high-dose methotrexate; and the highest risk is with cisplatin, high-dose cyclophosphamide, and dacarbazine.

For patients at a low risk of emesis, pretreatment with an oral phenothiazine (for example chlorpromazine, section 1.2), continued for up to 24 hours after chemotherapy, is often helpful. For patients at a higher risk dexamethasone 6–10 mg

by mouth (section 10.3) may be added before chemotherapy. For patients at a high risk of emesis or when other therapies are ineffective, high doses of intravenous metoclopramide (section 4.5) may be used.

NOTE: HIGH DOSES OF METOCLOPRAMIDE ARE PREFERABLY GIVEN BY CONTINUOUS INTRAVENOUS INFUSION: AN INITIAL DOSE OF 2–4 MG/KG IS GIVEN OVER 15 TO 20 MINUTES, FOLLOWED BY A MAINTENANCE DOSE OF 3–5 MG/KG OVER 8 TO 12 HOURS; THE TOTAL DOSE SHOULD NOT EXCEED 10 MG/KG IN 24 HOURS.

Dexamethasone is the drug of choice for the prevention of delayed symptoms; it is used alone or with metoclopramide.

Good symptom control is the best way to prevent anticipatory symptoms and the addition of diazepam to antiemetic therapy is helpful because of its sedative, anxiolytic and amnesic effects.

Hyperuricaemia. Hyperuricaemia may complicate treatment of conditions such as non-Hodgkin lymphomas and leukaemia. Renal damage may result from the formation of uric acid crystals. Patients should be adequately hydrated and hyperuricaemia may be managed with allopurinol (section 2.2.2) initiated 24 hours before cytotoxic treatment and continued for 7 to 10 days afterwards.

Alopecia. Alopecia is common during treatment with cytotoxic drugs. There is no drug treatment, but the condition often reverses spontaneously once treatment has stopped.

12.1.1 Alkylating drugs

Alkylating drugs are among the most widely used drugs in cancer chemotherapy. They act by damaging DNA and therefore interfering with cell replication. However, there are two complications. Firstly, they affect gametogenesis and may cause permanent male sterility; in women, the reproductive span may be shortened by the onset of a premature menopause. Secondly, they are associated with a marked increase in the incidence of acute non-lymphocytic leukaemia, in particular when combined with extensive radiation therapy.

Cyclophosphamide requires hepatic activation; it can therefore be given orally and is not vesicant when given intravenously. Like all alkylating drugs its major toxic effects are myelosuppression, alopecia, nausea and vomiting. It can also cause haemorrhagic cystitis; an increased fluid intake for 24 to 48 hours will help to avoid this complication. Cyclophosphamide is used either as part of treatment or as an adjuvant in non-Hodgkin lymphomas, breast cancer, childhood leukaemia, and ovarian cancer. It is also used in several palliative regimens.

Chlorambucil is used to treat chronic lymphocytic leukaemia, non-Hodgkin lymphomas, Hodgkin disease, ovarian cancer and Waldenstrom (primary) macroglobulinaemia. Adverse effects, apart from bone marrow suppression, are uncommon. However, severe widespread rash can develop and may progress to Stevens-Johnson syndrome or toxic epidermal necrolysis. If a rash occurs, further treatment with chlorambucil is contraindicated.

Chlormethine (mustine) forms part of the regimen for treatment of advanced Hodgkin disease and malignant lymphomas. Its toxicity includes myelosuppression, severe nausea and vomiting, alopecia and thrombophlebitis due to vesicant effect.

Further information on Alkylating drugs

Busulfan is limited to chronic granulocytic leukemia, polycythemia vera and myelofibrosis with myeloid metaplasia. It has a selective myelosuprressive action, affecting primarily granulocyte production and to some extent platelets.

Melphalan is particularly useful in multiple myeloma, alone or in combination with other agents. It can be given orally and marrow toxicity is delayed. It is usually given at intervals of 4-6 weeks. Nausea, vomiting and alopecia are infrequent.

Carmustine (BCNU) and Lomustine (CCNU) are nitrosoureas used in the treatment of brain tumours and advanced Hodgkin's disease refractory to other agents. BCNU has been used to treat colon and stomach cancer. Permanent marrow damage may occur with prolonged use of these agents. Nausea and vomiting are common and moderately severe.

BUSULFAN

Pharmacology: Acts by inhibition of DNA replication like other alkylating drugs. See notes above.

Indications: Chronic myeloid leukaemia

Contra-indications: Porphyria, pregnancy,

lactation.

Precautions: May induce severe bone marrow hypoplasia (frequent blood count required); if WBC is high, give hydration and allopurinol to prevent hyperuricaemia.

Adverse effects: Bone marrow suppression and blood disorders; endocardial fibrosis; hyperpigmentation of skin, urticaria, alopecia; nausea, vomiting, diarrhoea; muscle weakness.

Advice to patients: Watch for signs of bleeding; excellent oral hygiene is needed to minimize oral discomfort.

Nursing considerations: •Give at the same time each day, on empty stomach.

•Avoid all I.M injections when platelets are below 100,000/mm^{3}.

•Observe for signs of infection (fever, sore-throat, fatigue), bleeding from gum or nose, and report to physician.

•Educate patient on good oral hygiene; maintain strict medical asepsis.

•Instruct patient to report cough and progressive dyspnoea with alveolar exudate which may be due to drug toxicity and not pneumonia; dosage may need to be adjusted.

•Encourage deep breathing exercises.

•Anticoagulants and aspirin products including ibuprofen should be used cautiously; instruct patient to avoid aspirin-containing OTC products.

•Monitor serum uric acid; allopurinol may be given with adequate hydration to prevent hyperuricaemia.

Dose: *Induction of remission*, 60 mcg per kg to max. 4 mg daily; maintenance, 0.5- 2 mg daily.

POM **Busulfan** *(EDL 8)*
Tablet, Busulfan 2 mg.

POM **MYLERAN®** *(SKG)*
Tablet, Busulfan 0.5 mg, 2 mg.
0.5 mg - 25
2 mg - 25.

CHLORAMBUCIL

Chlorambucil is a complementary cytotoxic drug.

Indications: Chronic lymphocytic leukaemia; some non-Hodgkin lymphomas; Hodgkin disease, ovarian cancer and Waldenstrom (primary) macroglobulinaemia.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; renal impairment (Appendix 4); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Advice to patients: Notify physician immediately if sore throat or bleeding occurs; contraceptive measures are recommended during therapy (Drug is potentially teratogenic).

Nursing considerations: •*See under Busulfan*.

Dose: Consult specialist literature.

POM **Chlorambucil** *(WMF 8.2)*
Tablets, Chlorambucil 2 mg.

POM **Chlorambucil** *(EDL 8)*
Tablets, Chlorambucil 2 mg, 5 mg.

POM **LEUKERAN®** *(SKG)*
Tablet, Chlorambucil 2 mg, 5 mg; both yellow tabs.
2 mg - 25
5 mg - 25.

CHLORMETHINE

Chlormethine is a complementary cytotoxic drug.

Synonym: Mustine hydrochloride

Indications: Hodgkin disease; some non-Hodgkin lymphomas; polycythaemia vera; mycosis fungoides; brain tumours, neuroblastoma.

Contra-indications: see notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Dose: Consult specialist literature.

POM **Chlormethine** *(WMF 8.2)*
Injection (Powder for solution for injection), chlormethine HCl 10-mg vial.

CYCLOPHOSPHAMIDE

Cyclophosphamide is a complementary cytotoxic drug.

Indications: Malignant lymphomas including non-Hodgkin lymphomas, lymphocytic lymphoma, Burkitt lymphoma; multiple myeloma; leukaemias, mycosis fungoides; neuroblastoma; adenocarcinoma of the ovary; retinoblastoma; breast cancer.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; renal

RETURN

impairment (Appendix 4) and hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Advice to patients: See Label 27 in Appendix 6. Drink plenty of fluids before and after doses; report any blood in urine.

Nursing considerations: •Give in the morning so that drug can be eliminated before bedtime; do not give at bedtime because voiding is too infrequent in the night to prevent cystitis..

•Avoid all I.M. injections when platelets are below 100,000/mm^3.

•Encourage adequate fluid intake and frequent voiding to help prevent haemorrhagic cystitis.

•Advise both male and female patients to use contraceptive measures during treatment and for 12 weeks after end of therapy; drug is potentially teratogenic.

•Monitor serum uric acid; allopurinol may be given with adequate hydration to prevent hyperuricaemia.

•Warn patient that alopecia, which is reversible, may occur; a wig or hairpiece may make him/her feel better.

Dose: Consult specialist literature.

POM **Cyclophosphamide** *(WMF 8.2)*
Tablets, Cyclophosphamide 25 mg.
Injection (Powder for solution for injection), Cyclophosphamide 500-mg vial.

POM **Cyclophosphamide** *(EDL 8)*
Tablets, Cyclophosphamide 25 mg, 50 mg.
Injections, Cyclophosphamide 100 mg, 500 mg, 1 g; powder in vials.

MELPHALAN

Pharmacology: Acts by inhibition of DNA replication like other alkylating drugs. See notes above.

Indications: Multiple myeloma; advanced ovarian adenocarcinoma (AOA); breast carcinoma.

Contra-indications: Hypersensitivity to melphalan; severe bone marrow depression.

Precautions: To be used only under direction of experienced physician; impaired renal function; monitor blood count and renal function.

Advice to patients: Any signs of infection, easy bruising or bleeding, shortness of breath, or painful or burning urination should be brought to physicians attention. Nausea, vomiting, or hair loss sometimes occurs; drug may cause permanent sterility and birth defects. The drug may be excreted in breast milk, therefore, an alternative form of feeding your baby should be used.

Nursing considerations: •Administer on an empty stomach because absorption is decreased by food; may give antiemetic 30-60 min prior to medication to prevent vomiting.

•Do not allow drug to come in contact with skin or mucous membrane.

•Increase fluid intake to prevent urate deposits and calculi formation.

•Instruct patient to avoid aspirin products, NSAIDs, alcohol.

•Educate patient on good oral hygiene; maintain strict medical asepsis.

•Observe for signs of infection and bleeding, and report to physician.

Dose: Adult, by mouth, *Multiple myeloma*, 0.15 mg/kg bd. wt. daily in divided doses for 4 days; to be repeated at 6 weeks intervals.

Advanced ovarian adenocarcinoma (AOA), 0.2 mg/kg bd. wt. daily for 5 days; repeat at 4-8 week intervals or as soon as peripheral blood count has recovered.

Breast carcinoma, 0.15 mg/kg bd. wt. or 6 mg/m^2 bd. surface area daily for 5 days; repeat at 6 week intervals.

POM **ALKERAN®** *(SKG)*
Tablets, Melphalan 2 mg, 5 mg.
2 mg - 25
5 mg - 25.

12.1.2 Cytotoxic antibiotics

Bleomycin is used in regimens for the treatment of Hodgkin disease and testicular cancer. It has several antineoplastic drug toxicities; it is known to cause dose-related pneumonitis and fibrosis which can be fatal, and is associated with rare acute hypersensitivity reactions. Cutaneous toxicity has also been reported.

Doxorubicin is the most widely used anthracycline antibiotic. It is used for acute leukaemias although other anthracyclines are more commonly used in these circumstances. Doxorubicin also plays a palliative role in the treatment of other malignancies. The primary toxic effects are myelosuppression, alopecia, nausea, vomiting, and dose-related cardiomyopathy. It is also vesicant and can cause severe skin ulceration on extravasation.

Dactinomycin is used to treat paediatric cancers. Its toxicity is similar to that of doxorubicin, but it is not cardiotoxic.

Daunorubicin is used in acute leukaemias.

Its toxicity is similar to that of doxorubicin.

BLEOMYCIN

Bleomycin is a complementary cytotoxic drug.

Indications: Adjunct to surgery and radiotherapy in palliative treatment of Hodgkin and non-Hodgkin lymphomas; reticulum cell sarcoma and lymphoma; carcinomas of the head, neck, larynx, cervix, penis, skin, vulva, testicles and including embryonal cell carcinoma, choriocarcinoma and teratoma; malignant effusions.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; renal impairment (Appendix 4); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Advice to patients: Hair will reappear after discontinuance of medication; maintain excellent oral hygiene habits; report any coughing, shortness of breath, or wheezing; skin rashes, shaking, chills, or transient fever may occur following administration.

Nursing considerations: •Check injection site for signs of irritation.

•Give anti-emetic 30-60 min before giving drug to reduce nausea.

•Encourage deep breathing exercises; raise HOB to facilitate breathing.

•Patients should be monitored for signs of pulmonary toxicity; check body weight at regular intervals.

•Monitor for signs of anaphylaxis; allergic reactions may be delayed for several hours, especially in patients with lymphoma.

•Inform patient that alopecia may occur, but is reversible.

•Check temperature and pulse for bleomycin-induced fever; may treat with antipyretic.

•More stable in glass bottles than in plastic I.V. bags.

Dose: Consult specialist literature.

NOTE: DOSES OF BLEOMYCIN ARE EXPRESSED IN INTERNATIONAL UNITS. 1 BLEOMYCIN UNIT IN THE USP IS EQUIVALENT TO 1000 INTERNATIONAL UNITS.

POM **Bleomycin** *(WMF 8.2)*

Injection (Powder for solution for injection), Bleomycin (as sulfate) 15 000-unit vial.

POM **Bleomycin** *(EDL 8)*

Injection, Bleomycin sulphate 15 units; powder in vial.

DACTINOMYCIN

Dactinomycin is a complementary cytotoxic drug.

Synonym: Actinomycin D; ACT.

Indications: Trophoblastic tumours, Wilm tumour, Ewing sarcoma, rhabdomyosarcoma.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Advice to patients: Notify physician of symptoms of infection viz fever, persistent sore throat, bleeding, bruising, fatigue or malaise.

Nursing considerations: •Administer by slow I.V. push over 10-15 minutes; do not give I.M or S.C.; avoid extravasation (extremely damaging to soft tissue and can lead to tissue necrosis, pain and ulceration).

•Give anti-emetic 30-60 min before giving drug to reduce nausea; increase fluid intake.

•Observe for signs of infection and bleeding, and report to physician.

•Inform patient that alopecia may occur, but is reversible; recommend wig to patient.

Management of extravasation: Stop infusion; apply ice immediately for 30-60 minutes; then alternate off/on every 15 minutes for one day.

Dose: Consult specialist literature.

POM **Dactinomycin** *(WMF 8.2)*

Injection (Powder for solution for injection), Dactinomycin 500-microgram vial.

POM **Dactinomycin** *(EDL 8)*

Injection, Dactinomycin 0.5 mg; powder in vial.

DAUNORUBICIN

Daunorubicin is a complementary cytotoxic drug.

Indications: Acute leukaemias.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; renal and hepatic impairment (Appendices 4 and 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Dose: Consult specialist literature

POM **Daunorubicin** *(WMF 8.2)*
Infusion (Powder for solution for infusion), daunorubicin (as HCl) 20-mg vial.

DOXORUBICIN

Doxorubicin HCl is a complementary cytotoxic drug.

Synonym: ADR; Hydroxydaunomycin.

Indications: Acute leukaemias; carcinomas of the breast, bladder, ovary and thyroid; neuroblastoma; Wilm tumour; non-Hodgkin and Hodgkin lymphomas; soft tissue sarcomas, osteosarcoma.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Advice to patients: Discolours urine red/orange; immediately report any change in sensation (e.g., stinging) at injection site during infusion (may be an early sign of infiltration).

Nursing considerations: •Administer by slow I.V. push into tubing of freely flowing I.V.; never give I.M. or S.C.; avoid extravasation. Local erythematous streaking along the vein and/or facial flushing may indicate too rapid a rate of administration.

•Give anti-emetic before giving drug to reduce nausea.

•Inform patient that alopecia may occur, but is reversible.

•Advise patient that orange or red urine for 1-2 days is normal and does not indicate the presence of blood.

•Monitor serum uric acid; allopurinol may be given with adequate hydration to prevent hyperuricaemia.

•Observe for signs of infection and bleeding, and report to physician.

•**Management of extravasation**: Apply ice immediately for 30-60 minutes; then alternate off/on every 15 minutes for one day.

Dose: Consult specialist literature.

POM **Doxorubicin** *(WMF 8.2)*
Injection (Powder for solution for injection), Doxorubicin HCl 10-mg vial, 50-mg vial.

POM **Adriamycin** *(EDL 8)*
Injections, Adriamycin HCl 10 mg, 50 mg; powder in vials.

EPIRUBICIN

Therapeutic category: Antineoplastic Antibiotic.

Indications: Antimitotic and cytotoxic, neoplastic conditions including breast, ovarian, gastric lymphomas, leukaemias and multiple myelomas.

Contra-indications: Marked myelosuppression, cardiac impairment; patients previously treated with max. doses of other anthracyclines.

Precautions: Protection of personnel e.g. protective clothing, good technique; advise patient against conception and breast feeding.

Adverse effects: Alopecia, mucositis, nausea and vomiting which are reversible.

Dose: See lit.

POM **Epirubicin** *(EDL 8)*
Injection, Epirubicin 10 mg, 20 mg; in vials.

12.1.3 Antimetabolites and related therapy

Cytarabine is used in the treatment of acute leukaemia; children may tolerate high doses better than adults. Its effects are highly dependent upon the schedule of administration. It causes myelosuppression, mucositis, and in high doses, central neurotoxicity.

Fluorouracil is primarily used in the adjuvant treatment of colorectal and breast cancer. It is also employed in the palliative treatment of other malignancies. It causes myelosuppression and the palmar-plantar syndrome (erythema and painful desquamation of the hands and feet). When its action is modified by other drugs (such as calcium folinate), its toxicity profile can change; mucositis and diarrhoea may be significant problems. Central neurotoxicity can also occur.

Mercaptopurine is frequently used in the therapy of childhood leukaemia. It can be administered orally and myelosuppression and nausea are the only important toxic effects.

Methotrexate is used to treat a variety of malignancies and it plays a major role as an adjuvant for the treatment of breast cancer. Like fluorouracil, methotrexate is myelotoxic, but nausea and vomiting are minimal. It also causes mucositis. Renal impairment reduces methotrexate excretion and can exacerbate toxicity.

Calcium folinate is used to counteract the folate-antagonist action of methotrexate

and thus speed recovery from methotrexate-induced mucositis or myelosuppression. Calcium folinate also enhances the effects of fluorouracil when the two are used together for metastatic colorectal cancer.

CYTARABINE

Cytarabine is a complementary cytotoxic drug.

Indications: Acute lymphoblastic leukaemia; chronic myeloid leukaemia; meningeal leukaemia; erythroleukaemia; non-Hodgkin lymphomas.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Advice to patients: Notify physician of signs of infection viz fever, sore throat, bleeding, or bruising.

Nursing considerations: •Give anti-emetic before giving drug to reduce nausea.
•Reconstituted solution is stable for 48 hours; discard cloudy reconstituted solution.
•Avoid I.M. injections in patients with thrombocytopenia to prevent bleeding.
•Observe for signs of infection and bleeding and report to physician.
•Educate patient on good oral hygiene which prevent stomatitis.
•Nausea and vomiting are more frequent in large doses; anti-emetic may be given before giving drug.
•Monitor serum uric acid; allpurinol may be given with increased fluid intake to prevent urate nephropathy.

Dose: Consult specialist literature.

POM **Cytarabine** *(WMF 8.2)*
Injection (Powder for solution for injection), Cytarabine 100-mg vial.

POM **Cytarabine** *(EDL 8)*
Injection, Cytarabine 100 mg; powder in vial.

FLUOROURACIL

Fluorouracil is a complementary cytotoxic drug.

Synonym: 5-Fluorouracil; 5FU.

Therapeutic category: Cytostatic antineoplastic.

Indications: Carcinomas of the colorectum, breast, stomach, pancreas, cervix, prostate, ovary and endometrium; liver tumours; head and neck tumours; actinic keratosis (section 15.6).

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Advice to patients: Avoid unnecessary exposure to sunlight; any signs of infection, easy bruising or bleeding, shortness of breath, or painful or burning urination should be brought to the attention of the physician. Nausea, vomiting, or hair loss sometimes occur. The drug may cause permanent sterility and may cause birth defects. The drug may be excreted in breast milk, therefore, an alternative form of feeding your baby should be used.

Nursing considerations: •Cool to body temperature before using; after vial has been entered, any unused portion should be discarded within 1 hour.
•I.V. administration is unpredictable; I.V. formulation may be given orally mixed in water, grape juice, or carbonated beverage.
•Do not refrigerate and avoid using cloudy solutions; if crystals form, redissolve by warming. Solution is more stable in plastic I.V. bags than in glass bottles.
•Avoid I.M. injection in patients with thrombocytopenia to prevent bleeding.
•Anti-emetic may be given before giving drug to prevent nausea.
•Educate patient on good and frequent oral hygiene.
•Instruct patient to avoid aspirin products or NSAIDs.
•Inform patient that alopecia may occur; recommend use of wig.
•Stomatitis and diarrhoea are signs of toxicity; discontinue therapy.
•Warn patient that alopecia, which is reversible, may occur.

Dose: Consult specialist literature.

POM **Fluorouracil** *(WMF 8.2)*
Injection (Solution for injection), Fluorouracil 50 mg/ml, 5-ml ampoule.

POM **Fluorouracil** *(EDL 8)*
Injection, Fluorouracil 50 mg per ml; in 5 ml amp.

POM **Fluoro-Uracil** *(Swipha)*
Injection, Fluorouracil 250 mg per 5 ml; colourless liquid in transparent glass amp.

POM **5 F.U-ABC®** *(Dizpharm)*
Injection, Fluorouacil 50 mg per ml; in 5 ml amp

Pack - 10.

MERCAPTOPURINE

Mercaptopurine is a complementary cytotoxic drug.

Synonym: 6-Mercaptopurine; 6-MP.

Therapeutic category: Antineoplastic Agent, Antimetabolite (Purine).

Indications: Acute leukaemias.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; renal impairment (Appendix 4) and hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Advice to patients: Should not be taken with meals; notify physician of any signs of infection, easy bruising or bleeding, shortness of breath or painful or burning urination; nausea, vomiting, or hair loss sometimes occurs. The drug may cause permanent sterility and may cause birth defects. The drug may be excreted in breast milk, therefore, an alternative form of feeding your baby should be used. Contraceptive measures are recommended during therapy.

Nursing considerations: •Give after evening meal before bedtime; encourage patient to drink 10-12 glasses of fluid daily.
•Give iron, vitamin supplements as ordered.
•Avoid I.M. injection in patients with thrombocytopenia to prevent bleeding.
•Monitor serum uric acid; allopurinol may be given with increased fluid intake to prevent hyperuricaemia.
•Instruct patient to avoid aspirin products or NSAIDs.
•Observe for signs of bleeding and infection and report to physician.
•Watch for signs of hepatic dysfunction; discontinue if liver tenderness occurs.

Dose: Consult specialist literature.

POM **Mercaptopurine** *(WMF 8.2)*
Tablets, Mercaptopurine 50 mg.

POM **Mercaptopurine** *(EDL 8)*
Tablet, Mecaptopurine 50 mg.

METHOTREXATE

Methotrexate is a complementary cytotoxic drug.

Synonym: MTX; Amethopterin.

Therapeutic category: Antineoplastic Agent, Antimetabolite; Immunosuppressant.

Indications: Carcinoma of the breast, head and neck, and lung; trophoblastic tumours; acute lymphoblastic leukaemia, meningeal leukaemia; non-Hodgkin lymphomas; advanced cases of mycosis fungoides; non-metastatic osteosarcoma; severe rheumatoid arthritis (section 2.4)

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; renal and hepatic impairment (Appendices 4 and 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Nursing considerations: •Give after evening meal before bedtime; encourage patient to drink 10-12 glasses of fluid daily.
•Avoid I.M. injection in patients with thrombocytopenia.
•Anti-emetic may be given before giving drug to prevent nausea.
•Give iron, vitamin supplements as ordered.
•Advise patient to avoid prolonged exposure to sunlight; to avoid conception during and immediately after therapy due to possible abortion or congenital anomalies.
•May discontinue drug if GI or pulmonary adverse reactions occur.
•Observe for bleeding (especially GI) and infection.
•Monitor serum uric acid; allopurinol may be given with increased fluid intake to prevent hyperuricaemia.

Dose: Consult specialist literature.

POM **Methotrexate** *(WMF 8.2)*
Tablets, Methotrexate 2.5 mg.
Injection (Solution for injection), Methotrexate (as sodium salt) 25mg/ml, 2-ml vial.

POM **Methotrexate** *(EDL 8)*
Tablet, Methotrexate (as sodium salt) 2.5 mg
Injection, Methotrexate (as sodium salt) 50 mg; powder in vial.

POM **ABITREXATE®** *(Dizpharm)*
Injection, Methotrexate 50 mg per 2 ml; in 2 ml vial.

CALCIUM FOLINATE

Calcium folinate is a complementary drug.

Indications: High-dose methotrexate therapy ('folate rescue'); inadvertent overdose of methotrexate; with fluorouracil in the palliative treatment of advanced colorectal cancer.

Precautions: Not for pernicious anaemia

or other megaloblastic anaemias due to vitamin B_{12} deficiency; pregnancy (Appendix 2); breastfeeding; **interactions**: Appendix 1.

Adverse effects: Allergic reactions; pyrexia after parenteral administration.

Dose: *Antidote to methotrexate (usually started 24 hours after methotrexate)*, by intramuscular or intravenous injection or by intravenous infusion, ADULT and CHILD up to 120 mg in divided doses over 12–24 hours, then 12–15 mg by intramuscular injection or 15 mg by mouth every 6 hours for 48–72 hours.

Methotrexate overdosage (started as soon as possible, preferably within 1 hour of methotrexate), by intravenous injection or infusion, ADULT and CHILD , dose equal to or higher than that of methotrexate, at rate not exceeding 160 mg/minute.

With Fluorouracil in colorectal cancer, consult specialist literature.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

NOTE: INTRATHECAL INJECTION OF CALCIUM FOLINATE IS CONTRAINDICATED.

POM **Calcium folinate** *(WMF 8.2)*

Tablets, Folinic acid (as calcium folinate) 15 mg.

Injection (Solution for injection), Folinic acid (as calcium folinate) 3 mg/ml, 10-ml ampoule.

12.1.4 Vinca alkaloids and etoposide

The vinca alkaloids, **vinblastine** and **vincristine**, are primarily used in the treatment of acute leukaemias. Vinblastine is also used for Hodgkin disease and some solid tumours. Vincristine is also used in the management of non-Hodgkin lymphomas. Both can cause neurotoxicity, but this is more of a problem with vincristine. Myelosuppression is more common with vinblastine.

Etoposide is an important component of the treatment of testicular carcinoma, and is also used in several regimens for lung cancers and lymphomas. It causes myelosuppression and alopecia and it can cause hypotension during infusion. It does not produce significant nausea and vomiting.

ETOPOSIDE

Etoposide is a complementary cytotoxic drug.

Indications: Refractory testicular tumours; lung cancer.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Dose: Consult specialist literature.

POM **Etoposide** *(WMF 8.2)*

Capsules, Etoposide 100 mg.

Concentrate for infusion (Concentrate for solution for infusion), Etoposide 20 mg/ml, 5-ml vial.

VINBLASTINE

Vinblastine is a complementary cytotoxic drug.

Synonym: VLB.

Indications: Disseminated Hodgkin and non-Hodgkin lymphomas; advanced testicular carcinoma, breast carcinoma; palliative treatment of Kaposi sarcoma; trophoblastic tumours; Letterer-Siwe disease.

Contra-indications: See notes above and consult specialist literature; pregnancy and breastfeeding (Appendices 2 and 3).

IMPORTANT: INTRATHECAL INJECTION IS CONTRAINDICATED.

Precautions: See notes above and consult specialist literature; hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Advice to patients: Hair may be lost during treatment but will regrow to its pretreatment extent even with continued treatment; report any bleeding; examine mouth daily and report soreness to a physician; avoid constipation, use softener for prophylaxis; notify physician of any signs of infection, easy bruising or bleeding, shortness of breath, or painful or burning urination; nausea, vomiting may occur. The drug may cause permanent sterility and may cause birth defects. The drug may be excreted in breast milk, therefore, an alternative form of feeding your baby should be used.

Nursing considerations: •Administered by I.V. only, avoid extravasation; fatal if given intrathecally.
•Anti-emetic may be given before giving drug to prevent nausea.
•Encourage deep breathing exercises; raise HOB to facilitate breathing.
•Give iron, vitamin supplements as ordered.
•Inform patient that alopecia may occur; recommend use of wig.
•Educate patient on good and frequent oral hygiene.
•Maintain adequate hydration; allopurinol may be given to prevent uric acid nephropathy; may cause sloughing upon extravasation.
•**Management of extravasation**: Mix 150 units hyaluronidase with 1 ml NS. Inject the hyaluronidase solution S.C. through 6 clockwise injections into the infiltrated area using a 25-gauge needle; change the needle with each new injection. Apply warm compress immediately for 1 hour; repeat 4 times daily for 3-5 days.
Application of cold or hydrocortisone is contraindicated.

Dose: Consult specialist literature.

NOTE: VINBLASTINE IS FOR INTRAVENOUS ADMINISTRATION ONLY. INTRATHECAL INJECTION CAUSES SEVERE NEUROTOXICITY WHICH IS USUALLY FATAL.

POM **Vinblastine** *(WMF 8.2)*
Injection (Powder for solution for injection), Vinblastine sulfate 10-mg vial.

POM **Vinblastine** *(EDL 8)*
Injection, Vinblastine sulphate 10 mg; powder in vial.

VINCRISTINE

Vincristine is a complementary cytotoxic drug.

Synonym: VCR.

Indications: Acute lymphoblastic leukaemia; neuroblastoma, Wilm tumour, Hodgkin and non-Hodgkin lymphomas; rhabdomyosarcoma, Ewing sarcoma; mycosis fungoides.

Contra-indications: See notes above and consult specialist literature; pregnancy and breastfeeding (Appendices 2 and 3).

IMPORTANT: INTRATHECAL INJECTION IS CONTRAINDICATED.

Precautions: See notes above and consult specialist literature; hepatic impairment (Appendix 5); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

NOTE: IRRITANT TO TISSUES.

Advice to patients: Maintain adequate fluid intake; rinse mouth with water 3-4 times daily, brush teeth with soft brush and floss with waxed floss; nausea, vomiting or hair loss sometimes occur; report any nerve effects to physician; stool softener should be used for constipation prophylaxis; report to physician any persistent or severe fever, sore throat, bleeding or bruising, shortness of breath.

Nursing considerations: •Administer by I.V. only; draw up the solution into a syringe and inject either directly into a vein or into the tubing of a running I.V. infusion, whichever is more suitable for the patient; injection may be completed in about 1 minute; avoid infiltration of subcutaneous tissues and if it occurs, stop the injection immediately and any remaining dose should be introduced into another vein.
•Avoid contamination of the eyes which may cause severe irritation and even corneal ulceration (accidental contamination should be washed thoroughly and immediately).
•Calculate and administer the dose carefully to avoid overdosage which may have serious or fatal outcome.
•*See also under Vinblastine*.

Dose: Consult specialist literature.

NOTE: VINCRISTINE IS FOR INTRAVENOUS ADMINISTRATION ONLY. INTRATHECAL INJECTION CAUSES SEVERE NEUROTOXICITY WHICH IS USUALLY FATAL.

POM **Vincristine** *(WMF 8.2)*
Injection (Powder for solution for injection), Vincristine sulfate 1-mg vial, 5-mg vial.

POM **Vincristine** *(EDL 10)*
Injections, Vincristine sulphate 1 mg, 2 mg, 5 mg; powder in vials.

POM **CRISTOVIN®** *(Dizpharm)*
Injection, Vincristine sulphate 1 mg; powder in vial with diluent.

POM **Vincristine** *(Dizpharm)*
Injection (Solution), Vincristine sulphate 1 mg per ml; in multidose vials of 1 ml, 2 ml and 5 ml.
Injection (Lyophilised powder), Vincristine sulphate 1 mg; in 1 mg vial plus solvent.

12.1.5 Other antineoplastic drugs

The enzyme **asparaginase** is an important component in the management of childhood leukaemia, but is not used in any other malignancy. Its toxicity profile is broad and the drug must be carefully administered because of the risk of anaphylaxis.

Cisplatin is a platinum compound used in the treatment of ovarian and testicular malignancies. It is also a component of regimens used in non-small cell and small cell lung cancer and plays a palliative role in other malignancies. Cisplatin is myelosuppressive and also produces slight alopecia. However, it causes severe dose-related nausea and vomiting. It is also

nephrotoxic and neurotoxic. Nephrotoxicity can be reduced by maintaining high urine output during cisplatin administration and immediately afterwards, but neurotoxicity is often dose-limiting.

Dacarbazine, thought to act as an alkylating drug, is a component of a regimen for Hodgkin disease. It is also used in the palliative therapy of metastatic malignant melanoma. Its major toxic effects are myelosuppression, and intense nausea and vomiting.

Levamisole is an anthelminthic with immunostimulating properties; it is used in combination with fluorouracil as adjuvant therapy for colorectal cancer following resection of the tumour. Its major toxic effects are a variety of CNS symptoms, nausea, dermatitis and hypersensitivity reactions.

Procarbazine is used in the treatment of advanced Hodgkin disease. Toxic effects include myelosuppression, nausea, vomiting, CNS symptoms and depression. Procarbazine possesses a weak monoamine oxidase inhibitory effect but dietary restriction is not necessary.

ASPARAGINASE

Asparaginase is a complementary cytotoxic drug.

Synonym: Crisantaspase

Indications: Acute lymphoblastic leukaemia.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Dose: Consult specialist literature.

POM **Asparaginase** *(WMF 8.2)*
Injection (Powder for solution for injection), asparaginase 10 000-unit vial.

CISPLATIN

Cisplatin is a complementary cytotoxic drug.

Therapeutic category: Antineoplastic Agent, Alkylating Agent.

Indications: Metastatic testicular tumours, metastatic ovarian tumours, advanced bladder carcinoma and other solid tumours.

Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).

Precautions: See notes above and consult specialist literature; renal impairment (Appendix 4); **interactions**: Appendix 1.

Adverse effects: See notes above and consult specialist literature.

Advice to patients: Drink plenty of fluids to maintain urine output; be prepared for severe nausea and vomiting following drug administration which can be delayed for up to 48 hours; notify physician of numbness or tingling in extremities or hearing loss.

Nursing considerations: •Pretreatment hydration with 1-2 L of fluid is recommended prior to cisplatin administration; adequate hydration and urinary output (more than 100 ml per hour) should be maintained for 4 consecutive hours before therapy and for 24 hours after administration.
•Nausea and vomiting may be severe and prolonged (up to 24 hours); an anti-emetic e.g metoclopramide can be started 24 hours before therapy.
•Increase fluid intake to prevent urate deposits and calculi formation.
•Instruct patient to avoid aspirin products, NSAIDs, alcohol.
•Educate patient on good oral hygiene.
•Instruct patient to report tinnitus immediately to prevent permanent hearing loss; and to also report signs of infection and bleeding.
•Withhold drug when platelets are below 100,000/mm^3 or CBC is below 4000/mm^3.
•Do not allow drug to come in contact with skin or mucous membrane; use soap and water if contact occurs.
•Observe for signs of infection and bleeding, and report to physician.
•Monitor for possible anaphylactoid reaction; monitor renal, haematologic, otic, and neurologic functions frequently.

Dose: Consult specialist literature.

POM **Cisplatin** *(WMF 8.2)*
Injection (Powder for solution for injection), Cisplatin 10-mg vial, 50-mg vial.

POM **Cisplatin** *(EDL 8)*
Injections, Cisplatin 10 mg, 50 mg; powder in vials.

POM **ABIPLATIN®** *(Dizpharm)*
Injection, Cisplatin 500 mcg per ml; in 20 ml vial.

DACARBAZINE

Dacarbazine is a complementary cytotoxic drug.

Indications: Metastatic malignant melanoma; Hodgkin disease.
Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).
Precautions: See notes above and consult specialist literature; renal and hepatic impairment (Appendices 4 and 5); **interactions**: Appendix 1.
Adverse effects: See notes above and consult specialist literature.
NOTE: IRRITANT TO TISSUES.
Dose: Consult specialist literature.

POM **Dacarbazine** *(WMF 8.2)*
Injection (Powder for solution for injection), Dacarbazine 100-mg vial.

DOCETAXEL

Indications: Treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.
Contra-indications: History of severe hypersensitivity reactions to docetaxel or polysorbate 80. Avoid use in patients with neutrophil counts below 1500 cells/mm^3.
Precautions: To be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents; all patients should be premedicated with oral corticosteroids such as dexamethasone to reduce the severity of fluid retention and hypersensitivity reactions; observe closely for hypersensitivity reactions especially during the first and second infusions; monitor blood counts frequently and adjust dose accordingly (discontinue if neutrophil count falls below 1500 cells/mm^3); avoid use in pregnancy, lactation; not recommended for use in children below 16 years ; hepatic impairment.
Interactions:
•Metabolism of docetaxel may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4, such as ciclosporin, terfenadine, ketoconazole, erythromycin.
Adverse effects: Neutropenia, leukopenia, thrombocytopenia, anaemia, toxic deaths, fever, infections,hypersensitivity reactions, fluid retention, neurotoxicity, cutaneous reactions, GI effects, alopecia, stomatitis, asthenia, myalgia, athralgia, local reaction at infusion site.
Nursing considerations: •Administer by I.V. infusion over hour under ambient room temperature and lighting conditions; put on gloves.
•Avoid contact of the drug concentrate, premix solution, or infusion solution with the skin or mucous membrane; wash off immediately and thoroughly with water if contact occurs.
•Both the drug concentrate and the diluent vial contain an overfill, for example Docetaxel 80 mg contains 94.4 mg/2.36ml in the vial while the diluent vial has 7.33 ml of diluent (to give a final premix concentration of 10 mg docetaxel per ml).
•Preparation of the Premix Solution and Infusion Solution from the Concentrate:
1. Remove the drug and the diluent vials from the refrigerator and keep at room temperature for about 5 minutes.
2. Aseptically withdraw the diluent from its vial into a syringe and transfer to the vial containing the drug concentrate.
3. Gently rotate for about 15 seconds to ensure full mixture of the concentrate and diluent.
4. The resultant premix solution (10 mg docetaxel / ml) should be clear; allow to stand for a few minutes to allow any foam formed (due to the polysorbate 80) to dissipate.
5. Aseptically withdraw the required amount of premix solution into a syringe and inject into a 250 ml infusion bag or bottle of either 0.9% NaCl solution or D_5W to produce a final concentration of 0.3-0.9 mg/ml.
6. Thoroughly mix the infusion by manual rotation.
7. Inspect the resultant infusion solution for particulate matter or discolouration prior to administration.
•Discard the premix solution or infusion solution if it is not clear or appears to have precipitate.
•Avoid contact of the drug concentrate with plasticised PVC equipment or devices.
•Store drug in a refrigerator at 2° to 8°C, and protect from bright light. Freezing does not adversely affect the product.
Dose: By I.V. infusion (over 1 hour), 60-100 mg/m^2 every 3 weeks.
Note: **Premedication Regimen** - Dexamethasone 16 mg per day (e.g., 8 mg b.i.d) for 3 days, starting on the day before each course of docetaxel.

POM **TAXOTERE®** *(May & Baker)*
Concentrate for I.V. infusion, Docetaxel 40 mg per ml; in 2 ml vial plus 13% ethanol in Water for Injection as diluent.

LEVAMISOLE

Levamisole is a complementary drug.
Indications: With fluorouracil for the treatment of colorectal carcinoma after complete resection of primary tumour; intestinal nematode infections (section 9.4.1.2).
Contra-indications: See notes above and consult specialist literature; breastfeeding (Appendix 3).
Precautions: See notes above and consult specialist literature; pregnancy (Appendix 2); **interactions**: Appendix 1.

Adverse effects: Abdominal pain, nausea, vomiting, dizziness, headache.
Dose: Consult specialist literature.

POM **Levamisole** *(WMF 8.2)*
Tablets, Levamisole (as HCl) 50 mg.

PROCARBAZINE

Procarbazine is a complementary cytotoxic drug.
Indications: Part of MOPP regimen in Hodgkin and non-Hodgkin lymphomas.
Contra-indications: See notes above and consult specialist literature; pregnancy (Appendix 2) and breastfeeding (Appendix 3).
Precautions: See notes above and consult specialist literature; renal and hepatic impairment (Appendices 4 and 5); **interactions**: Appendix 1.
Adverse effects: See notes above and consult specialist literature.
Advice to patients: Avoid food with high tyramine content; do not take any new prescription or OTC drug without consulting your physician or pharmacist; avoid alcohol and alcohol containing products including topicals; notify physician of persistent fever, sore throat, bleeding or bruising; may impair judgement and coordination; avoid prolonged exposure to sunlight.
Nursing considerations: •Administer in divided doses and at bedtime to minimize nausea and vomiting; give nonphenothiazine antiemetic before and after treatment as ordered to prevent vomiting.
•Warn patient not to drink alcoholic beverages while taking this drug.
•Instruct patient to stop medication and report to doctor immediately if disulfiram-like reaction occurs namely chest pains, rapid or irregular heartbeat, severe headache and stiff neck.
•Avoid co-administration with other MAOIs, TCAs, or foods with high tyramine content; procarbazine inhibits MAO and can cause disulfiram-like reaction if given with these drugs.
•Avoid all I.M. injections in patients with thrombocytopenia
•Warn patient to avoid hazardous activities that require alertness until the CNS effects of drug are known.
•Inform patient that alopecia may occur; recommend use of wig.
•Observe for signs of infection and bleeding, and report to physician.

Dose: Consult specialist literature.

POM **Procarbazine** *(WMF 8.2)*
Capsules, Procarbazine (as HCl) 50 mg.

POM **Procarbazine** *(EDL 8)*
Capsule, Procarbazine HCl 50 mg.

12.2 Immunosuppressive drugs

12.2.1 Cytotoxic immunosuppressants
12.2.2 Corticosteroids and other immunosuppressants
12.2.3 Interferons

NOTE: WHO ADVISES THAT THIS CLASS OF DRUGS IS FOR USE ONLY WHEN ADEQUATE RESOURCES AND SPECIALIST CARE ARE AVAILABLE. SPECIFIC EXPERTISE, DIAGNOSTIC PRECISION, INDIVIDUALIZATION OF DOSAGE OR SPECIAL EQUIPMENT ARE REQUIRED FOR THEIR PROPER USE.

Immunosuppressive drugs are used in organ transplant recipients to suppress rejection; they are also used as second-line drugs in chronic inflammatory conditions. Treatment should only be initiated by a specialist. Careful monitoring of blood counts is required in patients receiving immunosuppressive drugs and the dose should be adjusted to prevent bone-marrow toxicity. Immunosuppressed patients are particularly prone to atypical infections.

12.2.1 Cytotoxic immunosuppressants

Azathioprine is the most widely used drug in transplant recipients. It is useful when corticosteroid therapy alone has proven inadequate or for other conditions when a reduction in the dose of concurrently administered corticosteroids is required. It is metabolized to mercaptopurine and, as with mercaptopurine, doses need to be reduced when given with allopurinol. The predominant toxic effect is myelosuppression, although hepatic toxicity also occurs.

AZATHIOPRINE

Azathioprine is a complementary immunosuppressive drug.
Therapeutic category: Immunosuppressant antimetabolite
Indications: To prevent rejection in transplant recipients; rheumatoid arthritis (section 2.1.2); inflammatory bowel disease (section 4.7).
Contra-indications: Hypersensitivity to azathioprine and mercaptopurine; breastfeeding (Appendix 3).
Precautions: Monitor for toxicity throughout treatment; full blood counts necessary every week (or more frequently with higher doses and in renal or hepatic

impairment) for first 4 weeks of treatment, and at least every 3 months thereafter; reduce dose in elderly; pregnancy (Appendix 2); renal impairment (Appendix 4); liver disease (Appendix 5); **interactions**: Appendix 1.

BONE MARROW SUPPRESSION: PATIENTS SHOLD BE WARNED TO REPORT IMMEDIATELY ANY SIGNS OR SYMPTOMS OF BONE MARROW SUPPRESSION, FOR EXAMPLE UNEXPLAINED BRUISING OR BLEEDING, INFECTION.

Adverse effects: Hypersensitivity reactions including malaise, dizziness, vomiting, fever, muscular pains, arthralgia, rash, hypotension or interstitial nephritis call for immediate withdrawal; haematological toxicity includes leukopenia and thrombocytopenia (reversible upon withdrawal); liver impairment, cholestatic jaundice; hair loss; increased susceptibility to infections and colitis in patients also receiving corticosteroids; nausea; rarely pancreatitis, pneumonitis, hepatic veno-occlusive disease.

Advice to patients: Take with meals; response in rheumatoid arthritis may not occur for up to 3 months; do not stop taking without the physician's approval, do not have any vaccinations before checking with your physician; notify your physician if you have a persistent sore throat, unusual bleeding or bruising, or fatigue.

Nursing considerations: •Give with meals to reduce GI upset.

•Give IV only if oral route is not possible; IM inj may cause bleeding and should be avoided.

•Advise patient to use soft toothbrush to prevent bleeding.

•Monitor blood tests; discontinue drug if leukocytes <3000/mm^3 or platelets <100,000/mm^3.

•Observe for signs of infection and report to physician.

Dose: *Transplant rejection*, by mouth or by intravenous injection (over at least 1 minute and followed by 50 ml sodium chloride intravenous infusion)or by intravenous infusion, ADULT up to 5 mg/kg on day of surgery, then reduced to 1–4 mg/kg daily according to response for maintenance.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

NOTE: INTRAVENOUS INJECTION IS ALKALINE AND VERY IRRITANT; THE INTRAVENOUS ROUTE SHOULD THEREFORE ONLY BE USED IF ORAL ADMINISTRATION IS NOT POSSIBLE.

POM **Azathioprine** *(WMF 8.1)*
Tablets, Azathioprine 50 mg.
Injection (Powder for solution for injection), Azathioprine (as sodium salt), 100-mg vial

POM **Azathioprine** *(EDL 8)*
Tablet, Azathioprine 50 mg
Injection, Azathioprine (as sodium salt) 50 mg; powder in vial.

POM **IMURAN®** *(GSK)*
Tablets, Azathioprine 25 mg, orange f-c scored tab marked 'L3C'; 50 mg, yellow f-c scored tab marked 'WELLCOME K7A'.
Injection, Azathioprine (as sodium salt) 50 mg; yellow to amber coloured powder in clear glass vial.

Dose: *Transplantation*, adult and child by mouth or I.V. up to 5 mg/kg b.wt daily on first day, depending on immuno suppressive regimen used.
Maintenance, 1-4 mg/kg b.wt daily; adjusted according to clinical requirements and haematological tolerance.
Treatment should be continued indefinitely because of the risk of graft rejection.
Other conditions, adult and child, initially 1-3 mg/kg b.wt daily; to be adjusted within these limits accordingly. Treatment may be withdrawn if no improvement occurs within 3 months.
Maintenance, between 1 mg/kg or less to 3 mg/kg b.wt daily.

Note: Azathioprine injection should be used only when the oral route is impractical and should be discontinued as soon as oral therapy is tolerated. Specialist medical literature should be consulted for guidance as to clinical experience in particular conditions. In patients with renal and/or hepatic insufficiency, dosages should be given at the lower end of the normal range.

12.2.2 Corticosteroids and other immunosuppressants

Ciclosporin is a potent immunosuppressant which is virtually free of myelotoxic effects, but is markedly nephrotoxic. It is particularly useful for the prevention of graft rejection and for the prophylaxis of graft-versus-host disease. The dose is adjusted according to plasma-ciclosporin concentrations and renal function. Dose-related increases in serum creatinine and blood urea nitrogen (BUN) during the first few weeks may necessitate dose reduction.

Corticosteroids have significant

immunosuppressant activity and can also be used to prevent rejection of organ transplants.

The corticosteroids **prednisolone**, **dexamethasone** and **hydrocortisone** are synthetic hormones given at pharmacological doses particularly for haematological malignancies. Although there is no evidence for therapeutic superiority, prednisolone is used more commonly than dexamethasone or hydrocortisone (section 8.3); prednisolone is an important component of curative regimens for lymphomas and childhood leukaemias and elsewhere it has a palliative role. However, chronic use leads to the development of a cushingoid syndrome.

CICLOSPORIN

Ciclosporin is a complementary immunosuppressive drug.

Synonym: Cyclosporin

Therapeutic category: Immunosupressive agent.

Indications: Rejection in kidney, liver, heart or bone-marrow transplantation; graft-versus-host disease.

Precautions: Monitor kidney function (dose dependent increase in serum creatinine and urea during first few weeks may necessitate dose reduction, exclude rejection if kidney transplant, also Appendix 4); monitor liver function (adjust dosage according to bilirubin and liver enzymes, also Appendix 5); monitor blood pressure (discontinue if hypertension cannot be controlled by antihypertensives); monitor serum potassium, particularly if marked renal impairment (risk of hyperkalaemia); monitor serum magnesium; hyperuricaemia; measure blood lipids before and during treatment; avoid in porphyria; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.

Adverse effects: Dose-related and reversible increases in serum creatinine and urea unrelated to tissue rejection; burning sensation in hands and feet during initial therapy; electrolyte disturbances including hyperkalaemia, hypomagnesaemia; hepatic dysfunction; hyperuricaemia; hypercholesterolaemia; hyperglycaemia, hypertension (especially in heart transplant patients); increased incidence of malignancies and lymphoproliferative disorders; increased susceptibility to infections due to immunosuppression; gastrointestinal disturbances; gingival hyperplasia; hirsutism; fatigue; allergic reactions; thrombocytopenia (sometimes with haemolytic uraemic syndrome); also mild anaemia, tremors, convulsions, neuropathy; dysmenorrhoea or amenorrhoea; pancreatitis, myopathy or muscle weakness; cramp; gout; oedema; headache.

Advice to patients: To mask taste, mix oral solution with milk, chocolate drink, cola, or orange juice immediately before taking (and rinse with more to ensure total dose); stir well and drink at once; take dose at the same time each day. Do no mix with grapefruit juice. Do not use plastic cup. Keep medicine measure away from other liquids (including water).

Nursing considerations: •Give dosage once daily in the morning and encourage patient to do so at the same time, each day.

•Do not administer from plastic cup; use a glass container instead to minimize adherence to container walls.

•Mixing with milk, chocolate drink, cola, or orange juice preferably at room temperature, improves palatability; stir well; do not allow to stand before drinking; rinse with more diluent to ensure that the total dose is taken; after use, dry outside of pipette; do not rinse mouth with water or other cleaning agents; may cause inflamed gums.

•Advise patient to take drug with meals if nausea occurs; anorexia, nausea and vomiting are transient, occuring frequently at the start of therapy.

•Stress that drug should not be withdrawn without doctor's knowledge.

•To prevent thrush, patient should swish and swallow nystatin 4 times daily as ordered.

Dose: NOTE: LOWER DOSES ARE REQUIRED WHEN CICLOSPORIN IS USED WITH OTHER IMMUNOSUPPRESSANTS.

Organ transplantation, by mouth, ADULT and CHILD over 3 months 10–15 mg/kg 4–12 hours before surgery, then 10–15 mg/kg daily for 1–2 weeks, reducing to 2–6 mg/kg daily for maintenance (adjust dose according to blood concentration and kidney function).

Organ transplantation, by intravenous infusion over 2–6 hours, ADULT and CHILD one-third of the corresponding dose by mouth.

Bone marrow transplantation, graft-versus-host disease, by mouth, ADULT and CHILD over 3 months 12.5–15 mg/kg daily for 2 weeks, starting on day before surgery, followed by 12.5 mg/kg daily for 3–6 months, then gradually tailed off (may

take up to 1 year after transplant)
Bone marrow transplantation, graft-versus-host disease, by intravenous infusion over 2–6 hours, ADULT and CHILD over 3 months 3–5 mg/kg daily for 2 weeks, starting on day before surgery, followed by maintenance by mouth.

CONVERSION: ANY CONVERSION BETWEEN BRANDS SHOULD BE UNDERTAKEN VERY CAREFULLY, AND THE MANUFACTURER CONSULTED FOR FURTHER INFORMATION
DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.
NOTE: CONCENTRATE FOR INFUSION CONTAINS POLYETHOXYLATED CASTOR OIL, WHICH HAS BEEN ASSOCIATED WITH ANAPHYLAXIS; OBSERVE PATIENT FOR 30 MINUTES AFTER STARTING INFUSION, AND THEN AT FREQUENT INTERVALS.

POM **Ciclosporin** *(WMF 8.1)*
Capsules, Ciclosporin 25 mg
Concentrate for infusion (Concentrate for solution for infusion), Ciclosporin 50 mg/ml, 1-ml ampoule.

POM **Ciclosporin** *(EDL 8)*
Oral solution, Ciclosporin 100 mg per ml
Injection, Ciclosporin 50 mg per ml.

POM **SANDIMMUN®** *(Novartis)*
Oral solution, Ciclosporin 100 mg per ml; yellow oily solution.
Pack - 50 ml.
Concentrate for IV Infusion, Ciclosporin 50 mg per ml; oily solution in amps. To be diluted before use.
Pack - 10 x 1 ml
Pack - 10 x 5 ml.

DEXAMETHASONE

Indications: Diagnosis of Cushing's disease; congenital adrenal hyperplasia; cerebral oedema
Precautions: Perineal irritation may occur after intravenous administration of the phosphate ester.
Nursing considerations: *See Dexamethasone in Section 10.3*.
Dose: 0.5-2 mg daily in divided doses;
Adrenal hyperplasia, 0.5-1.5 mg daily in divided doses.

POM **Dexamethasone** *(EDL 8)*
Tablets, Dexamethasone 0.5 mg, 4 mg.
Injection, Dexamethasone (as sodium phosphate) 4 mg per ml.

See section 10.3 for the proprietory Preparations

PREDNISOLONE

Prednisolone is a representative corticosteroid. Various drugs can serve as alternatives.
Prednisolone is a complementary drug for the treatment of malignant neoplasms.
Indications: With antineoplastic drugs for acute lymphoblastic and chronic lymphocytic leukaemias, Hodgkin disease, and non-Hodgkin lymphomas; inflammatory and allergic reactions (sections 8.3 and 10.3); eye (section 13.2)
Contra-indications: Untreated bacterial, viral, and fungal infections; avoid live virus vaccines.
Precautions: Monitor body weight, blood pressure, fluid and electrolyte balance, and blood glucose concentration throughout treatment; adrenal suppression during and for some months after withdrawal—intercurrent infection or surgery may require increased dose of corticosteroid (or temporary reintroduction if already withdrawn); quiescent amoebiasis, strongyloidiasis, or tuberculosis possibly reactivated; increased severity of viral infections, particularly chickenpox and measles—passive immunization with immunoglobulin required; hypertension, recent myocardial infarction, congestive heart failure; renal impairment; hepatic impairment (Appendix 5); diabetes mellitus; osteoporosis; glaucoma; severe psychosis, epilepsy; peptic ulcer; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.
Adverse effects: Gastrointestinal effects including dyspepsia, oesophageal ulceration, development of or aggravation of peptic ulcers, abdominal distension, acute pancreatitis; increased appetite and weight gain; adrenal suppression with high doses, leading to cushingoid symptoms (moon face, acne, bruising, abdominal striae, truncal obesity, muscle wasting); menstrual irregularities and amenorrhoea; hypertension; osteoporosis, with resultant vertebral collapse and long-bone fractures; avascular osteonecrosis; ophthalmic effects including glaucoma, subcapsular cataracts, exacerbation of viral or fungal eye infections; diabetes mellitus; thromboembolism; delayed tissue healing; myopathy, muscle weakness of arms and legs; depression, psychosis, epilepsy; raised intracranial pressure; hypersensitivity reactions.
Nursing considerations: *See Prednisolone in Section*

10.3.

Dose: *Leukaemias and lymphomas*, by mouth, ADULT initially up to 100 mg daily, then gradually reduced if possible to 20–40 mg daily; CHILD up to 1 year, initially up to 25 mg, then 5–10 mg; 2–7 years, initially up to 50 mg, then 10–20 mg; 8–12 years, up to 75 mg, then 15–30 mg.

POM **Prednisolone** *(WMF 8.3)*
Tablets, Prednisolone 5 mg, 25 mg.

POM **Prednisolone** *(EDL 8)*
Tablet, Prednisolone 5 mg.
Injections, Prednisolone (as sodium phosphate or sodium succinate) 20 mg, 25 mg per ml; in vials.

See Proprietary Preparations in section 10.3

12.2.3 Interferons

Interferons are naturally occurring proteins which affect the immune response as well as the cell function. There are alfa, beta and gamma interferons.

Interferon alfa-2a *(Roferon-A®)* is a highly purified sterile protein consisting of 165 aminoacids. It is produced by DNA recombinant technology. Following binding to specific cell membrane receptor, transcytoplasmic signals initiate the appearance of up to 15 major new protein species in the cytoplasm, the products of interferon inducible genes. These lead to morphological and behavioural changes in cells which include gene activation, modulation of cell growth and division and modulation of the cells of the immune system.

INTERFERON ALFA–2A

Indications: Hairy cell leukaemia (HCL), cutaneous T-cell lymphoma (CTCL), chronic myelogenous leukaemia (CML), multiple myeloma, thrombocytosis in CML, thrombocytosis in myeloproliferative diseases other than CML, low-grade non-Hodgkin's lymphoma (NHL), AIDS-related kaposis's sarcoma (KS), renal cell carcinoma, malignant melanoma, chronic active hepatitis-B, chronic hepatitis-C, condylomata acuminata.

Contra-indications: Hypersensitivity to recombinant interferon alfa-2a or any component of the preparation; severe cardiac disease or any history of cardiac illness; severe renal, hepatic or myeloid dysfunction; seizure disorders and/or compromised CNS function; chronic hepatitis with advanced, decompensated hepatic disease or cirrhosis of the liver; chronic hepatitis in patients who are being or have recently been treated with immunosuppressive agents, excluding short-term "steroid withdrawal"; CML patients who have an HLA-identical relative and for whom allogeneic bone marrow transplantation is planned or possible in the immediate future.

Precautions: Administration should be under the supervision of a qualified physician experienced in the management of the respective indications. Mild to moderate renal, hepatic or myeloid dysfunction (close monitoring of these functions is required); careful periodic neuropsychiatric monitoring of all patients is recommended; suppressive effect on bone marrow in patients with severe myelosuppression; therapeutic immunosuppression may be weakened in transplant patients; children (safety and effectiveness not yet established); neurotoxicity, haematotoxicity or cardiotoxic effects of previously or concurrently administered centrally-acting drugs may be increased; pregnancy (to be used only if the benefit to the woman justifies the potential risk to the foetus); breast-feeding (not yet established whether it is excreted in human milk).

Interactions: •Theophylline (its metabolism is inhibited leading to enhanced effect).

Adverse effects: Flu-like symptoms; reactivation of peptic ulcer and non-life-threatening GI bleeding; rarely, hepatitis, pulmonary oedema, CHF, cardiorespiratory arrest and myocardial infarction; severe somnolence, coma, cerebrovascular adverse events, transient impotence and ischaemic retinopathy are rare complications; rarely, cardiovascular problems in patients with hepatitis-B; transient leukopaenia in about one third to over one half of cancer patients; thrombocytopenia and decrease of haemoglobin in non-myelosuppressed patients. Recovery of severe haematological deviations to pretreatment levels usually occurs within 7-10 days after discontinuing treatment.

Nursing considerations: •Administer at bedtime to minimize daytime drowsiness.
•Use S.C. route in patients with platelets count below 50,000/mm^3; inspect injection site and skin for signs of bruising.
•Ensure patient is properly hydrated especially during the early stage of therapy.
•Paracetamol may be given to minimize flu-like symptoms experienced by almost all patients.
•Instruct patient on proper oral hygiene during treatment, because the suppressive effect of the drug on

RETURN

bone marrow may cause microbial infection, delayed healing, and gingival bleeding. Interferon may also decrease salivary flow.

•Co-administration with a live vaccine may potentiate replication of vaccine virus, increase adverse reactions, and decrease patient's antibody response; advise patient to inform the doctor before having any immunization.

•Reassure patient that loss of hair is temporary and normal growth of hair will resume when drug is stopped.

•Monitor for CNS adverse reactions such as decreased mental status and dizziness; careful periodic neuropsychiatric monitoring of all patients is recommended.

•Store drug in a refrigerator; use reconstituted solution within 30 days.

Dose: By S.C. or I.M. injection, *HCL*, initially, 3 m.i.u. daily for 16-24 weeks; maintenance, 3 m.i.u. thrice weekly.

CTCL, initially, 18 m.i.u. daily for 12 weeks; maintenance, thrice weekly injections at doses acceptable to patient, but not exceeding 18 m.i.u.

CML, initially, 9 m.i.u. daily for 8-12 weeks or for a max. of 18 months; for patients with complete haematological response, continue with 9 m.i.u. daily or thrice weekly (minimum) - optimum duration yet to be determined.

Multiple Myeloma, 3 m.i.u. thrice weekly indefinitely unless rapid progression or severe intolerance develops.

Thrombocytosis in CML, initially as for CML.

Thrombocytosis in other myeloproliferative diseases, 6 m.i.u. daily for up to 30 days; maintenance, 1-3 m.i.u. 1-3 times daily.

Low grade NHL, concomitantly with chemotherapy, 6 m.i.u./sq. m from day 22-26 of each 28-day cycle; or as maintenance after chemotherapy (usually after 4-6 weeks), 3 m.i.u. thrice weekly for at least 12 months.

AIDS-related KS, initially, 18-36 m.i.u. for 12 weeks; maintenance, thrice weekly injections at dose acceptable to patient, but not exceeding 36 m.i.u. for 12 weeks - optimum duration yet to be determined.

Renal cell carcinoma, initially, when used with Vinblastine, 18 m.i.u. thrice weekly for 8-12 weeks; maintenance with Vinblastine, 18 m.i.u. (max.) thrice weekly.

Malignant melanoma, initially, 18 m.i.u. thrice weekly for 8-12 weeks; maintenance, 18 m.i.u. thrice weekly or at max. dose acceptable to patient - optimum duration yet to be determined.

Chronic active Hepatitis-B, 2.5-5 m.i.u./sq. m thrice weekly for 4-6 months.

Chronic Hepatitis-C, initially 6 m.i.u. thrice weekly for 3 months; maintenance, patients whose ALT has normalised should then receive 3 m.i.u. thrice weekly for another 3 months.

Condylomata acuminata, 1-3 m.i.u. thrice weekly for 1-2 months.

POM **ROFERON–A®** *(Swipha)*
Injections, Interferon alfa-2a (rbe) 4.5, 9 million i.u.; powder for reconstitution in vials. All with syringes, needles and ampoules containing 1 ml sterile water for injection. Pack - 1 x 5.

12.3 Sex hormones and antagonists used in malignant diseases

Tamoxifen is an estrogen-receptor antagonist. Its important role in breast cancer is use after surgery and for palliative management in patients with advanced disease. When given at recommended doses, it has few adverse effects, although, it can induce uterine endometrial malignancies.

Diethylstilbestrol, a synthetic estrogen, is used to manipulate the hormonal environment in patients with hormone-sensitive tumours (for example breast and testes). It has few significant adverse effects in women but in men it causes gynaecomastia, and, more importantly, increases the risk of cardiovascular disease. For breast cancer diethylstilbestrol has been superseded by tamoxifen but it can be used for its anti-androgen effect in prostate cancer as an adjunct or for palliation.

DIETHYLSTILBESTROL

Therapeutic category: Synthetic estrogen

Indications: Carcinoma of the prostate; breast cancer.

Contra-indications, Precautions, etc.: See Diethylstilboestrol in Section 10.4.1.

Dose: By mouth, *Breast cancer*, 10-20 mg daily.

Prostate cancer, 1-3 mg daily.

POM **Diethylstilboestrol** *(EDL 8)*
Tablets, Diethylstilboestrol 1 mg, 5 mg, 25 mg.

TAMOXIFEN

Tamoxifen is a complementary drug for the

treatment of breast cancer.

Therapeutic category: Estrogen antagonist.

Indications: Adjuvant treatment of estrogen-receptor-positive breast cancer; metastatic breast cancer.

Contra-indications: Pregnancy (exclude before treatment and advise non-hormonal contraception if appropriate, see also Appendix 2); breastfeeding (Appendix 3).

Precautions: Monitor for endometrial changes (increased incidence of hyperplasia, polyps, and cancer); cystic ovarian swellings in premenopausal women; increased risk of thromboembolism when used with antineoplastic drugs; avoid in porphyia; **interactions**: Appendix 1.

Adverse effects: Hot flushes; endometrial changes (symptoms such as vaginal bleeding and other menstrual irregularities, vaginal discharge, pelvic pain require immediate investigation); increased pain and hypercalcaemia with bony metastases; tumour flare; nausea and vomiting; liver enzyme changes (rarely cholestasis, hepatitis, hepatic necrosis); hypertriglyceridaemia (sometimes with pancreatitis); thromboembolic events; decreased platelet count; oedema; alopecia; rash; headache; visual disturbances including corneal changes, cataracts, retinopathy; rarely interstitial pneumonitis, hypersensitivity reactions including angioedema, Stevens-Johnson syndrome, bullous pemphigoid.

Advice to patients: Report any vomiting that occurs after taking dose; patient should be adivsed to notify their physician of vaginal bleeding, weakness, mental confusion; increased bone and tumour pain and local disease flare may occur with start of therapy.

Nursing considerations: •Give after evening meal before bedtime; increase fluid intake to prevent dehydration.

•Anti-emetic may be given before giving drug to prevent nausea.

•Give iron, vitamin supplements as ordered.

•Reassure patient that increased bone pain during tamoxifen therapy usually indicates a good therapeutic response; give analgesic to relieve pain.

•Inform patient that alopecia may occur but it is temporary; recommend use of wig.

Dose: *Breast cancer*, by mouth, ADULT
20 mg daily.

POM **Tamoxifen** *(WMF 8.3)*
Tablets, Tamoxifen (as citrate) 10 mg, 20 mg.

POM **Tamoxifen** *(EDL 8)*
Tablets, Tamoxifen 10 mg, 20 mg.

POM **APO-TAMOX®** *(Lahams)*
Tablet, Tamoxifen citrate 20 mg; off-white tab. marked 'APO T20'.
20 mg-100.

POM **NOLVADEX®** *(Reals)*
Tablet, Tamoxifen (as citrate)10 mg; white round, bionvex tab marked 'NOLVADEX 10 and ICI'.

POM **NOLVADEX-D®** *(Reals)*
Tablets, Tamoxifen (as citrate) 20 mg; white, octagonal biconvex tab marked 'NOLVADEX–D AND ICI'.

POM **Tamoxifen** *(Dizpharm)*
Tablets, Tamoxifen (as citrate) 10 mg, 20 mg
10 mg - 30
20 mg - 30.

FINASTERIDE

Therapeutic category: Antiandrogen.

Pharmacology: The development of the prostate gland and subsequent benign prostatic hyperplasia (BPH) is dependent upon conversion of testosterone to dihydrotestosterone (DHT) within the prostrate. Finasteride belongs to a class of specific inhibitors of 5-alpha reductase, an intracellular enzyme which metabolises testosterone into the more potent androgen, DHT. Finasteride has no affinity for the androgen receptor.

Indications: Treatment and control of benign prostatic hyperplasia (BPH) to cause regression of the enlarged prostate, improve urinary flow, and improve the symptoms associated with BPH.

Contra-indications: Hypersensitivity to finasteride; women who are or may become pregnant; children.

Precautions: Monitor for obstructive uropathy in patients with large residual urine volume and/or severely diminished urinary flow. Perform digital rectal examination and other evaluations for prostate cancer on patients with BPH before initiating therapy and periodically thereafter.

Adverse effects: Impotence, decreased lipido, decreased volume of ejaculate, breast tenderness and enlargement, hypersensitivity reactions including lip swelling and skin rash.

Nursing considerations: •Administer with or without meals.

•Drug may have adverse effect on developing male foetus; advise pregnant women to avoid contact with drug or semen of a patient taking this medication.

•Therapeutic response may take 3-6 months including increased urinary flow, hair growth.

Dose: By mouth, Adult, 5 mg daily with or without food.
Not recommended for children.

POM **PROSCAR®** (*Bolax/BPP*)
Tablet, Finasteride 5 mg; blue, apple-shaped, f-c tab. marked 'PROSCAR' on one side and 'MSD 72' on the other.

GOSERELIN ACETATE

Therapeutic category: Antineoplastic agent; Luteinizing Hormone-Releasing Hormone (LHRH) Analogue.

Pharmacology: Goserelin is a synthetic analogue of naturally occurring LHRH also known as gonadotropin-releasing hormone (GnRH) incorporated into a biodegradable depot material which allows for continuous slow release over 28 days. Continuous daily administration results in suppression of ovarian and testicular steroidogenesis due to decreased levels of LH and FSH with subsequent decrease in testosterone (male) and oestrogen (female) levels. This suppression leads to prostate tumour regression and symptomatic improvement in the majority of patients.

Goserelin is inactive when administered orally. Absorption is rapid when administered subcutaneously and it can be detected in the serum in 10 minutes. Time to peak serum concentration is about 12-15 days.

Indications: Management of prostate cancer, breast cancer in premenopausal and perimenopausal women, endometriosis; uterine fibroids (in conjunction with iron therapy in the haematological improvement of anaemia patients with fibroids prior to surgery); prethinning of the endometrium prior to endometrial ablation or resection.

Assisted reproduction: Pituitary down regulation in preparation for superovulation.

Contra-indications: Hypersensitivity to the drug or other LHRH analogues; pregnancy or lactation; Children.

Precautions: Worsening of signs and symptoms especially cancer-related pain during the first few weeks of treatment (usually controlled by analgesics); ureteral obstruction and spinal cord compression in men (monitor carefully during the first month of therapy); women with metabolic bone disease (may cause loss of bone mineral density in women); children (not recommended).

Adverse effects: Rarely anaphylaxis; worsening of the signs and symptoms early in the treatment manifested by an increase in bone pain, increased difficulty in urinating, hot flashes, injection site irritation, weakness; sexual dysfunction, impotence, postmenopausal symptoms, gynaecomastia, oedema, headache, lethargy, dizziness, insomnia, skin rash, breast tenderness/enlargement, sweating, increased bone pain, bone loss, diarrhoea, nausea, vomiting.

Advice to patients: Females must use reliable contraceptive during therapy; symptoms may worsen temporarily during first week of therapy.

Dose: By s.c. injection (into the upper abdomen), 3.6 mg every 28 days. No dosage adjustment for patients with renal or hepatic impairment, or for the elderly.
Prostate carcinoma: intended for long-term administration.
Endometriosis: recommended duration is 6 months (safety data is not available for longer treatment periods).
Endometrial thinning: Two depots to be administered 4 weeks apart, with surgery timed for between zero and two weeks after the second depot.
Uterine fibroid: 3.6 mg depot with supplementary iron may be given for up to three months before surgery.
Not recommended for children.

Note: *Administration:* Do not remove the sterile syringe until immediately before use. After cleaning with an alcohol swab, a local anaesthetic may be used on an area of skin on the upper abdominal wall. Stretch the patient's skin with one hand, and grip the needle into the s.c. fat.

Do not aspirate: If the hypodermic needle penetrates a large vessel, blood will be seen instantly in the syringe chamber. Change the direction of the needle so it parallels the abdominal wall. Push the needle in until the barrel hub touches the patient's skin.

Withdraw the needle 1cm to create a space to discharge the drug; fully depress the plunger to discharge.

Withdraw needle and bandage the site. Confirm discharge by ensuring tip of the plunger is visible within the tip of the needle.

POM **ZOLADEX®** *(Reals)*
Injection (Depot), Goserelin acetate 3.6 mg; in a single dose syringe applicator.

12.4 Drugs used in palliative care

NOTE: THE EXPERT COMMITTEE ON THE SELECTION AND USE OF ESSENTIAL MEDICINES RECOMMENDS THAT ALL

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THE DRUGS MENTIONED IN CANCER PAIN RELIEF: WITH A GUIDE TO OPIOID AVAILABILITY, 2ND EDITION. GENEVA: WHO 1996 BE CONSIDERED ESSENTIAL. THESE DRUGS ARE INCLUDED IN THE RELEVANT SECTIONS OF THE MODEL LIST ACCORDING TO THEIR THERAPEUTIC USE, FOR EXAMPLE ANALGESICS.

Palliative care includes both pain relief and the symptomatic relief of conditions including dyspnoea, restlessness and confusion, anorexia, constipation, pruritus, nausea and vomiting, and insomnia. Health authorities should be encouraged to develop their own palliative care services.

Pain relief can be achieved with drugs and neurosurgical, pyschological and behavioural approaches adapted to individual patient needs. If carried out correctly, most patients with cancer pain can obtain effective relief. Pain is best treated with a combination of drug and non-drug measures. Some types of pain respond well to a combination of a non-opioid and an opioid analgesic. Other types of pain are relieved by combining a corticosteroid and an opioid. Neuropathic pains often show little response to non-opioids and opioids, but may be eased by tricyclic antidepressants and anticonvulsants (see below). Cancer patients often have many fears and anxieties, and may become depressed. Very anxious or deeply depressed patients may need an appropriate psychotropic drug in addition to an analgesic. If this fact is not appreciated, the pain may remain intractable.

In the majority of patients, cancer pain can be relieved with analgesics:

- **by mouth**: if possible analgesics should be given by mouth. Rectal suppositories areuseful in patients with dysphagia, uncontrolled vomiting or gastrointestinal obstruction. Continuous subcutaneous infusion offers an alternative route.
- **by the clock**: analgesics are more effective in preventing pain than in the relief of established pain, therefore doses should be given at fixed time intervals and titrated against the patient's pain; if pain occurs between doses, a rescue dose should be given, and the next dose increased.
- **by the ladder**: the first step is to give a non-opioid analgesic such as **acetylsalicylic acid**, **paracetamol** or **ibuprofen**, if necessary with an adjuvant drug. If this does not relieve the pain, an opioid for mild to moderate pain such as **codeine** should be added. When this combination fails to relieve pain, an opioid for moderate to severe pain such as **morphine** should be substituted.
- **for the individual**: there are no standard doses for opioid drugs. The range for oral morphine is from as little as 5 mg to more than 100 mg every 4 hours.
- **with attention to detail**: the first and last doses of the day should be linked to the patient's waking time and bedtime. Ideally the drug regimen should be written out in full for the patient and his or her family. The patient should be warned about possible adverse effects.

Drugs for neuropathic pain

Neuropathic pain often responds to a tricyclic antidepressant, such as **amitriptyline** (section 1.4), or to an anticonvulsant such as **carbamazepine** or **sodium valproate** (both section 1.7.1); **ketamine** (section 3.1.1) or **lidocaine** (section 5.4) by intravenous infusion may be useful in some situations. Neuropathic pain responds only partially to opioids, but they my be considered when other options fail. A corticosteroid may be required, particularly to relieve pressure and therefore pain in patients with nerve compression.

13. Ophthalmological preparations

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13.1 Anti–infective drugs

13.2 Anti–inflammatory/Anti–allergic/Anti–infective drugs

13.3 Mydriatics and cycloplegics

13.3.1 Antimuscarinics

13.3.2 Sympathomimetics

13.4 Drugs used in glaucoma

13.4.1 Miotics

13.4.2 Beta-blockers

13.4.3 Sympathomimetics

13.4.4 Carbonic anhydrase inhibitors

13.4.5 Prostaglandin analogue

13.5 Local anaesthetics

13.6 Miscellaneous eye preparations

Administration of eye preparations

Preparations for the eye should be sterile when issued. Use of single-application containers is preferable; multiple-application preparations include antimicrobial preservatives and when used particular care should be taken to prevent contamination of the contents, including the avoidance of contact between the applicator and the eye or other surfaces.

Eye drops are generally instilled into the lower conjunctival sac which is accessed by gently pulling down the lower eyelid to form a pocket into which one drop is instilled. The eye should be kept closed for as long as possible after application, preferably 1–2 minutes. A small amount of eye ointment is applied similarly; the ointment melts rapidly and blinking helps to spread it.

When two different eye drops are required at the same time, dilution and overflow may occur when one immediately follows the other; an interval of 5 minutes should be allowed between the two applications.

Systemic absorption, which may occur after topical application of eye drops, can be minimized by using the finger to compress the lacrimal sac at the medial canthus for at least one minute after instillation of the drops. This helps block the passage of the drops through the naso-lacrimal duct.

PERFORMANCE OF SKILLED TASKS

Application of eye preparations may cause blurring of vision which is generally transient; patients should be advised not to carry out skilled tasks such as operating machinery or driving until their vision has cleared.

13.1 Anti–infective drugs

Blepharitis, conjunctivitis, keratitis and endophthalmitis are common acute infections of the eye and can be treated topically. However, in some cases, for example, in gonococcal conjunctivitis, both topical and systemic anti-infective treatment may be necessary. Blepharitis and conjunctivitis are often caused by staphylococcus, while keratitis and endophthalmitis may be bacterial, viral or fungal. Bacterial blepharitis is treated with an antibacterial eye ointment or drops. Although most cases of acute bacterial conjunctivitis may resolve spontaneously, anti-infective treatment shortens the infectious process and prevents complications. Acute infective conjunctivitis is treated with antibacterial eye drops by day and eye ointment applied at night. A poor response may indicate viral or allergic conjunctivitis. Keratitis requires immediate specialist treatment.

Gentamicin is a broad-spectrum bactericidal aminoglycoside antibiotic with particular activity against *Pseudomonas aeruginosa*, *Neisseria gonorrhoea* and other bacteria that may be implicated in blepharitis or conjunctivitis. Topical application may lead to systemic absorption and possible adverse effects.

Idoxuridine is an antiviral used in the treatment of keratitis due to herpes simplex virus. Idoxuridine is effective against epithelial infections of recent origin. These

may respond to treatment within a week and resolve completely in 1–2 weeks. Eye drops must be applied frequently to maintain a high concentration and achieve a successful therapeutic outcome; however, if there is no relief within 7 days, treatment should be discontinued and alternative treatment is indicated. For systemic treatment with antivirals such as aciclovir, see section 9.5.1.

Silver nitrate is a topical anti-infective. Its antibacterial activity is attributed to precipitation of bacterial proteins by silver ions. It is available in 1% ophthalmic solutions and is used for prophylaxis of gonococcal ophthalmia neonatorum.

Tetracycline is a broad spectrum antibiotic with activity against many Gram-positive and Gram-negative bacteria including *N. gonorrhoea*, and most chlamydia, rickettsia, mycoplasma and spirochetes. Ophthalmic tetracycline is used in blepharitis, conjunctivitis, and keratitis produced by susceptible bacteria. Tetracycline is also used in the treatment of trachoma caused by *Chlamydia trachomatis* and in the prophylaxis of neonatal conjunctivitis (ophthalmia neonatorum) caused by *N. gonorrhoea* and *C. trachomatis*.

ACYCLOVIR

Indications: Treatment of herpes simplex keratitis.
Dose: Apply 5 times daily at 4 hourly intervals for at least 3 days.

POM **Acyclovir** *(EDL 21.1)*
Eye Ointment, Acyclovir 3%.

POM **ZOVIRAX®** *(SKG)*
Eye Ointment, Acyclovir 3%.

CHLORAMPHENICOL

Indications: Ocular infections
Adverse effects: Blood dyscrasias
Advice to patients: Wash hands, clean crusts or discharge from eye, instil eye drops and apply pressure to lacrimal sac for 1 minute to prevent systemic absorption; do not share make-up and towel with family members during infection; do not allow the container tip to touch the eye; discontinue therapy and notify physician immediately of any signs of sensitivity viz itching, increased redness, burning or stinging sensation; ointment may temporarily blur vision, apply in the night.
Dose: 1-2 drops 4 times daily; up to hourly in severe cases.
Apply ointment in the night in conjuction with daily drops.

POM **Chloramphenicol** *(EDL 21.1)*
Eye-drops, Chloramphenicol 0.5%
Eye Ointment, Chloramphenicol 1%

POM **Chloramphenicol** *(Hovid)*
Eye-drops, Chloramphenicol 0.5%
Pack - 5 ml x 12

POM **ISOPTO FENICOL®** *(Summit Healthcare)*
Eye-drops, Chloramphenicol 0.5%
Pack - 15 ml.
Eye Ointment, Chloramphenicol 1%
Pack - 3.5 g.

CHLORTETRACYCLINE

Indications: Local treatment of eye infection, including trachoma.
Dose: Apply ointment every 2 hours especially for acute infections.

POM **Chlortetracycline** *(EDL 21.1)*
Eye Ointment, Chlortetracyline HCl 1%.

CIPROFLOXACIN

Pharmacology: Ciprofloxacin is a fluoro-quinolone antibacterial active against a broad spectrum of gram-negative and gram-positive ocular pathogens.
Indications: Treatment of bacterial infections caused by susceptible strains of the microorganisms; corneal ulcers.
Contra-indications: History of hypersensitivity to other quinolones.
Precautions: Not recommend for children under 1 year; pregnancy and lactation.
Adverse effects: Local burning or discomfort; lid margin crusting; crystals/scales; foreign body sensation; itching; conjunctival hyperaemia and a bad taste following instillation.
Dose: *Corneal ulcer*, apply throughout day and night, Day 1 2 drops into the affected eye every 15 minutes for the first 6 hours and then every 30 minutes for the remainder of the day; Day 2 instill 2 drops hourly; Day 3 to 14 apply 2 drops every 4 hours. Treatment may be continued after 14 days if corneal re-epithelialization has not occured.
Bacterial conjunctivitis, apply 1-2 drops

into the conjunctival sac (s) every 2 hours while awake for 2 days and 1-2 drops every 4 hours while awake for the next 5 days.

POM **CILOXAN®** *(Summit Healthcare)*
Eye-drops, Ciprofloxacin (as HCl) 3 mg per ml.
Pack - 5 ml (in plastic DROP-TAINER® dispenser)

FRAMYCETIN

Indications: Local treatment of eye infections
Dose: Apply eye drop or ointment every 3 hours

POM **Framycetin** *(EDL 21.1)*
Eye drops, Framycetin sulphate 0.5%
Eye Ointment, Framycetin sulphate 0.5%

POM **SOFRAMYCIN®** *(NGC)*
Eye-drops, Framycetin sulphate 0.5%
Pack - 8 ml.
Eye Ointment, Framycetin sulphate 0.5%
Pack - 5 g.

GENTAMICIN

Gentamicin is a representative antibacterial. Various drugs can serve as alternatives.
Therapeutic category: Topical antibiotic, aminoglycoside
Indications: Blepharitis; bacterial conjunctivitis; systemic infections (section 9.1.2.5).
Contra-indications: Hypersensitivity to aminoglycoside group of antibiotics.
Precautions: Prolonged use may lead to skin sensitization and emergence of resistant organisms including fungi; discontinue if purulent discharge, inflammation or exacerbation of pain.
Adverse effects: Burning, stinging, itching, dermatitis.
Advice to patients: Wash hands, clean crusts or discharge from eye, instil eye drops and apply pressure to lacrimal sac for 1 minute to prevent systemic absorption; do not share make-up and towel with family members during infection; do not allow the container tip to touch the eye; discontinue therapy and notify physician immediately of any signs of sensitivity viz itching, increased redness, burning or stinging sensation; ointment may temporarily blur vision, apply in the night.
Administration: *Mild to moderate infection*, by instillation into the eye, ADULT and CHILD 1 drop every 2 hours, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete. *Severe infection*, by instillation into the eye, ADULT and CHILD 1 drop every hour, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete.

POM **Gentamicin** *(WMF 21.1)*
Eye drops, solution, Gentamicin (as sulfate) 0.3%.

POM **Gentamicin** *(EDL 21.1)*
Eye-drops or ointment, Gentamicin sulphate 0.3%.

POM **ALCOMICIN®** *(CHI)*
Eye-drops, Gentamicin sulphate 3 mg per ml.

POM **CIDOMYCIN®** *(NGC)*
Drops (Eye or Ear), Gentamicin (as sulphate) 0.3%; colourless solution.
Pack - 8 ml.
Eye Ointment, Gentamicin (as sulphate) 0.3%
Pack - 3 g.

POM **GENTADAR®** *(Supreme)*
Eye/ear drops, Gentamicin 0.3%
Pack - 10 ml.

POM **GENTALEK®**(*Taylek*)
Eye/Ear drops, Gentamicin sulphate 3 mg per ml.
Pack - 5 ml.
Eye/Ear ointment, Gentamicin sulphate 3 mg per g.
Pack - 3 g (in tubes).

GRAMICIDIN plus NEOMYCIN plus POLYMYXIN B

Pharmacology: A broad-spectrum, bactericidal preparation active against pathogens commonly found in bacterial infections of the eye.
Indications: Prevention or treatment of infections of the eye and its adnexa. Prophylaxis pre- and post-operatively, including surgical procedures and removal of foreign bodies from the eye. Treatment of bacterial infections including conjuctivitis, keratitis, corneal ulceration, ulcerative blepharitis with asociated conjuctivitis, and chronic dacryocystitis.
Contra-indications: Hypersensitivity to the product or any of its constituents, or to cross-sensitizing substances such as Framycetin, Kanamycin, Gentamicin and other related antibiotics; any condition where the product can gain access to intraocular fluids; neonates and infants (high absorption through immature skin

may impair renal function).

Precautions: Prolonged use may result in overgrowth of non-susceptible organisms including fungi; irreversible ototoxicity may occur with high doses or prolonged treatment; pregnancy and lactation (not recommended).

Adverse effects: Low incidence of allergic reactions following topical applications of neomycin sulphate, polymyxin B sulphate and gramicidin.

Advice to patients: Wash hands, cleanse crusts or discharge from the eye, tilt head back, place medication in conjunctival sac, and close eyes; apply finger pressure on lacrimal sac for 1 minute following instillation; notify physician of any signs of sensitivity viz itching, reddening, swelling or worsening condition.

Dose: Apply 1-2 drops into the affected eye 2-4 times daily; frequency may be inreased depending on the severity of the condition. Continue treatment for at least 2 days after the condition has resolved. See lit. for use in children and elderly. Not recommended for neonates and infants

Note: If during application a drop does not adequately cover the eye, a further drop should be administered. To prevent contamination of the eye drops, do not allow the applicator tip to touch any surface (including the eye), and keep the container tightly closed.

POM **Gramicidin plus Neomycin plus Polymyxin** *(EDL 21.1)*

Eye drops, Gramicidin 25 units, neomycin sulphate 1700 units, polymyxin B sulphate 5000 units per ml.

POM **NEOSPORIN®** *(GSK)*

Eye drops, Gramicidin 25 units, neomycin sulphate 1700 units, polymyxin B sulphate 5000 units per ml; a colourless to very pale yellow, slightly hazy solution.

IDOXURIDINE

Idoxuridine is a representative antiviral. Various drugs can serve as alternatives.

Indications: Keratitis or keratoconjunctivitis caused by herpes simplex.

Contra-indications: Pregnancy; concurrent use of an eye preparation containing boric acid.

Precautions: Existing deep ulceration of cornea; prolonged or excessive use may damage the cornea; do not exceed frequency or duration of treatment, discontinue if no relief within 7 days; concurrent use of a corticosteroid.

Adverse effects: Occasionally burning, itching, irritation, pain, conjunctivitis, oedema, inflammation, photophobia, pruritus; rarely allergic reactions.

Advice to patients: Patient should understand how to instil the drug. May cause sensitivity to bright light; minimize by wearing sunglasses; notify physician if improvement is not seen in 7-8 days, if condition worsens, or if pain, decreased vision, itching, or swelling of the eye occur; do not exceed recommended dose.

Nursing considerations: •Teach patient how to instill drops.

•Idoxuridine solution should not be mixed with other topical eye medications.

•Store Idoxuridine 0.1% solution in a refrigerator.

•Idoxuridine may cause sensitivity to bright light; advise patient to minimize this by wearing sunglasses, and to avoid prolonged exposure to sunlight.

Administration: *Herpes simplex keratitis*, by instillation into the eye, ADULT and CHILD 1 drop every hour during daytime and every 2 hours at night-time, reducing frequency as infection is controlled to 1 drop every 2 hours during daytime and every 4 hours at night-time, then continue for 3–5 days after healing is complete; maximum length of treatment 21 days.

Herpes simplex keratitis, by application to the eye, ADULT and CHILD 1 application of ointment every 4 hours during daytime and once at night-time (5 applications), then continue for 3–5 days after healing is complete; maximum length of treatment 21 days.

POM **Idoxuridine** *(WMF 21.1)*

Eye drops, solution, Idoxuridine 0.1%.

Eye ointment, Idoxuridine 0.2%.

POM **Idoxuridine** *(EDL 21.1)*

Eye-drops, Idoxuridine 0.1%

Eye Ointment, Idoxuridine 0.5%

POM **DENDRID®** *(CHI)*

Eye-drops, Idoxuridine 0.1%

Pack - 15 ml

Eye Ointment, Idoxuridine 0.5%

Pack - 3.5 g.

LOMEFLOXACIN

Therapeutic category: Ophthalmic antibiotic.

Pharmacology: Lomefloxacin, a difluorinated quinolone derivative, is a bacterial gyrase

inhibitor (which impairs bacterial enzyme functions) effective against gram-positive and gram-negative bacteria. Systemic absorption following topical ophthalmic application of 0.3% eye drops is very low.
Indications: Bacterial infections of the anterior segment including conjunctivitis, blepharitis and blepharo-conjunctivitis.
Contra-indications: Hypersensitivity to the drug, or quinolones generally.
Precautions: Long term treatment with antibiotics may enhance development of secondary fungal infections or the growth of resistant bacteria. Pregnancy and lactation (to be used only when the potential benefit to the pregnant/lactating woman outweighs the potential risk to the foetus or infant).
Interactions:
•Avoid co-administration with bacteriostatic ophthalmic antibiotics.
Adverse effects: Slight and transient burning immediately after the instillation; rarely, allergic reactions.
Dose: Instil one drop 2 times daily into the lower conjunctival sac. At the beginning of treatment, applications should be more frequent: apply 5 drops within 20 minutes or 1 drop every hour for the first 6-10 hours.

POM **OKACIN®** *(Novartis Ophthalmics)*
Eye-drops, Lomefloxacin 3 mg per ml.
Pack - 5 ml.

NATAMYCIN

Indications: Local infection of the eye of fungal origin.
Adverse effects: Ocular oedema, hyperemia.
Advice to patients: Shake well before using, do not touch dropper to eye; notify physician if condition worsens or does not improve after 3-4 days.
Nursing considerations: •Teach patient how to instill the drug: wash hands, cleanse crusts or discharge from the eye, tilt head back, place medication in conjunctival sac, and close eyes; apply light finger-pressure on lacrimal sac for 1 minute following instillation to prevent systemic absorption.
•Natamycin is the only antifungal available as ophthalmic preparation.
Dose: 2-3 drops, 3 times daily

POM **Natamycin** *(EDL 21.1)*
Eye Ointment, Natamycin 1%
Eye Suspension, Natamycin 5%

OXYTETRACYCLINE plus POLYMYXIN B

Indications: Prophylaxis and treatment of superficial ocular infection due to susceptible organisms.
Advice to patients: See under Gramicidin plus Neomycin plus Polymyxin B.
Dose: Apply the Ointment 3-6 times daily usually for 10-15 days in acute and up to 3 months in chronic cases.

POM **Oxytetracycline plus Polymyxin B** *(EDL 21.1)*
Eye ointment, Oxytetracycline HCl 5 mg, polymyxin B sulphate 10,000 units per g; in 3.5 g tube.

PROPAMIDINE

Indications: Treatment of blepharitis and conjunctivitis due to bacterial infection; prevention of infection when trauma of conjunctiva has occured.
Dose: Drops, instil 1-2 drops 4 times daily
Ointment, apply 2-3 times daily.

POM **Propamidine** *(EDL 21.1)*
Eye-drops, Propamidine isethionate 0.1%
Eye Ointment, Propamidine isethionate 0.1%

RIFAMYCIN

Therapeutic category: Topical antibiotic
Pharmacology: Rifamycin sodium is a water-soluble bactericidal antibiotic for topical use in ocular infections. It is produced by *Streptomyces mediterranei* and is active against most of the pathogens responsible for ocular infections, both Gram-positive and Gram-negative bacteria.
Indications: Infections of the external eye and its adnexae including acute, subacute or chronic bacterial conjunctivitis; blepharitis, keratitis, dacryocystitis.
Precautions: Overgrowth of non-succeptible organisms on prolonged use and sensitisation reaction (discontinue treatment); pregnancy, breast-feeding.
Adverse effects: Transient irritation, allergic reactions.
Dose: Instil 1-2 drops every 4-6 hours; frequency of administration may be increased in severe infections.

POM **RIFAMYCINE CHIBRET®** *(Bolax/BPP)*
Eye–drops, Rifamycin sodium 1%.
Pack - 10 ml vial
Eye Ointment, Rifamycin sodium 1%.
Pack - 5 g tube

SILVER NITRATE

Indications: Prophylaxis of neonatal conjunctivitis (ophthalmia neonatorum) due to *Neisseria gonorrhoea*, if tetracycline not available.
Precautions: Avoid use of old, concentrated drops; wipe excess drops from skin near the eye to prevent staining.
Adverse effects: Skin and mucous membrane irritation; mild conjunctivitis; repeated use may cause skin discoloration, corneal cauterization and blindness.
Administration: *Prophylaxis of neonatal conjunctivitis*, by instillation into the eye, NEWBORN at birth after cleansing eyes with sterile gauze, 2 drops into each eye.

POM **Silver nitrate** *(WMF 21.1)*
Eye drops, solution, Silver nitrate 1%.

SULFACETAMIDE

Indications: Mild infections of the conjunctiva and eyelid like conjunctivitis, corneal ulcer.
Precautions: Incompartible with silver preparations.
Adverse effects: Sensitivity reactions.
Advice to patients: See under Gentamicin.
Nursing considerations: •Teach patient how to instill the drug: wash hands, cleanse crusts or discharge from the eye (purulent exudate interferes with sulphacetamide action), tilt head back, place medication in conjunctival sac, and close eyes; apply light finger-pressure on lacrimal sac for 1 minute following instillation to prevent systemic absorption.
•Wait at least 5 minutes before applying other eyedrops.
•Warn patient not to touch dropper or tip of tube to eye or sorrounding tissue; that eyedrop burns slightly and that solution may stain clothing.
•Advise patient to notify physician immediately of any signs of sensitivity viz itching, increased redness, burning or stinging sensation.
•Instruct patient not to share make-up, towel and the medication with other family members.
•Sulfacetamide may cause sensitivity to bright light; advise patient to minimize this by wearing sunglasses, and to avoid prolonged exposure to sunlight.
Dose: Instil 1-2 drops 3-6 times daily.

POM **Sulfacetamide** *(EDL 21.1)*
Eye-drops, Sulfacetamide sodium 10%, 30%.
Eye Ointment, Sulfacetamide sodium 10%

POM **ISOPTO CETAMIDE®** *(CHI)*
Eye-drops, Sulfacetamide sodium 15%
Pack - 15 ml
Eye Ointment, Sulfacetamide sodium 10%
Pack - 3.5 g

SULFACETAMIDE plus CHLORAMPHENICOL

Pharmacology: Both chloramphenicol and sulfacetamide act bacteriostatically due to their interference with the metabolism of the bacteria cell. Chloramphenicol is a lipophilic, low molecular weight antibiotic which acts by inhibiting the protein synthesis due to a supression of the transfer of activated amino acids. Sulfacetamide, an antagonist of P-aminobenzoic acid (PABA) inhibits the synthesis of folic acid inside the bacterial cell. The combination of both drugs results in an increased antibacterial spectrum.
Indications: Bacterial infections of the eyelids, the conjunctiva, the cornea (corneal ulcer), the anterior uvea as well as of the lacrimal system. Trachoma and other infections caused by chlamydozoa, benign lymphoreticulosis (cat-scratch fever) and Parinaud's conjunctiva. Prophylaxis of infection before and after rinsing of the lacrimal duct, before and after eye surgery as well as after cauterizations and burns.
Contra-indications: Hypersensitivity to the ingredients.
Interactions:
• Avoid co-administration with other topical preparations containing heavy metals particularly copper, zinc and silver due to chemical incompatibilities.
• Avoid co-administration with bactericidal substances such as penicillins,cephalosporins (antagonism is possible).
Adverse effects: Rarely allergic reactions which manifest as eczema of the eyelid margin. Prolonged topical therapy (2-3 months) with chloramphenicol may cause aplastic anaemia.
Dose: Instil 1 drop 2-4 times daily; up to 1 drop hourly in acute cases.

POM **SPERSACET C®** *(Novartis Ophthalmics)*
Eye-drops, Sulfacetamide sodium 100 mg, chloramphenicol 5 mg per ml.
Pack - 10 ml.

TETRACYCLINE

Tetracycline is a representative antibacterial. Various drugs can serve as alternatives.
Indications: Superficial bacterial infection of the eye; mass treatment of trachoma in endemic areas; prophylaxis of neonatal conjunctivitis (ophthalmia neonatorum) due to *Neisseria gonorrhoea* or *Chlamydia trachomatis*.

RETURN

Contra-indications: Hypersensitivity to tetracycline group of antibiotics.
Precautions: Prolonged use may lead to overgrowth of non-susceptible organisms.
Adverse effects: Rash; rarely stinging, burning.
Administration: *Superficial bacterial infection*, by application to the eye, ADULT and CHILD aged over 8 years 1 application of ointment 3–4 times daily.
Prophylaxis of neonatal conjunctivitis, by application to the eye, NEWBORN at birth after cleansing eyes with sterile gauze, 1 application of ointment into each eye; close eyelids and massage gently to aid spread of ointment.
Trachoma, intermittent treatment, by application to the eye, ADULT and CHILD 1 application of ointment into each eye either twice daily for 5 days or once daily for 10 days, every month for 6 consecutive months each year, repeated as necessary.
Trachoma, continuous intensive treatment, by application to the eye, ADULT and CHILD 1 application of ointment into each eye twice daily for at least 6 weeks.

POM **Tetracycline** *(WMF 21.1)*
Eye ointment, Tetracycline HCl 1%.

13.2 Anti-Inflammatory/Anti-allergic/ Anti-infective drugs

Ophthalmic corticosteroids should only be used under supervision of an ophthalmologist as inappropriate use is potentially blinding. Dangers include the development of open-angle glaucoma (chronic simple glaucoma) and cataracts, and the aggravation of a simple herpes simplex epithelial lesion into an extensive corneal ulcer and subsequent permanent corneal scarring, with possible damage to vision and even loss of the eye.

Corticosteroids such as **prednisolone** are useful in the treatment of inflammatory conditions including uveitis and scleritis. They are also used for reducing postoperative ocular inflammation. Before administration of an ophthalmic corticosteroid, the possibility of bacterial, viral or fungal infection should be excluded. Treatment should be the lowest effective dose for the shortest possible time; if long-term therapy (more than 6 weeks) is unavoidable, withdrawal of an ophthalmic corticosteroid should be gradual to avoid relapse.

Further clinical notes
Topical corticosteroids as well as subconjunctival and systemic applications are valuable for the treatment of uveitis, scleritis and post-operative inflammation. The topical use of corticosteroids should however be left for the experts to decide and not used for undiagnosed *'red eye'*. There are two main dangers from topical corticosteroids: enhancement of herpetic corneal disease (due to misdiagnosis) when applied in eye-drops, and production of a 'steroid glaucoma' after a few weeks treatment with eye-drops in patients predisposed to chronic simple glaucoma, especially with **dexamethasone** and **prednisolone**.
Oxyphenbutazone eye ointment does not have the disadvantages of corticosteroids and is used in the treatment of episcleritis. Topical preparations of antihistamines plus vaso-constrictors are used for the short-term treatment of allergic conjunctivitis. For this purpose, **antazoline** with **naphazoline** or **tetrahydrozoline** are used.
Corticosteroids are often combined with anti-bacterial agents for topical application to treat inflammatory eye conditions. Such preparations should be used under expert supervision.
Sodium cromoglycate eye-drops may be useful for vernal catarrh and other allergic forms of conjunctivitis.
Conjunctival oedema and hyperaemia secondary to ocular allergies are treated with ophthalmic decongestants like **tetrahydrozoline, hydrastine, synephrine** and **naphazoline** eye preparations (often in combinations). They should be used cautiously also and watch out for hypersensitivity reactions.

ANTAZOLINE plus NAPHAZOLINE

Therapeutic category: Mucosal decongestant with antihistaminic effect.
Pharmacology: Naphazoline is a vasoconstrictor which has both a rapid and prolonged action in suppressing conjunctival hyperaemia. Antazoline is an antihistamine with an antiallergic action which reduces vascular permeability.
Indications: Irritative conjunctivitis, allergic disorder of the conjunctiva (vernal catarrh).
Precautions: Some sensitive patients might have a passing prickling feeling during instillation which, however, does not affect the

treatment's efficacy. Close the bottle immediately after use and discard any remaining product at the end of treatment.

Advice to patients: Discontinue eye drops if visual changes or ocular pain occurs. Notify physician of insomnia, tremor, or irregular heartbeat; do not use for more than 72 hours unless directed to do so; remove contact lenses before using in eye.

Nursing considerations: •Teach patient how to instill the drug: wash hands before and after instillation, avoid touching dropper tip to eye or sorrounding tissue, tilt head back, place medication in conjunctival sac, and close eyes. Apply light finger-pressure on lacrimal sac for 1minute following instillation.
•Instruct patient to report changes in vision, blurring or loss of sight, headache, respiratory dysfunction, sweating, anxiety, weakness, lid oedema.
•Reassure patient that the blurring of vision will decrease with repeated use of drugs; he should avoid hazardous tasks until he can see properly.
•Inform patient that rebound congestion and conjunctivitis may occur with frequent and prolonged use.

Dose: Instil 1-2 drops into the conjunctival sac 3-4 times daily.
Child: 1-2 drops daily.

POM **Antazoline plus Naphazoline** *(EDL 21.2)*
Eye-drops, Antazoline (as sulphate or phosphate) 0.5%, naphazoline HCl 0.05%.

POM **ANTISTINE-PRIVINE®** *(Novartis Ophthalmics)*
Eye-drops, Antazoline sulphate 5 mg, naphazoline nitrate 0.25 mg per ml.
Pack - 10 ml.

POM **OPHTHAZOLIN®** *(Supreme)*
Eye-drops, Antazoline 0.5%, naphazoline 0.05%.
Pack - 10 ml.

ANTAZOLINE plus TETRAHYDROZOLINE

Therapeutic category: Antiallergic/Vasoconstrictor

Pharmacology: The antihistamine antazoline blocks the histamine receptors and in this way protects the cell membrane from the effects of liberated histamine and prevents the pathological changes that would otherwise occur. The vasoconstrictor tetrahydrozoline rapidly relieves irritation of the conjunctiva and brings a subjective improvement. Lacrymal secretion is slightly reduced but the preparation has no effect on pupillary diameter, accommodation or intraocular pressure.

Indications: Inflammatory conditions of the conjunctiva of allergic origin, especially hay-fever and vernal conjuctivitis, and in drug hypersensitivity reactions, excessive lacrymal secretion and stenosis of the lacrymal canal.

Nursing considerations: •*See under Antazoline plus Naphazoline.*

Dose: *In acute cases*, one drop 3 hourly.
In protracted treatment, one drop 2-3 times daily.
In severe cases, can be applied hourly.
Child: 1-2 drops daily

POM **Antazoline plus Tetrahydrozoline** *(EDL 21.2)*
Eye-drops, Antazoline (as sulphate or phosphate) 0.5%, tetrahydrozoline HCl 0.05%.

POM **SPERSALLERG®** *(Novartis Ophthalmics)*
Eye-drops, Antazoline HCl 0.5 mg, tetrahydrozoline HCl 0.4 mg per ml.
Pack - 10 ml.

BETAMETHASONE

Therapeutic category: Corticosteroid

Indications: Short-term treatment of steroid responsive inflammatory conditions of the eye after clinical exclusion of bacterial, viral and fungal infections. Non-infected inflammatory conditions of the ear.

Contra-indications: Bacterial, viral and fungal infections, tuberculosis or purulent conditions of the eye; glaucoma, herpetic keratitis (e.g. dendritic ulcer); patients who wear soft lenses.

Precautions: Should not be administered to "red eyes" until definitive diagnosis is made; prolonged use without regular check to exclude raised intra-ocular pressure.

Adverse effects: Rise in intra-ocular pressure, corneal perforation, cataract.

Dose: Eyes: 1-2 drops, 1-2 hourly or the ointment 2-3 times daily and/or at night
Ears: 2-3 drops, 2-3 hourly.

POM **Betamethasone** *(EDL 21.2)*
Drops (Ear or Eye), Betamethasone sodium phosphapte 0.1%
Eye ointment, Betamethasone sodium phosphate 0.1%

POM **BETNESOL®** *(GSK)*
Drops (Ear or Eye), Betamethasone sodium phosphate 0.1%
Pack - 5 ml; 10 ml
Eye Ointment, Betamethasone sodium phosphate 0.1%
Pack - 3 g.

BETAMETHASONE plus NEOMYCIN

Therapeutic category: Corticosteroid/ antibacterial.
Pharmacology: Betamethasone has topical corticosteroid activity. The presence of neomycin should prevent the development of bacterial infection.
Indications: For short-term treatment of steroid responsive inflammatory conditions of the eye after clinical exclusion of bacterial, viral and fungal infections but where prophylaxis against secondary bacterial infection is required, such as allergic conjunctivitis, blepharitis, uveitis, etc.
Contra-indications, Precautions, etc: See under betamethasone.
Dose: 1-2 drops, 1-2 hourly or the ointment 3-4 times daily and/or at night.

POM **Betamethasone plus Neomycin** *(EDL 21.2)*
Eye-drops, Betamethasone sodium phosphate 0.1%, neomycin sulphate 0.5%.
Eye-Ointment, Betamethasone sodium phosphate 0.1%, neomycin sulphate 0.5%.

POM **BETNESOL-N**® *(GSK)*
Eye-drops, Betamethasone sodium sulphate 0.1%, neomycin sulphate 0.5%.
Pack - 5 ml, 10 ml
Eye Ointment, Betamethasone sodium phosphate 0.1%, neomycin sulphate 0.5%
Pack - 3 g.

POM **OPHTHAMESONE**® *(Supreme)*
Eye/Ear/Nasal Drops, Betamethasone 0.1%, neomycin 0.5%
Pack - 10 ml.

DEXAMETHASONE

Therapeutic category: Corticosteroid
Indications: Vernal catarrh, allergic noninfectious blepharitis and conjunctivitis, noninfectious keratitis; iritis, myositis, sympathetic ophthalmia.
Contra-indications, Precautions, etc: See under betamethasone.
Advice to patients: Ensure patient understands instillation method; shake suspension well before use; notify physician of exacerbation of cornea or ulceration; do not discontinue drug abruptly.
Nursing considerations: •Teach patient how to instill the drug: wash hands before and after instillation, avoid touching dropper tip to eye or sorrounding tissue, shake suspension well before use, tilt head back, place medication in conjunctival sac, and close eyes. Apply light finger-pressure on lacrimal sac for 1 minute following instillation to prevent systemic absorption.
•Advise patient to stop medication and inform doctor immediately if visual acuity is affected or visual field diminishes.
•Watch for corneal ulceration; may require stopping medication.
•Instruct patient not to share medication with other family members.
Dose: One drop 3-5 times daily; up to one drop hourly in severe cases.

POM **SPERSADEX**® *(Novartis Ophthalmics)*
Eye-drops, Dexamethasone phosphate 1 mg per ml.
Pack - 5 ml.

POM **MAXIDEX**® *(Summit Healthcare)*
Eye-drops, Dexamethasone 0.1%
Pack - 5 ml.
Eye Ointment, Dexamethasone 0.1%.

DEXAMETHASONE plus CHLORAMPHENICOL

Therapeutic category: Corticosteroid/ antibiotic.
Indications: Non-purulent forms of infectious conjunctivitis and blepharitis of allergic origin; Kerato-conjunctivitis, non-viral keratitis, acne rosacea keratitis, iritis, post operative anti-exudative treatment after eye surgery.
Contra-indications: Injuries and ulcerating conditions of the cornea, particularly those of viral origin, purulent infections of the conjunctiva and eyelids, tuberculous infections, mycosis, glaucoma.
Precautions: Primary infection of the eye may be masked by corticosteroid; children, prolonged use.
Adverse effects: Rise in intraocular pressure.
Advice to patients: Ensure patient understands instillation method; shake suspension well before use; notify physician of exacerbation of cornea or ulceration; do not discontinue drug abruptly.
Dose: One drop 3-5 times daily; up to one drop hourly in severe cases.

POM **SPERSADEX COMP.**® *(Novartis Ophthalmics)*
Eye-drops, Dexamethasone phosphate 1mg, Chloramphenicol 5 mg per ml
Pack - 5 ml.

DEXAMETHASONE plus CHLORAMPHENICOL plus TETRAHYDROZOLINE

Therapeutic category: Antibiotic, anti-inflammatory (corticosteroids) and decongestant combination.

Pharmacology: Dexamethasone is a glucocorticoid with an anti-inflammatory effect about 25 times stronger than that of hydrocortisone. Chloramphenicol is a lipophilic antibiotic which selectively inhibits bacterial protein synthesis. It is effective against gram-(+ve) and gram- (-ve) bacteria, spirochaetes, salmonella, rickettsiae and chlamydiae (trachoma). Tetrahydrozoline (tetryzoline) is a sympathomimetic agent which causes local vasoconstriction through its alpha-adrenergic receptor agonist activity. Following topical application, it quickly reduces swelling, hyperaemia and conjunctival irritation.

Indications: Acute and chronic keratitis and conjunctivitis of an infectious nature; inflammation of the anterior uvea (iritis, iridocyclitis); scleritis, episcleritis and myositis; sympathetic Ophthalmia.

Contra-indications: Hypersensitivity to the ingredients; injuries and ulcerous processes of the cornea including those related to Herpes simplex, other viral infections and mycosis; glaucoma; severe blood disorders due to bone marrow depression; acute intermittent porphyria; family history of bone marrow depression; new-born babies; pregnancy and lactation; dry eyes, especially in cases of keratoconjunctivitis sicca.

Precautions: Avoid prolonged therapy; Chloramphenicol therapy is associated with a potential risk of aplasic anaemia or other blood dyscrasias; Corticosteroids could mask, activate or aggravate an infection in the eye; topical application of corticosteroids may cause perforation when there is stromal damage of cornea or sclera; avoid use in children under 2 years or in those suffering from hypertension or hypotension due to the danger of systemic reactions; due care should be taken in the presence of rhinitis sicca, hyperthyroidism, diabetes mellitus and cardiac disorders.

Interactions:

•Avoid co-administration of chloramphenicol with bactericidal substances or with drugs which have an adverse effect on bone marrow function.

Adverse effects: Slight nd transient burning sensation and bitter taste in the mouth. Rarely, allergic reactions and blood dyscrasias. Systemic sympathomimetic effects such as palpitation, hypertension, tremor due to tetryzoline (tetrahydrozoline). Periocular dermatitis, immunosuppression followed by secondary infections and impairment of wound healing may be associated with topical corticosteroids. Long-term therapy with corticosteroids may cause reversible increase in eye pressure, posterior subcapsular cataracts, corneal perforation and adverse systemic effects (especially in children).

Dose: Instil one drop into the conjunctival sac 1-4 times per day.
Acute cases, up to 1 drop every hour if necessary.

POM **SPERSADEXOLINE®** *(Novartis Ophthalmics)*
Eye-drops, Dexamethasone (as sodium phosphate) 1 mg, chloramphenicol 5 mg, tetrahydrozoline 0.25 mg per ml.
Pack - 5 ml (in dropper bottle).

DEXAMETHASONE plus NEOMYCIN

Therapeutic category: Anti-inflammatory/ Antiallergic/Antibiotic.

Indications: Eye infection and inflammation such as keratits, conjunctivitis, iritis; ulcers, burns and injuries of the cornea.

Contra-indications: Ophthalmic herpes simplex, fungal infections of the eye and ear, acute phase of most viral infections of the cornea and conjunctiva.

Precautions: Raised I.O.P.; prolonged application of steroids to the eyes may cause subcapsular cataracts.

Adverse effects: Rarely hypersensitivity reactions; secondary bacterial or fungal infections.

Dose: Instil 1-2 drops hourly during the day and every 2 hours at night; when controlled, reduce to 1drop 4 hourly or even less frequently. Ointment, apply as a thin layer 3-4 times daily until controlled then reduce frequeuency.

POM **BIVACYN-N®** *(Taylek)*
Eye / Ear-drops, Dexamethasone 1 mg, neomycin sulphate 3500 I.U. (5 mg) per ml; in 5 ml vials.
Pack - 5 ml
Eyes / Ear Ointment, Dexamethasone 0.5 mg, neomycin sulphate 3500 I.U. per g.
Pack - 3 g; 5 g (in tubes).

FLUOROMETHOLONE

Therapeutic category: Corticosteroid.

Pharmacology: Corticosteroids suppress the inflammatory response to inciting agents of mechanical, chemical or immunological nature.

Indications: Conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the eye.

Contra-indications: Hypersensitivity to any component of this preparation in acute superficial herpes simplex keratitis, vaccinia,

varicella and most other viral diseases of cornea and conjunctiva; tuberculosis; fungal diseases; acute purulent untreated infections which, like other diseases caused by microorganisms, may be masked or enhanced by the presence of the steroid.

Precautions: Pregnancy, lactation; herpes simplex infections. Prolonged use may result in glaucoma, damage to the optic nerve, defects in visual acuity and visual field, cataract formation and /or may aid in the establishment of secondary ocular infections from pathogens due to suppression of host response. Acute purulent infections of the eye may be masked or exacerbated by presence of steroid medication. In those diseases causing thinning of the cornea or sclera, perforation has been known to occur with chronic use of topical steroids. It is advisable that the intraocular pressure be checked frequently.

Adverse effects: Glaucoma with optic nerve damage, visual acuity and field defects, cataract formation, secondary ocular infection following suppression of host response, and perforation of the globe may occur.

Advice to patients: Do not touch dropper tip to any surface, as this may contaminate the suspension. Shake well before using.

Dose: 1-2 drops instilled into the conjunctival sac(s) 4 times daily; may be increased during initial 24-48 hours to 2 drops every 2 hours.

POM **FLAREX**®*(Summit Healthcare))*
Eye- drops, Fluorometholone acetate 0.1%. Pack-5 ml (inplastic DROP-TAINER® dispenser).

FLUOROMETHOLONE plus TETRAHYDROZOLINE

Therapeutic category: Anti-inflammatory and decongestant combination.

Pharmacology: Like all anti-inflammatory glucocorticoids, fluorometholone reduces prostaglandin synthesis by inhibiting the enzyme phospholipase A2. It also inhibits the chemostatic infiltration of neutrophils into the focus of inflammation. In contrast to other topical glucocorticoids, fluorometholone does not significantly raise the intraocular pressure as it is more rapidly degraded in ocular tissue. Its anti-inflammatory action is at least 40 times stronger than that of hydrocortisone.

Tetrahydrozoline (Tetryzoline) is a sympathomimetic, which causes local vasoconstriction due to its alpha-adrenergic receptor agonist activity. The vasoconstrictive action of tetryzoline sets in rapidly and alleviates swelling, hyperaemia and irritation of the conjunctiva.

Indications: Acute allergic non-infectious conjunctivitis and keratitis; non-infectious inflammation of the anterior segment of the eye (including anterior uveitis, episcleritis and scleritis); postoperative inflammation following squint, cataract and glaucoma operations.

Contra-indications: Hypersensitivity to any component of the preparation; infectious conjunctivitis or keratitis; injuries and ulcerous processes of the cornea, especially infections caused by virus, bacteria and fungi; glaucoma; diseases associated with stromal damage to the cornea or sclera; dry eyes, especially keratoconjunctivitis sicca; children under 2 years. Not recommended for use during pregnancy and lactation.

Precautions: May temporarily affect visual acuity; if affected do not drive or operate machinery. Administer after careful risk/ benefits evaluation in the following cases:

(1) Severe circulation disorders e.g. hypertension;

(2) Metabolic disturbances e.g. diabetes;

(3) History of ocular herpes simplex infection.

Avoid prolonged use. Reactive hyperaemia may occur after discontinuation of therapy. Regularly examine patients on long-term treatment for intraocular pressure, systemic adverse reactions and secondary infections. May mask, activate or aggravate an infection in the eye. Use with caution in children and elderly due to possibility of systemic adverse effects

Interactions:

•Avoid co-administration with TCAs or with MAOIs (for the latter there must be an interval of at least 10 days since last treatment).

Adverse effects: Slight and transient burning sensation. Prolonged use may cause reactive hyperaemia. Rarely, allergic reactions. Local application of steroids may cause: increased susceptibility to infections (especially mycosis/ herpes simplex), delayed wound healing and very rarely mydriasis, ptosis and exophthalmos. Long-term application of steroids may cause: increase in intraocular pressure, posterior subcapsular cataracts, corneal melting and perforation of the globe and systemic adverse reactions (especially with children and geriatric patients). Tetryzoline may cause irritation of the conjunctiva and in rare cases mydriasis. In spite of the low doses for topical application, systemic sympathomimetic adverse reactions are possible: palpitations, arrhythmia, angina,

hypertension, occipital headaches, pallor, central excitation, tremor and sweating.
Dose: Adult, instil 1 drop 2-3 times daily into the conjunctival sac. In the first 24-48 hours, the dose may be increased to 1 drop hourly for adults. Not recommended for children below 2 years.

POM **EFEMOLINE**® *(Novartis Ophthalmics)*
Eye-drops, Fluorometholone 1 mg, Tetrahydrozoline HCl 0.25 mg per ml.
Pack - 5 ml.

HYDRASTINE plus SYNEPHRINE

Therapeutic category: Decongestant.
Indications: Conjunctival irritation such as allergic and seasonal conjunctival hyperaemia; ocular reactions to wind, dust, smoke, natural or artifical light and environmental irritants.
Contra-indications: Narrow-angle glaucoma; hypersensitivity to any component of the preparation.
Precautions: Continued or increased eye irritation; pregnancy, nursing mothers.
Adverse effects: Rarely, mydriasis.
Dose: Instil 1-2 drops in each eye 2-6 times daily.

POM **DACRINE**® *(Bolax/BPP)*
Eye-drop, Hydrastine chloride 0.05%, synephrine tartrate 0.5% in a methylcellulose buffered solution; sterile solution in 10 ml vial.
Pack - 10 ml.

HYDROCORTISONE plus CHLORAMPHENICOL

Indications: Local infection of the eye associated with inflammation.
Precautions: Prolonged use of steroid eye drops may lead to steroid glaucoma.
Advice to patients: Ensure patient understands instillation method; shake suspension well before use; notify physician of exacerbation of cornea or ulceration; do not discontinue drug abruptly.
Dose: Apply ointment or drops 2-3 times daily

POM **Chloramphenicol plus Hydrocortisone** *(EDL 21.2)*
Eye-drops or Ointment, Chloramphenicol 1%, hydrocortisone 0.5%.

HYDROCORTISONE plus CHLORAMPHENICOL plus COLISTINE

Therapeutic category: Corticosteroid/antibiotic
Pharmacology: A combination of two antibiotics, chloramphenicol and colistine (a polymyxin antibiotic), and a corticosteroid. The eye-ear solution associates anti-inflammatory effects to very effective antibiotic therapy
Indications: Bacterial conjunctivitis caused by Gram-positive or Gram-negative bacteria; blepharo and kerato-conjunctivitis; infections of the lacrymal ducts. Acute and chronic external otitis; catarrhal otitis.
Contra-indications: Epithelial herpes simplex keratitis and other viral diseases of the cornea and conjunctiva; mycobacterial infection of the eye; fungal diseases of the ocular structures; after removal of a corneal foreign body.
Precautions: Avoid prolonged use; discontinue treament if overgrowth of non–susceptible organisms occurs.
Adverse effects: Blood dyscrasia; allergic sensitizations; elevation of intraocular pressure; cataract formation; delayed wound healing; secondary infections on prolonged use.
Advice to patients: See under Dexamethasone.
Dose: 3-8 instillations daily.

POM **BACICOLINE**® *(Bolax/BPP)*
Eye-ear drops, Hydrocortisone acetate 1%, chloramphenicol 0.5%, colistine 2%; sterile lyophilized powder in 5 ml bottle plus 5 ml ampoule of diluent.

HYDROCORTISONE plus NEOMYCIN

Indications: EYE - Steroid-responsive allergic and inflammatory disorders of the anterior segment of the eye (conjunctival, corneal or uveal tract inflammation) or mechanical, chemical or thermal trauma, where bacterial infection or a risk of bacterial ocular infection exists.
NOSE - Allergic and vasomotor rhinitis and as an adjuvant treatment in affections of the sinus.
EAR - Inflammation and infection of the external auditory canal, seborrheic dermatitis, infected eczematoid dermatitis.
Contra-indications: Hypersensitivity to either component of the preparation; topical corticosteroids should be avoided in tuberculosis of the skin, herpes simplex, vaccinia, varicella and untreated fungal or viral ear infections; avoid application to the external auditory canal of patients with perforated eardrum.
Precautions: Pregnancy, breastfeeding; ototoxicity and nephrotoxicity may occur with topical neomycin in patients with aural or renal

disease especially when co-administered with aminoglycoside antibiotic; discontinue therapy if sensitisation or irritation occurs; intraocular pressure should be routinely monitored if used in the eye for 10 days or longer; advise patients to refrain from tasks requiring visual acuity until they feel able to do so.

Adverse effects: Rarely irritation or burning may occur; prolonged ophthalmological use may cause elevated intraocular pressure and/or glaucoma, posterior subcapsular cataract formation and an increased possibility of secondary ocular infections due to host-response suppression.

Dose: Instil 2-3 drops into the affected eye, nostril or ear every 1-4 hours according to the severity of the case; after the inflammation has subsided, the dosage may be gradually reduced to 1-2 drops 3-4 times daily.

POM **Hydrocortisone plus Neomycin** *(EDL 21.2)*
Eye-drops and Ointment, Hydrocortisone acetate 1.5%, neomycin sulphate 0.5%.

POM **HYCOMYCIN**® *(Dizpharm)*
Drops(Eye, Nose or Ear), Hydrocortisone acetate 1.5%, neomycin sulphate 0.5%; as an isotonic buffered suspension.
Pack - 5 ml.

POM **NEOCORTISONE**® *(Orange Drugs)*
Drops (Eye or Ear), Hydrocortisone acetate 1.5%, neomycin sulphate 0.5%.

HYDROCORTISONE plus OXYTETRACYCLINE plus POLYMYXIN B

Therapeutic category: Corticosteroid/antibiotic.

Indications: Blepharitis, Conjunctivitis, Scleritis; infected inflammatory conditions of the external ear canal.

Contra-indications: Viral diseases of the cornea and conjunctivitis; mycobacterial infection of the eye; fungal diseases of the ocular structures; perforated eardrum.

Precautions: Avoid prolonged use; secondary fungal infections of the cornea after prolonged use; monitor the intraocular pressure.

Adverse effects: Elevation of intraocular pressure, optic nerve damage, development of cataract, delayed wound healing, secondary infection.

Dose: Instil 1-2 drops 3 times daily.
Ear conditions, Instil 2-4 drops 3 times daily.

Note: Avoid contamination of the dropper with exudate from the infected site and replace the dropper immediately after use.

POM **Oxytetracycline plus Hydrocortisone plus Polymyxin B** *(EDL 21.2)*
Ear/Eye Suspension, Hydrocortisone 15 mg, Oxytetracycline HCl 5 mg, polymyxin B (as sulphate) 10,000 units per ml.

POM **OXYCORTRIL-B**® *(Drugfield)*
Eye/Ear Suspension, Hydrocortisone, oxytetracycline HCl, polymyxin B.
Pack - 5 ml

POM **TERRA-CORTRIL**® *(Pfizer/Neimeth)*
Eye/Ear Suspension, Hydrocortisone acetate 5 mg, Oxytetracycline HCl 10 mg, polymyxin B sulphate 10,000 units per ml; in a gel-like base.
Pack - 4 ml (in tube with nozzle).

KETOTIFEN

Therapeutic category: Anti-allergic.

Pharmacology: Ketotifen is a histamine H_1-receptor antagonist; it also inhibits the release of mediators (such as histamines, prostaglandins, leukotrienes) from cells involved in type 1 or immediate allergic reactions (mast cells, eosinophils, basophils and neutrophils). Ketotifen also reduces the chemotaxis, activation and degranulation of eosinophils. cAMP levels increased by phosphodiesterase inhibition can contribute to the cell-stabilising action of ketotifen. The antihistamine effect of ketotifen eye drops has a rapid onset following instillation into the eye and persists for 8-12 hours. Ketotifen eye drops alleviate the symptoms of allergic conjunctivitis such as pruritus and hyperaemia.

Indications: Treatment and prevention of signs and symptoms of allergic conjunctivitis.

Contra-indications: Hypersensitivity to ketotifen or any of the excipients.

Precautions: In principle, contact lenses should not be worn if the eyes are red and/or inflammed. The eye drops in bottles of 5ml contain benzalkonium chloride as preservative, which can permeate into soft hydrophilic contact lenses. For this reason, soft hydrophilic contact lenses must be taken out before applying ketotifen eye drops, and not replaced for at least 15 minutes (this does not apply to single dose units which do not contain preservative). Avoid use in irritation caused by contact lenses. Pregnancy.

Interactions: If several medicines are to be

administered into the eye, there should be an interval of at least 5 minutes between each application.

Adverse effects: Occasionally changes in visual acuity, dry eyes, headaches, fatigue, skin rash. Isolated cases of burning/stinging, conjunctivitis, subconjunctival haemorrhage, ophthalmalgia, sensitivity to light, allergic reaction, dry mouth, eczema.

Advice to patients: Ketotifen can impair the patient's reaction and therefore his ability to drive, operate machinery or perform other hazardous tasks.

Dose: Adult, elderly and children above 12 years, instil 1 drop twice daily into the conjuctival sac of each eye.
Children below 12 years: Efficacy has not been tested but it has beeb shown to be safe in children as young as 3 years.

Note: Maximum duration for treatment is 6 weeks. May be used up to 1 month after first opening the bottle (taking into account the expiring date).

POM **ZADITEN®** *(Norvatis Ophthalmics)*
Eye drops, Ketotifen (as fumarate) 0.25 mg per ml.
Pack - Dropper bottle of 5 ml.

LODOXAMIDE

Pharmacology: Lodoxamide is a mast cell stabilizer that inhibits the *in vivo* type 1 immediate hypersensitivity reaction. It inhibits the release of histamine and other mast cell inflammatory mediators(i.e. SRA-A). It has no intrinsic vasoconstrictor, antihistaminic, cyclooxygenase inhibition or other anti-inflammatory activity.

Indications: Allergic conjunctivitis

Contra-indications: Hypersensitivity to any component of the preparation.

Adverse effects: Mild and transient burning, stinging, itching, and lacrimation; flushing and dizziness.

Dose: Adult and child over 2 years, apply 1-2 drops in each eye 4 times daily at regular intervals. Not recommended for children below 2 years of age.

POM **ALOMIDE®** *(Summit Healthcare)*
Eye-drops, Lodoxamide (as tromethamine) 0.1%.
Pack - 10 ml (in polyethylene bottle).

NAPHAZOLINE plus PHENIRAMINE

Pharmacology: A combination of an antihistamine (pheniramine maleate) and a decongestant (naphazoline).

Indications: For the relief of ocular irritation and /or congestion.

Contra-indications: Hypersensitivity to any component of the preparation; narrow angle glaucoma.

Precautions: Severe cardiovascular disease including cardiac arrhythmia; poorly controlled hypertension; diabetes; pregnancy.

Adverse effects: Pupillary dilation; increase in ocular pressure; systemic effects due to absorption (i.e. hypertension, cardiac irregularities, hyper-glycaemia); drowsiness.

Dose: Instil 1-2 drops in each eye every 3-4 hours or less frequently as needed.

POM **NAPHCON-A®** *(Summit Healthcare)*
Eye-drops, Naphazoline HCl 0.025%, pheniramine maleate 0.3%.
Pack - 15 ml (in plastic DROP- TAINER® dispenser).

OXYTETRACYCLINE plus POLYMYXIN B

Indications: Prophylaxis and treatment of superficial ocular infections due to susceptible organisms.

Dose: Apply the ointment 3-6 times daily usually for 10-15 days in acute and up to 3 months in chronic cases.

POM **Oxytetracycline plus Polymyxin B** *(EDL 21.1)*
Eye ointment, Oxytetracycline HCl 5 mg, polymyxin B sulphate 10,000 units per g; in 3.5 g tube.

OXYPHENBUTAZONE

Indications: Local treatment of inflammation of the eye.

Dose: Apply ointment 2-5 times daily.

POM **Oxyphenbutazone** *(EDL 21.2)*
Eye ointment, Oxyphenbutazone 10%.

OXYPHENBUTAZONE plus CHLORAMPHENICOL

Therapeutic category: Topical antibiotic and anti-inflammatory agent.

Indications: Acute or chronic ocular inflammation with bacterial infections such as conjunctivitis, keratitis, blepharitis, keratoconjunctivitis without perforation; pre- and post-operative treatment of cataract, squint, glaucoma.

Precautions: Allergic reactions (without treat-

ment), Children, long-term treatment.
Adverse effects: Rarely allergic reactions.
Dose: Apply 3 times daily.

POM **MINADRIL**® *(Novartis Ophthalmics)*
Eye ointment, Oxyphenbutazone 100 mg, Chloramphenicol 10 mg per g
Pack - 5 g.

PREDNISOLONE

Prednisolone is a representative corticosteroid. Various drugs can serve as alternatives.
Indications: Short-term local treatment of inflammation of the eye; malignant disease (section 12.2.2); inflammatory and allergic reactions (section 10.3, also section 8.3).
Contra-indications: Undiagnosed 'red eye' caused by herpetic keratitis; glaucoma.
Precautions: Cataract; corneal thinning, corneal or conjunctival infection; discontinue treatment if no improvement within 7 days; risk of adrenal suppression after prolonged use in infants.
Adverse effects: Secondary ocular infection; impaired corneal healing (due to corneal thinning), optic nerve damage, cataract; glaucoma, mydriasis, ptosis, epithelial punctate keratitis, delayed hypersensitivity reactions including burning, stinging.
Administration: NOTE: USE ONLY UNDER THE SUPERVISION OF AN OPHTHALMOLOGIST.

Inflammation of the eye, by instillation into the eye, ADULT and CHILD 1 drop every 1–2 hours, reducing frequency as inflammation is controlled.

POM **Prednisolone** *(WMF 21.2)*
Eye drops, solution, Prednisolone sodium phosphate 0.5%.

SODIUM CROMOGLYCATE

Indications: Allergic conjunctivitis.
Dose: Apply eye-drops 4 times daily;
Eye ointment, apply 2-3 times daily.

POM **Sodium cromoglycate** *(EDL 21.2)*
Eye drops, Sodium cromoglycate 2%
Eye ointment, Sodium cromoglycate 4%.

TETRAHYDROZOLINE

Therapeutic category: Ophthalmic decongestant.
Pharmacology: Tetrahydrozoline is a sympathomimetic agent which brings about decongestion by vasoconstriction. It whitens reddened eyes by constricting the small blood vessels. It does not produce a dilation of the pupil or cause rebound hyperaemia.
Indications: Symptomatic relief of conjunctival oedema and hyperaemia secondary to ocular allergies, minor irritations, nonspecific or catarrhal conjunctivitis.
Precautions: Glaucoma.
Adverse effects: Ocular stinging, burning, reactive hyperaemia
Advice to patients: See under Antazoline plus Tetrahydrozoline.
Nursing considerations: •*See under Antazoline plus Naphazoline*.
Dose: Instil 1-2 drops in each eye 2-3 times daily.

OTC **Tetrahydrozoline** *(EDL 21.2)*
Eye-drops, Tetrahydrozoline HCl 0.05%

OTC **VISINE**® *(Neimeth)*
Eye-drops, Tetrahydrozoline HCl 0.05%; clear colourless solution in a dropper container.
Pack - 15 ml.

13.3 Mydriatics and cycloplegics

13.3.1 Antimuscarinics
13.3.2 Sympathomimetics

Antimuscarinics, by blocking the cholinergic effects of acetylcholine, paralyse the pupillary constrictor muscles causing dilation of the pupil (mydriasis) and paralyse the ciliary muscles resulting in paralysis of accommodation (cycloplegia). Mydriasis may precipitate acute angle-closure glaucoma particularly in elderly or long-sighted patients. In patients with dark iridic pigmentation, higher concentrations of mydriatic drugs are usually required and care should be taken to avoid overdosing.

Atropine is a long-acting antimuscarinic used for cycloplegic refraction procedures, particularly in children. It is also used to immobilize the ciliary muscle and iris and to prevent formation of posterior synechiae in the treatment of inflammatory eye disorders such as iritis and uveitis.

Further clinical notes
Antimuscarinics are used to dilate the pupil and to paralyse the ciliary muscles in order to facilitate surgical procedures. **Atropine** is the most potent whilst **Tropicamide** is least potent. They also vary in their duration of action. Whilst tropicamide effects may last for 3 hours,

RETURN

the effect of atropine is seen up to 7 days or longer. **Cyclopentolate**, and **Homatropine** have intermediate potencies and their effects last for up to 24 hours.

Sympathomimetics like **Phenylephrine** are also used as mydiatrics and decongestants.

Contact dermatitis is common with the antimuscarinic mydriatic drugs, especially atropine. In addition, toxic systemic reactions to atropine may occur in the very young and the very old.

Mydriasis may precipitate acute closed-angle ('congestive') glaucoma in a few patients, usually aged over 60 years, who are predisposed to the condition because of a small eyeball with a shallow anterior chamber and small diameter cornea. A family history is significant and mydriatics should be avoided in such patients.

Phenylephrine may interact with systematically administered monoamine-oxidase inhibitors.

Patients should be warned not to drive for 1 to 2 hours after mydriasis.

13.3.1 Antimuscarinics

Short-acting, relatively weak mydriatics, such as **Tropicamide** 0.5%, facilitate the examination of the fundus of the eye. **Cyclopentolate** 1% or **Atropine** are preferable for producing cycloplegia for refraction in young children. Atropine 1% as ointment is preferred for children under 5 years of age. Atropine is also used for the treatment of iridocyclitis mainly to prevent posterior synechiae, often with phenylephrine 10% eye-drops.

ATROPINE

Therapeutic category: Mydriatic

Indications: Iritis, uveitis; cycloplegic refraction procedures; premedication (section 3.2); organophosphate poisoning (section 19.2.3); antispasmodic (section 4.2).

Contra-indications: Angle-closure glaucoma.

Precautions: May precipitate acute attack of angle-closure glaucoma, particularly in the elderly or long-sighted; risk of systemic effects with eye drops in infants under 3 months—eye ointment preferred.

SKILLED TASKS: MAY CAUSE SENSITIVITY TO LIGHT AND BLURRED VISION. DO NOT CARRY OUT SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY OR DRIVING, UNTIL VISION IS CLEAR.

Adverse effects: Transient stinging and raised intra-ocular pressure; on prolonged administration, local irritation, hyperaemia, oedema and conjunctivitis may occur; contact dermatitis; systemic toxicity may occur in the very young and the elderly.

Advice to patients: Ensure patient knows how to instil drug; do not allow dropper bottle or tube to touch eye or surrounding tissue during administration; may cause blurred vision, increased sensitivity to light or eye pain, notify physician if it becomes severe or persists.

Nursing considerations: •Finger pressure should be applied to lacrimal sac for 1-2 minutes after instillation to decrease risk of absorption and systemic reactions.

•Advise patient to use chewing gum if dry mouth becomes a problem.

•Advise patient to avoid hazardous activities until the visual impairment caused by this drug wears off; sunglasses can relieve the discomfort of photophobia.

•Observe for signs of glaucoma namely increased I.O.P., eye pain, headache, progressive blurring of vision; report to physician.

Administration: *Cycloplegic refraction*, by instillation into the eye, ADULT 1 drop (1%) twice daily for 1–2 days before procedure or a single application of 1 drop (1%) 1 hour before procedure; CHILD under 3 months (see Precautions), 3 months–1 year (0.1%), 1–5 years (0.1–0.5%), over 5 years (0.5–1%), 1 drop twice daily for 1–3 days before procedure with a further dose given 1 hour before procedure.

Iritis, uveitis, by instillation into the eye, ADULT 1 drop (0.5 or 1%) up to 4 times daily; CHILD 1 drop (0.5 or 1%) up to 3 times daily.

POM **Atropine** *(WMF 21.5)*
Eye drops, solution, Atropine sulfate 0.1%, 0.5%, 1%.

POM **Atropine** *(EDL 21.5)*
Eye drops or Ointment, Atropine sulphate 1%.

POM **Atropine** *(Novartis Ophthalmics)*
Eye-drops, Atropine sulphate 10 mg per ml.
Pack - 10 ml
Eye ointment, Atropine sulphate 10mg per g.
Pack - 4 g.

POM **CHIBRO-ATROPINE**® *(Bolax/BPP)*
Eye-drops, Atropine sulphate 1%

POM **Atropine** *(CHI)*
Eye-drops, Atropine sulphate 1%
Pack - 5 ml
Eye ointment, Atropine sulphate 1%

Pack - 3.5 g.

CYCLOPENTOLATE

Indications: Mydriasis and cycloplegia
Contra-indications: Narrow angle glaucoma or anatomical narrow angles.
Precautions: Elderly; patients with increased I.O.P
Adverse effects: Increased I.O.P., psychotic reactions usually in children.
Advice to patients: Ensure patient knows how to instil drug; do not allow tip of dropper bottle or tube to touch eye or surrounding tissue during administration; may cause blurred vision, increased sensitivity to light or eye pain, notify physician if it becomes severe or persist.
Nursing considerations: •Finger pressure should be applied to lacrimal sac for 1-2 minutes after instillation to decrease risk of absorption and systemic reactions.
•May cause burning sensation on instillation.
•Advise patient to avoid hazardous activities until the visual impairment caused by this drug wears off; sunglasses can relieve the discomfort of photophobia.
Dose: 1 drop (1%) followed by 2nd drop in 5 mins; complete recovery usually in 24 hours.

POM **Cyclopentolate** *(EDL 21.5)*
Eye-drops, Cyclopentolate HCl 0.5%, 1%.

POM **CYCLOGYL®** *(Summit Healthcare)*
Eye-drops, Cyclopentolate HCl 1%
Pack - 15 ml.

HOMATROPINE

Indications: Mydriatic and cycloplegic for refraction, uveitis.
Contra-indications: Glaucoma
Adverse effects: Loss of accommodation; raised intraocular pressure; local irritation on prolonged use.
Advice to patients: Ensure patient knows how to instil drug; do not allow dropper bottle or tube to touch eye or surrounding tissue during administration; may cause blurred vision, increased sensitivity to light or eye pain, notify physician if it becomes severe or persist.
Nursing considerations: •Teach patient how to instil the drug: wash hands before and after instillation, avoid touching dropper tip to eye or sorrounding tissue, tilt head back, place medication in conjunctival sac, and close eyes. Apply light finger-pressure on lacrimal sac for 1-2 minutes following instillation to decrease risk of absorption and systemic reactions.
•Advise patient to avoid hazardous tasks such as driving, until he can see clearly; sunglasses can relieve the discomfort of photophobia.
•Advise patient to use chewing gum if dry mouth becomes a problem.
Dose: *Cycloplegic refraction*, Adult and child, instil 1-2 drops (2% or 5%); repeat in 5-10 minutes if necessary for 2 or 3 doses. *Uveitis*, Adult and Child, instil 1-2 drops (2% or 5%) up to 3-4 hourly.

POM **Homatropine** *(EDL 21.5)*
Eye drops, Homatropine hydrobromide 1%, 2%

POM **ISOPTO HOMATROPINE®** *(Summit Healthcare)*
Eye-drops, Homatropine hydrobromide 2%.
Pack - 15 ml.

TROPICAMIDE

Indications: Mydriatic and cycloplegic (with a rapid recovery of accommodation) for refraction.
Contra-indications: Narrow angle glaucoma; soft lenses.
Precautions: Unknown I.O.P; in infants put pressure over lachrymal sac for 1 minute.
Adverse effects: Transient stinging, dry mouth, blurred vision, photophobia, tachycardia, headache, psychotic reactions, behavioural changes.
Advice to patients: See under Homa-tropine
Nursing considerations: •Teach patient correct method of instillation: wash hands before and after instillation, avoid touching dropper tip to eye, tilt head back, place medication in conjunctival sac, and close eyes. Apply light finger-pressure on lacrimal sac for 1 minute after instillation.
•Reassure patient that blurred vision will decrease with repeated use of drug; advise him not to engage in hazardous tasks such as driving until he can see clearly.
•Advise patient to wear dark sunglasses if photophobia occurs.
•Wait for 5 minutes before applying other eye drops.
Dose: 1-2 drops (1%) at 1-5 minute intervals. If patient not examined within 30 minutes, an additional drop shoud be used.

POM **Tropicamide** *(EDL 21.5)*
Eye-drops, Tropicamide 0.5%, 1%.

POM **MYDRIACYL®** *(Summit Healthcare)*
Eye-drops, Tropicamide 1%
Pack - 15 ml.

POM **MYDRIATICUM®** *(Bolax/BPP)*
Eye-drops, Tropicamide 0.5%.
Pack - 10 ml.

13.3.2 Sympathomimetics

Phenylephrine is used as a mydriatic/decongestant in combination with atropine. It is contraindicated in glaucoma and may induce loss of accommodation.

PHENYLEPHRINE

Indications: Mydriatic, decongestant and vasoconstrictor.

Contra-indications: Glaucoma, soft contact lense use.

Adverse effects: Occular effects include transient burning or stinging on instillation, blurred vision, allergic conjunctivitis, photophobia; systemic effects include hypertension, palpitations, tachycardia, trembling, sweating.

Advice to patients: Ensure patient knows how to instil drug; do not touch dropper tip to the eye; may cause blurred vision, do not drive; may cause photophobia, use sunglasses.

Nursing considerations: •Teach patient how to instil drug: wash hands before and after instillation, avoid touching dropper tip to eye, tilt head back, place medication in conjunctival sac, and close eyes. Apply light finger-pressure on lacrimal sac for 1-2 minutes following instillation to prevent systemic absorption.

•Monitor patient's B.P. and pulse.

•Avoid in patients with idiopathic orthostatic hypotension; may cause high blood pressure.

•Advise patient not to exceed recommended dose because systemic effects are common.

•May cause blurred vision; warn patient against driving or operating a machinery until this effect wears off.

•May cause photophobia; advise patient to wear dark sunglasses and to contact physician if condition persists for over 12 hours afer stopping the drug.

•Wait for 5 minutes before applying other eye drops.

Dose: *Mydriasis and Vasoconstruction*, Adult, instil 1 drop (2.5% or 10%); may repeat in 1 hour if necessary.
Child: instil 1 drop (2.5%) as above.
To relieve eye redness, Adult, instil 1-2 drops (0.12%) up to 4 times daily.
Chronic mydriasis, Adult, instil 1 drop (2.5% or 10%) 2-3 times daily.
Child: instil 1 drop (2.5%) 2-3 times daily.
Posterior synechia (adhesion of iris), Adult and child, instil 1 drop (10%)
Mydriasis (without cycloplegia), Adult and Child, instil 1 drop (2.5% or 10%) before examination.

Note:10% solution should not be used in infants; use cautiously in the elderly.

POM **Phenylephrine** *(EDL 21.5)*
Eye-drops, Phenylephrine HCl 2.5%, 10%.

POM **MYDFRIN**® *(Summit Healthcare)*
Eye- drops, Phenylephrine HCl 2.5%.
Pack - 5 ml.

13.4 Drugs used in glaucoma

13.4.1 Miotics
13.4.2 Beta-blockers
13.4.3 Sympathomimetics
13.4.4 Carbonic anhydrase inhibitors

Glaucoma is normally associated with raised intra-ocular pressure and eventual damage to the optic nerve which may result in blindness. The rise in pressure is almost always due to reduced outflow of aqueous humour, the inflow remaining constant. The most common condition is chronic open-angle glaucoma (chronic simple glaucoma) in which the intra-ocular pressure increases gradually and the condition is usually asymptomatic until well advanced. In contrast, angle-closure glaucoma (closed-angle glaucoma) usually occurs as an acute emergency resulting from a rapid rise in intra-ocular pressure; if treatment is delayed, chronic angle-closure glaucoma may develop. Ocular hypertension is a condition in which intra-ocular pressure is raised without signs of optic nerve damage.

Drugs used in the treatment of glaucoma lower the intra-ocular pressure by a variety of mechanisms including reduction in secretion of aqueous humour by the ciliary body, or increasing the outflow of the aqueous humour by opening of the trabecular network. Antiglaucoma drugs used include topical application of a beta-blocker (beta-adrenoceptor antagonist), a miotic, or a sympathomimetic such as epinephrine; systemic administration of a carbonic anhydrase inhibitor may be used as an adjunct.

Timolol is a non-selective beta-blocker that reduces the secretion of aqueous humour. A beta-blocker is usually the drug of choice for initial and maintenance treatment of chronic open-angle glaucoma. If further reduction in intra-ocular pressure is required a miotic, a sympathomimetic or a systemic carbonic anhydrase inhibitor may be used with timolol. In angle-closure glaucoma, timolol should be used with a miotic and not alone. Since systemic absorption can occur, an ophthalmic beta-blocker should be used with caution in

certain individuals.

A miotic such as **pilocarpine**, through its parasympathomimetic action, contracts the iris sphincter muscle and the ciliary muscle, and opens the trabecular network. It is used in chronic open-angle glaucoma either alone or, if required, with a beta-blocker, epinephrine or a systemic carbonic anhydrase inhibitor. Pilocarpine is used with systemic acetazolamide in an acute attack of angle-closure glaucoma prior to surgery; however, it is not advisable to use pilocarpine after surgery because of a risk of posterior synechiae forming. Systemic absorption of topically applied pilocarpine can occur producing muscarinic adverse effects.

The sympathomimetic drug **epinephrine** (adrenaline) probably acts by reducing the rate of production of aqueous humour and increasing the outflow through the trabecular network. Epinephrine is usually used with a miotic, a beta-blocker or a systemic carbonic anhydrase inhibitor in the treatment of chronic open-angle glaucoma; however, because epinephrine is also a mydriatic, it is contraindicated for angle-closure glaucoma unless an iridectomy has been carried out.

Acetazolamide, by reducing carbonic anhydrase in the eye, reduces the production of aqueous humour and so reduces intra-ocular pressure. It is used systemically as an adjunct in chronic open-angle glaucoma unresponsive to treatment with topically applied antiglaucoma drugs. Prolonged therapy with acetazolamide is not normally recommended, but if treatment is unavoidable blood count and plasma electrolyte concentration should be monitored. Acetazolamide is also used as part of emergency treatment for an acute attack of angle-closure glaucoma; however it should not be used in chronic angle-closure glaucoma as it may mask deterioration of the condition.

13.4.1 Miotics

PILOCARPINE

Pilocarpine is a representative miotic. Various drugs can serve as alternatives.

Indications: Chronic open-angle glaucoma, ocular hypertension; emergency treatment of acute angle-closure glaucoma; to antagonize effects of mydriasis and cycloplegia following surgery or ophthalmoscopic examination.

Contra-indications: Acute iritis, acute uveitis, anterior uveitis, some forms of secondary glaucoma; acute inflammation of anterior segment; not advisable after angle-closure surgery (risk of posterior synechiae).

Precautions: Retinal disease, conjunctival or corneal damage; monitor intra-ocular pressure in chronic open-angle glaucoma and in long-term treatment; cardiac disease, hypertension, asthma, peptic ulceration, urinary-tract obstruction, Parkinson disease; stop treatment if symptoms of systemic toxicity develop

SKILLED TASKS: CAUSES DIFFICULTY WITH DARK ADAPTATION; MAY CAUSE ACCOMMODATION SPASM. DO NOT CARRY OUT SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY OR DRIVING UNTIL VISION IS CLEAR.

Adverse effects: Eye pain, blurred vision, ciliary spasm, lacrimation, myopia, browache; conjunctival vascular congestion, superficial keratitis, vitreous haemorrhage and increased pupillary block have been reported; lens opacities have occurred following prolonged use; rarely systemic effects including hypertension, tachycardia, bronchial spasm, pulmonary oedema, salivation, sweating, nausea, vomiting, diarrhoea.

Advice to patients: May sting on instillation; notify physician of sweating, urinary retention; usually causes difficulty in dark adaptation; advice patients to use caution while night driving or performing hazardous tasks in poor illumination; after topical instillation, finger pressure should be applied to lacrimal sac for 1-2 minutes to decrease drainage into the nose and throat and minimize possible systemic absorption and reactions.

Administration: *Chronic open-angle glaucoma*, by instillation into the eye, ADULT 1 drop (2% or 4%) up to 4 times daily.

Acute angle-closure glaucoma before surgery, by instillation into the eye, ADULT 1 drop (2%) every 10 minutes for 30–60 minutes, then 1 drop every 1–3 hours until intra-ocular pressure subsides.

POM **Pilocarpine** *(WMF 21.4.1)*

Eye drops, solution, Pilocarpine hydrochloride 2%, 4%; Pilocarpine nitrate 2%, 4%.

POM **Pilocarpine** *(EDL 21.4.1)*

Eye drops, Pilocarpine HCl 1%, 2%, 3%, 4%

POM **CHIBRO-PILOCARPINE**® *(Bolax/BPP)*
Eye-drops, Pilocarpine nitrate 1%, 2%, 4%.
Pack - 10 ml

POM **ISOPTO CARPINE**® *(Summit Healthcare)*
Eye-drops, Pilocarpine 1%, 2%, 3%, 4%.
Pack - 15 ml.

PHYSOSTIGMINE

Indications: Primary glaucoma.
Adverse effects: Headache,weakness, slow or irregular heartbeats, blurred vision, eye irritation, nausea, vomiting, diarrhoea, loss of bladder control, increased sweating, shortness of breath.
Advice to patients: Burning or stinging may occur with application; may cause loss of dark adaptation; notify physician if abdominal cramps, sweating, salivation, or cramps occur.
Nursing considerations: •Teach patient how to instill the drug: wash hands before and after instillation, avoid touching dropper tip to eye or sorrounding tissue, tilt head back, place medication in conjunctival sac, and close eyes. Apply light finger-pressure on lacrimal sac for 1 minute following instillation to decrease drainage into the nose and throat and minimize possible systemic absorption and reactions.
Dose: 1-2 drops, 3-6 times daily

POM **Physostigmine** *(EDL 21.4.2)*
Eye drops, Physostigmine sulphate 0.25%, 0.5%

13.4.2 Beta-blockers

TIMOLOL

Timolol is a representative beta-blocker. Various drugs can serve as alternatives.
Therapeutic category: Anti-glaucoma (Ocular hypotensive)
Indications: Ocular hypertension; chronic open-angle glaucoma, aphakic glaucoma, some secondary glaucomas.
Contra-indications: Uncontrolled heart failure, bradycardia, heart block; asthma, obstructive airways disease.
Precautions: Older people (risk of keratitis); if used in angle-closure glaucoma, use with a miotic, and not alone; **interactions**: Appendix 1.
Adverse effects: Stinging, burning, pain, itching, erythema, transient dryness, allergic blepharitis, transient conjunctivitis, keratitis, decreased corneal sensitivity, diplopia, ptosis; systemic effects, particularly on the pulmonary, cardiovascular and central nervous systems, may follow absorption.
Advice to patients: Apply gentle pressure to lacrimal sac during and immediately following instillation (1 minute) to avoid systemic absorption; stop drug if breathing difficulty occurs.
Nursing considerations: •Teach patient how to instil drug: wash hands before and after instillation, avoid touching dropper tip to eye, tilt head back, place medication in conjunctival sac, and close eyes. Apply light finger-pressure on lacrimal sac for 1 minute following instillation to prevent systemic absorption. •Monitor for systemic effect of beta-blockade even when administering ophthalmic product.
Administration: *Ocular hypertension, chronic open-angle glaucoma, aphakic glaucoma, some secondary glaucomas*, by instillation into the eye, ADULT 1 drop (0.25% or 0.5%) twice daily.

POM **Timolol** *(WMF 21.4.2)*
Eye drops, solution, Timolol (as maleate) 0.25%, 0.5%.

POM **Timolol** *(EDL 21.4.1)*
Eye-drops, Timolol maleate 0.25%, 0.5%.

POM **CUSIMOLOL**®*(Summit Healthcare)*
*Eye- drops,*Timolol maleate 0.25%.

POM **NYOLOL**®*(Novartis Ophthalmics)*
Eye-drops, Timolol (as maleate) 0.5%.
Pack - 5 ml (in a dropper bottle).
Gel, Timolol (as maleate) 0.1%.

POM **OPHTHAMOLOL**® *(Supreme Pharm)*
Eye-drops, Timolol maleate 0.25%, 0.5%
0.25% - 10 ml
0.5% - 10 ml

POM **TIMOPTOL**® *(Bolax/BPP)*
Eye-drops, Timolol (as maleate) 0.25%, 0.5%; Clear, colourless to light yellow, sterile eye drops in metered-dose Ocumeter Dispensers
0.25% - 5 ml
0.5% - 5 ml.

POM **Timolol** *(Hovid)*
Eye-drops, Timolol maleate 0.25%, 0.5%; clear, colourless liquid.
Pack - 5 ml.

13.4.3 Sympathomimetics

EPINEPHRINE

Epinephrine is a complementary drug for use

when drugs in the main list cannot be made available.

Synonym: Adrenaline

Indications: Chronic open-angle glaucoma, ocular hypertension; anaphylaxis (section 8.2); cardiac arrest (section 5.4).

Contra-indications: Angle-closure glaucoma, unless an iridectomy has been carried out.

Precautions: Hypertension, heart disease, aneurysm, arrhythmia, tachycardia, hyperthyroidism, cerebral arteriosclerosis, diabetes mellitus.

Adverse effects: Stinging, blurred vision, photophobia, eye pain, conjunctival hyperaemia, headache or browache; occasionally, conjunctival sensitization and local skin reactions; after prolonged use conjunctival pigmentation and macular oedema in aphakia; systemic adverse reactions are rare following topical use at normal dosage but tachycardia, hypertension, arrhythmia, dizziness, sweating may occur.

Administration: *Chronic open-angle glaucoma*, by instillation into the eye, ADULT 1 drop (0.5% or 1%) 1–2 times daily.

POM **Epinephrine** *(WMF 21.4.3)*
Eye drops, solution, Epinephrine (as HCl) 0.5%, 1%.

13.4.4 Carbonic anhydrase inhibitors

ACETAZOLAMIDE

Therapeutic category: Diuretic; Carbonic anhydrase inhibitor.

Indications: As an adjunct in the treatment of chronic open-angle glaucoma; secondary glaucoma; as part of pre-operative treatment of acute angle-closure glaucoma.

Contra-indications: Hypersensitivity to sulfonamides; chronic angle-closure glaucoma (may mask deterioration); hypokalaemia, hyponatraemia, hyperchloraemic acidosis; renal impairment (Appendix 4), severe hepatic impairment.

Precautions: Elderly; pregnancy (Appendix 2); breastfeeding (Appendix 3); diabetes mellitus; pulmonary obstruction; monitor blood count and electrolytes if used for long periods; **interactions**: Appendix 1.

SKILLED TASKS: MAY IMPAIR ABILITY TO PERFORM SKILLED TASKS, FOR EXAMPLE OPERATING MACHINERY, DRIVING.

Adverse effects: Nausea, vomiting, diarrhoea, taste disturbance; loss of appetite, paraesthesia, flushing, headache, dizziness, fatigue, irritability, depression; thirst, polyuria; reduced libido; metabolic acidosis and electrolyte disturbances on long-term therapy; occasionally drowsiness, confusion, hearing disturbances, urticaria, melaena, glycosuria, haematuria, abnormal liver function, renal calculi, blood disorders including agranulocytosis and thrombocytopenia, rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis; transient myopia reported.

Advice to patients: May take with food; report numbness or tingling of extremities to physician; ability to perform tasks requiring mental alertness and/or physical co-ordination may be impaired; drug may cause substantial increase in blood glucose in some diabetic patients.

Nursing considerations: •Administer orally with food to reduce nausea; absorption may be reduced slightly.
•Patient may be placed on high potassuim diet.
•Advise patient to rise slowly from lying down or sitting position; to avoid hazardous activities if drowsiness occurs.
•Weigh patient daily as elderly patient is susceptible to excess diuresis; weight loss and hypotension should be assessed.
•Monitor fluid I&O, electrolytes viz sodium, bicarbonate and chloride.

Dose: *Chronic open-angle glaucoma*, secondary glaucoma, by mouth, ADULT 0.25–1 g daily in divided doses.

POM **Acetazolamide** *(WMF 21.4.4)*
Tablets, Acetazolamide 250 mg.

POM **Acetazolamide** *(EDL 21.5)*
Tablet, Acetazolamide 250 mg.

POM **APO-ACETAZOLAMIDE®** *(Lahams)*
Tablet, Acetazolamide 250 mg; white, double scored tab. marked 'APO 250'.
250 mg - 100; 500.

POM **ACETOMID®** *(Hovid)*
Tablet, Acetazolamide 250 mg
250 mg - 500.

13.4.5 Prostaglandin analogue

LATANOPROST

RETURN

Indications: Reduction of elevated IOP in patient with open angle glaucoma and ocular hypertension.
Contra-indications: Known hypersensitivity to latanoprost or benzalkonium chloride.
Precautions: Prostanglandin analogues may gradually change eye colour by increasing the amount of brown pigment in the iris; monitor patient. Pregnancy and breastfeeding.
Adverse effects: Major side effects include blurred vision, increased pigmentation of iris, conjunctival hyperaemia & punctuate epithelial erosions. Mild to moderate conjunctival or episcleral hyperaemia may occur during topical treatment and photophobia. Rarely (< 1%) conjunctivitis, diplopia & eye discharge have been reported. Most common systemic events include upper respiratory tract infections, cold & flu, pain in muscle, joints, back, chest & angina pectoris.
Dose: One drop once daily preferably in the evening, which should not be exceeded. Reduction of IOP starts 3-4 hours after administration; pressure reduction is maintained for at least 24 hours.
Note: Can be used concomitantly with other products - to be used 5 minutes apart.

POM **XALATAN®** *(Pharmacia)*
Drops, Latanoprost 50 µg with 50 µg benzalkonium chloride as preservative.
Pack – 5 ml bottle.

13.5 Local anaesthetics

Topical local anaesthetics are employed for simple ophthalmological procedures and for short operative procedures involving the cornea and conjunctiva. **Tetracaine**, available in 0.5% ophthalmic solution, provides a rapid local anaesthesia which lasts for 15 minutes or more. Prolonged or unsupervized use of tetracaine is not recommended.

TETRACAINE

Tetracaine is a representative local anaesthetic. Various drugs can serve as alternatives.
Synonym: Amethocaine
Indications: Short-acting local anaesthesia of cornea and conjunctiva.
Contra-indications: Hypersensitivity to ester-type local anaesthetics; eye inflammation or infection.
Precautions: Avoid prolonged use (cause of severe keratitis, permanent corneal opacification, scarring, delayed corneal healing); protect eye from dust and bacterial contamination until sensation fully restored.
Adverse effects: Burning, stinging, redness; rarely, allergic reactions may occur.
Advice to patients: May cause transient burning or stinging of eyes upon instillation; do not touch or rub eye until anaesthesia has worn off.
Administration: *Local anaesthesia*, by instillation into the eye, ADULT and CHILD 1 drop.

POM **Tetracaine** *(WMF 21.3)*
Eye drops, solution, Tetracaine HCl 0.5%

POM **Tetracaine** *(EDL 21.3)*
Eye-drops, Tetracaine HCl 0.5%, 1%.

13.6 Miscellaneous eye preparations

A variety of other agents are applied for local or systemic effects.
Chymotrypsin is a zonulolytic which is useful in intracapsular cataract extraction.
Hyaluronidase is used to promote resorption of excess fluids and extravasated blood in the tissue during ocular surgery.
Methylcellulose, an emollient, is used for tear deficiencies.
Zinc Sulphate, a traditional astringent, is used in eye–drops for treatment of excessive lachrymation. It should not be combined with epinephrine eye drops because of the risk in using epinephrine in patients predisposed to closed–angle glaucoma.

CHYMOTRYPSIN

Therapeutic category: Zonulolytic
Indications: For enzymatic zonulysis in intracapsular lens extraction.
Contra-indications: Significant anterior displacement of the lens iris diaphragm with impending vitreous loss or other conditions in which loss of vitreous is a significant problem.
Precautions: Rise in I.O.P, moderate uveitis, corneal oedema.
Dose: See lit.

POM **Chymotrypsin** *(EDL 21.7)*
Injection, alpha chymotrypsin 300 U.S.P. units; powder.

DICLOFENAC

Therapeutic category: Non-steroidal anti-inflammatory drug (NSAID).
Pharmacology: Diclofenac sodium is a non-

steroidal drug with anti-inflammatory and analgestic effects. It acts by inhibitions of prostaglandin synthesis. It has an anti-inflammatory effect when given after surgery or trauma to the eye and in other non-infectious inflammatory conditions. Prophylactic administration of diclofenac in patients undergoing cataract removal and intraocular lens implantation reduces the frequency and severity of intra-operative miosis and post-operative cystoid macular oedema.

Indications: Inhibition of miosis during cataract surgery. Postoperative inflammation after cataract surgery and other surgical procedures. Prevention of cystoid macular oedema associated with lens extraction and intraocular lens implantation. Non-infectious inflammatory conditions affecting the anterior segment of the eye (e.g. chronic non-infectious conjunctivitis). Post-traumatic inflammation in penetrating and non-penetrating wounds (as an adjuvant to local anti-infective therapy).

Adverse effects: Occasionally, mild or moderate**,** transient stinging and /or blurred vision directly after application of eye drops. Rarely, hypersensitivity reaction in the form of itching, reddening, and photosensitivity; Kertitis punctata.

Dose: Adults, *Preoperative,* up to 5 x 1 drop in the 3 hours preceding surgery.

Postoperative, 3 x 1 drop immediately after surgery, thereafter 3-5 x 1 drop daily for as long as required.

Other indications, 4-5 x 1 drop daily, depending on the severity of the condition.

POM **VOLTAREN OPHTHA®** *(Novartis Ophthalmics)*

Eye-drops, Diclofenac sodium 1.0 mg per ml Pack - 5 ml (in a dropper bottle).

HYALURONIDASE

Indications: To promote resorption of excess fluids and extravasated blood in the tissue during ocular surgery.

Contra-indications: Should not be injected into or around an infected area.

Precautions: Infections

Adverse effects: Occasional hypersensitivity reactions.

Nursing considerations: •Appropriate drugs for the management of an acute hypersensitivity (adrenaline, corticosteroids, and antihistamines) should be readily available.

•Avoid getting solution into the eyes; flush with water at once.

•Solution is unstable and should be used immediately after mixing it.

Dose: See lit.

POM **Hyaluronidase** *(EDL 21.7)*

Injection, Hyaluronidase 1,500 units; powder in amp.

METHYLCELLULOSE

Indications: An emolient used for tear deficiencies.

Contra-indications: Soft lenses.

Dose: See lit.

POM **Methylcellulose** *(EDL 21.7)*

Eye-drops, Methylcellulose 1%, 2%.

PHENYLMERCURIC BORATE

Indications: Ocular hygiene; irrigation of the eyelids or eye.

Dose: 1-3 times daily.

POM **DACRYOSERUM®** *(Bolax/BPP)*

Eye-lotion, Phenylmercuric borate 0.002%, boric acid 1.8%, sodium borate 1.2%, sodium chloride 0.3%; in plastic vial with nozzle allowing eyewash dropwise or under pressure. Pack - 150 ml vial.

POTASSIUM IODIDE plus SODIUM IODIDE

Therapeutic category: Anti-cataractogenic.

Pharmacology: Iodides can activate the metabolism and occasionally counteract cloudiness of the vitreous body. Potassium iodide diffuses rapidly into the vitreous humour after local administration.

Indications: Opacity of and bleeding in the vitreous body of any cause (age, myopia, hypertension, diabetes, periphlebitis etc.). Clouding of the lens as the first sign of senile cataract.

Contra-indications: Known hypersensitivity to iodine (iodism) or other components of the formulation. Functional disturbances of the thyroid.

Precautions: Gently compress the lacrimal sac with the index finger for 1-2 mins after instillation to minimize systemic absoprtion. Pregnancy and lactation.

Adverse effects: Slight and transient burning or pricking sensation. Occasionally, increased tear flow. Hyperthyroidism and acne-type effects may occur.

Dose: Apply one drop into the conjunctival sac 1-3 times a day.

Note: Gently compress the lacrimal sac with the index finger for 1-2 mins after instillation

RETURN

to minimize systemic absorption.

POM **VITREOLENT**® *(Novartis Ophthalmics)*
Eye-drops, Potassium iodide 3 mg, sodium iodide 3 mg per ml.
Pack - 10 ml (in a dropper bottle).

ZINC SULFATE

Indications: Excessive lachrymation
Advice to patients: Notify physician if irritation persists or continues.
Dose: Apply sufficient quantity to both eyes 3 times daily.

POM **Zinc Sulfate** *(EDL 21.7)*
Eye-drops, Zinc sulfate 0.22 - 0.28%

POM **ZINCFRIN**® *(CHI)*
Eye-drops, Zinc sulfate.

14. Ear, nose and throat (ENT) drugs

RETURN

14.1 Ear drugs
14.1.1 Anti-infective and/or Anti-inflammatory drugs
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14.1 Ear drugs

14.1.1 Anti-infective and/or Anti-inflammatory drugs
14.1.2 Preparations for the removal of ear wax

Drugs are applied locally as drops or ointment, into the ear for the treatment of ear infections and to remove excess ear wax. The major disorders of the ear are otitis externa, an eczematous reaction of the meatal skin, and otitis media which is the commonest cause of severe pain in small children and recurrent attacks especially in infants, are particularly distressing. For *otitis externa*, one must exclude an underlying chronic otitis media before treatment is started. Many cases recover after thorough cleansing of the meatus by suction, dry mopping or gentle syringing. For resistant cases, it is effective to introduce a ribbon gauze dressing soaked in an astringent such as aluminum acetate, or anti-inflammatory corticosteroid solution. When this is not possible, the ear should be gently cleared with a probe covered in cotton wool and the patient encouraged to lie with the affected ear uppermost for ten minutes after the canal has been filled with a liberal quantity of the appropriate solution. If infection is present, a topical anti-infective which is not used systemically (such as framycetin, neomycin or clioquinol) may be used for only about a week as excessive use may result in fungal infections. Sensitivity to the anti-infective or solvent may occur and resistance to antibacterial is a possibility with prolonged use.

For *acute otitis media* local treatment is ineffective and there is no place for drops containing a local anaesthetic. Many attacks are viral in origin and require only treatment with simple analgesics for pain. Severe attacks of bacterial origin should be treated with systemic antibiotics. Identification of the infecting organism by bacterial examination of the discharge, if present, is helpful in selecting the appropriate treatment. In recurrent acute otitis media a daily dose of a prophylactic antibiotic (co-trimoxazole or erythromycin)

during the cold season can be tried.

For *chronic otitis media*, thorough cleansing with an aural suction tube may completely control infection. However, acute exacerbations of chronic infection may require systemic antibiotics.

Ear wax may be readily removed by syringing with warm water. If necessary, wax can be softened before syringing with topical solutions, the most effective of which is sodium bicarbonate ear-drops. Other simple remedies are olive oil and almond oil. The patient should lie with the affected ear uppermost for 5 to 10 minutes after a generous amount of the solution has been introduced into the ear.

14.1.1 Anti-infective and/or Anti-inflammatory drugs

Chloramphenicol ear drugs contain propylene glycol and cause sensitivity in about 10% of patients. An eye ointment of chloramphenicol may be used. It is primarily indicated for bacterial infection of the external ear. Framycetin and Gentamicin are the other widely-used anti-infectives for bacterial infections of the external ear. However, when otitis externa is treated topically with preparations containing aminoglycosides or polymyxins in patients who have a perforation of the tympanic membrane, there is an increased risk of drug-induced deafness.

Solutions containing an anti-infective and a corticosteroid (such as Gentisone HC) are used for treating cases where infection is present with inflammation and eczema.

CHLORAMPHENICOL

Indications: Bacterial infections of the external ear.

Adverse effects: Hypersensitivity reactions.

Nursing considerations: •Teach patient how to instil ear drops correctly without touching dropper to the ear.

•Remove impacted cerumen by irrigation; clean stopper with methylated spirit; restrain child if necessary; warm solution to body temperature; drop drug into the ears.

•Inform patient that dizziness may occur after instilling drug.

•Monitor the ears for pain, redness, swelling and fever.

Dose: Apply 2-3 drops, 2-3 times daily.

POM **Chloramphenicol** *(EDL 17.1)*
Ear drops, Chloramphenicol 5%.

POM **CHLORAF**® *(Afrab-Chem)*
Eardrops, Chloramphenicol 5%; in a bottle of 10 ml solution with dropper.

FRAMYCETIN

Indications: Bacterial infection of the external ear.

Adverse effects: Hypersensitivity reactions

Nursing considerations: •*See under Chloramphenicol*.

Dose: Apply 2-3 drops, 2-3 times daily.

POM **Framycetin** *(EDL 17.1)*
Ear drops, Framycetin Sulphate 0.5%

See section 13.1 for the proprietory preparations

GENTAMICIN

Indications: Bacterial infection of the external ear.

Adverse effects: Hypersensitivity reaction.

Nursing considerations: •*See under Chloramphenicol*.

Dose: Apply 2 - 3 drops, 2 - 3 times daily.

POM **Gentamicin** *(EDL 17.1)*
Ear drops, Gentamicin sulphate 0.3%

See section 13.1 for the proprietory preparations

GENTAMICIN plus HYDROCORTISONE

Therapeutic category: Antibiotic/ Corticosteroid.

Indications: Otitis externa, chronic suppurative otitis media.

Precautions: Extensive or prolonged use in pregnancy or infants, perforated ear drum.

Adverse effects: Irritation, sensitisation or super-infection (discontinue if occur).

Nursing considerations: •*See under Chloramphenicol*.

Dose: Adult and Children, instil 2-4 drops 3-4 times daily and at night.

POM **Gentamicin plus Hydrocortisone** *(EDL 17.1.3)*
Ear drops, Gentamicin sulphate 0.3%, hydrocortisone acetate 1%.

BETAMETHASONE

Indications: Atopic/eczematous inflammation of the external ear.

Contra-indications: Perforated ear drum

Dose: Apply 2-3 drops, every 2-3 hours.

POM **Betamethasone** *(EDL 17.1.2)*
Ear drops, Betamethasone sodium phosphate

0.1%.

See section 13.2 for the proprietory preparations

DEXAMETHASONE plus NEOMYCIN

Therapeutic category**: Anti-inflammatory/ Antiallergic/Antibiotic.**
Indications**: Diseases of the external ear such as seborrhoeic dermatitis, eczema.**
Contra-indications**: Perforated ear drum, untreated infection.**
Precautions**: Avoid prolonged use**
Adverse effects**: Local sensitivity reactions.**
Dose**: Clean and dry the ear canal carefully. Apply the ointment as a thin layer 2-3 times daily until controlled then reduce frequency. The drops can be applied by placing a napkin soaked in the solution to the ear for 12-24 hours; reduce dose when controlled.**

POM BIVACYN-N® ***(Taylek)***
Eye / Ear -drops**, Dexamethasone 1 mg, neomycin sulphate 3500 I.U. per ml.; in 5 ml vials**
Pack - 5 ml.
Eye / Ear ointment**, Dexamethasone 0.5 mg, neomycin sulphate 3500 I.U. per g.**
Pack - 3 g; 5 g (in tubes).

HYDROCORTISONE plus NEOMYCIN

Indications: Inflammation and infection of the external auditory canal, seborrheic dermatitis, infected eczematoid dermatitis.
Contra-indications: Perforated ear drum, fungal or viral infections, tuberculosis.
Precautions: Extensive or prolonged use in pregnancy or infants.
Adverse effects: Superinfection, sensitisation.
Nursing considerations: •*See under Chloramphenicol*.
Dose: Instil 2-3 drops into the affected ear every 1-4 hours according to the severity of the case; after the inflammation has subsided, the dosage may be gradually reduced to 1-2 drops 3-4 times daily.

POM **Hydrocortisone plus Neomycin** *(EDL 17.1.3)*
Ear drops, Hydrocortisone acetate 1.5%, neomycin sulphate 0.5%.

See section 13.2 for the proprietory preparations

HYDROCORTISONE plus NEOMYCIN plus POLYMYXIN B

Indications: Bacterial infection with inflammation of the ear, e.g. otitis externa.
Nursing considerations: •*See under Chloramphenicol*.
Dose: Apply 2-3 drops every 8 hours.

POM **Hydrocortisone plus Neomycin plus Polymyxin B.** *(EDL 17.1.3)*
Ear drops, Hydrocortisone acetate 1%, Neomycin sulphate 0.44%, Polymyxin B 0.12%

POM **OTO-MED®** *(Afrab-Chem)*
Ear drops, Hydrocortisone acetate 1%, Neomycin sulphate 0.44%, Polymyxin B sulphate 0.12%.
Pack - 8 ml.
Dose: Apply 4-5 drops 2-4 times daily according to the seriousness and patient's response.

POM **OTOSPORIN®** *(SKG)*
Ear drops, Hydrocortisone acetate 10 mg, neomycin sulphate 3,400 units, polymyxin B sulphate 10,000 units per 10 ml.

HYDROCORTISONE plus OXYTETRACYCLINE plus POLYMYXIN B

Indications: Bacterial infection associated with inflammation of the ear.
Adverse effects: Hypersensitivity reactions.
Nursing considerations: •*See under Chloramphenicol*.
Dose: Apply 2-3 drops, 2-3 times daily.

POM **Hydrocortisone plus Oxytetracycline plus Polymyxin B** *(EDL 17.1.3)*
Ear drops, Hydrocortisone acetate 1.5%, Oxytetracycline HCl 0.5%, Polymyxin B sulphate 0.12%.

See section 13.2 for the proprietory preparations

14.1.2 Preparations for the removal of ear wax

Various formulations contain organic solvents and these can cause irritation of the meatal skin. **Glycerol plus sodium bicarbonate** ear drops does not cause this kind of irritation and is as effective for the removal of ear wax.

CHLORBUTOL plus TURPENTINE OIL

plus PARADICHLOROBENZENE

Indications: Removal of ear wax.
Dose: Apply 2-3 drops, 2-3 times daily.

POM **Chlorbutol plus Paradichlorobenzene plus Turpentine Oil** *(EDL 17.1.4)*
Ear drops, Chlorbutol 5%, Paradichlorobenzene 2%, Turpentine oil 10%.

GLYCEROL plus SODIUM BICARBONATE

Indications: To soften ear wax before removal.
Dose: Apply sufficient drops into the affected ear for 3 consecutive nights.

POM **Glycerol plus Sodium Bicarbonate** *(EDL 17.1.4)*
Ear drops, Glycerol 30 ml, Sodium bicarbonate 5 g, in 100 ml solution.

14.2 Nasal drugs

14.2.1 Topical nasal decongestants
14.2.2 Systemic nasal decongestants
14.2.3 Preparations for the cauterisation of nose

Nasal drugs are formulated as drops or sprays for the treatment of inflammatory nasal disorders. *Nasal allergy* is controlled by oral antihistamines and systemic nasal decongestants. Severe attacks are relieved by topical preparations of corticosteroids with no significant side-effects. Very disabling symptoms may justify the use of systemic corticosteroids for short periods. They may also be used at the beginning of a course of treatment with a corticosteroid spray to relieve severe mucosal oedema and allow the spray to penetrate the nasal cavity. Decongestant nasal drops and sprays are used for the symptomatic relief of nasal congestion which may accompany vasomotor rhinitis, nasal polypi and the common cold. The commonest sympathomimetic drugs used for this purpose are oxymetazoline, xylometazoline, tetrahydrozoline, antazoline and phenylephrine. They cause vasoconstriction of the mucosal blood vessels which in turn reduces the thickness of the nasal mucosa. The major problem with their use is that they often give rise to a rebound phenomena as their effects wear off due to a secondary vasodilation with a subsequent increase in nasal congestion. Ephedrine nasal drops is perhaps the safest, giving relief for several hours. Oxymetazoline, phenylephrine and xylometazoline are more potent and more likely to cause a rebound effect. All of these preparations may cause a hypertensive crisis if used during treatment with a monoamine-oxidase inhibitor.

14.2.1 Topical nasal decongestants

ANTAZOLINE plus NAPHAZOLINE

Indications: Nasal congestion of allergic origin.
Dose: 2-3 drops or 1 spray into each nostril, 3-4 times daily.

POM **Antazoline plus Naphazoline** *(EDL 17.2.1)*
Nasal drops or spray, Antazoline sulphate 0.5%, Naphazoline 0.025%.

BECLOMETHASONE

Therapeutic category: Corticosteroid.
Pharmacology:Beclomethasone dipropio- nate has a potent anti-inflammatory effect within the respiratory tract at doses which are not systemically active.
Indications: Prophylaxis and treatment of perennial and seasonal allergic rhinitis including hay fever and vasomotor rhinitis.
Precautions: Nasal infections should be appropriately treated, patients on systemic steroid treatment, pregnancy.
Adverse effects: Sneezing and very rarely, septal perforation.
Nursing considerations: •Ensure patient understands how to use medication: shake container and invert; blow the nose and clear nasal passages; tilt head slowly backward and insert nozzle into nostril, pointing it away from the septum; hold the other nostril, inspire gently and spray. Shake container again and repeat in the other nostril.
•Advise patient to continue with the drug even in the presence of mild nasal bleeding (this is only transient).
•Teach patient good oral and nasal hygiene.
•Warn patient not to exceed prescribed dosage.
•Explain to patient that therapeutic effect is not immediate unlike nasal decongestants.
•Instruct patient to notify the doctor if there is no improvement in symptoms within 3 weeks or if nasal irritation persists.
•Observe for fungal infections.
Dose: Adult and Children over 6 years, 2 puffs (100 mcg) into each nostril twice daily or 1 puff (50 mcg) 3-4 times daily; max. 8 puffs daily.

POM **Beclomethasone** *(EDL 17.2.1)*
Nasal spray, Beclomethasone dipropionate 50 mcg per metered spray.

POM **BECONASE**® *(GSK)*
Nasal spray, Beclomethasone dipropionate 50 mcg per dose; metered-dose aerosol with nasal applicator.
Pack - 200 dose unit.

EUCALYPTUS OIL

Indications: For the relief of colds, coughs, catarrh and headaches.
Adverse effects: Nausea and vomiting when taken excessively.
Administration: Put a few drops in boiling water and inhale the vapuor.
Alternatively, put 3 drops on a lump of sugar and take every 3 hours.

OTC **BELL'S SILVERBIRD EUCALYPTUS OIL**® *(De-Sears)*
Liquid, Eucalyptus oil BP; a colourless or pale yellow oil with a characteristic aromatic camphoraceous odour.
Pack - 30 ml.

OXYMETAZOLINE

Pharmacology: It acts by stimulating the alpha-adrenergic receptors in the arterioles of the nasal mucosa causing vasoconstriction. Onset of action is about 5-10 minutes and lasts for about 5-6 hours.
Indications: Nasal congestion.
Contra-indications: Hypersensitivity to oxymetazoline or any component.
Precautions: Prolonged or excessive use may cause rebound congestion. Hyperthyroidism, hypertension, diabetes mellitus, cardiac disease.
Adverse effects: Rebound congestion on prolonged or excessive use, transient burning or stinging,dryness of the nasal mucosa, sneezing; systemic effects may include headachce, drowsiness, nervousness, insomia, palpitations, hypertension.
Advice to patients: Do not use for longer than 3 days on self-medication; discontinue the drug and consult physician if symptoms persist; notify physician of insomnia, tremor, or irregular heartbeat; burning, stinging, or drying of the mucosa may occur.
Nursing considerations: •Teach patient how to use: hold head upright, sniff and spray briskly.
•Warn patient not to exceed recommended dosage.
•Instruct patient not to share dropper bottle or nasal spray with other family members.
•Therapy should not exceed 3-5 days.
Dose: 2-3 drops or 1 spray into each nostril, 3-4 times daily.

POM **Oxymetazoline** *(EDL 17.2.1)*
Nasal spray, Oxymetazoline HCl 0.025-0.05%.

TETRAHYDROZOLINE

Therapeutic category: Nasal decongestant.
Pharmacology: Tetrahydrozoline, a sympathomimetic amine, possesses vasoconstrictor and decongestant actions when applied to the nasal mucosa, resulting in constriction of the smaller arteriole of the nasal passages and effecting a decongesting action.
Indications: Decongestion of nasal and nasopharyngeal mucosa.
Contra-indications: Hypersensitivity to the drug; 0.1% solution not recommended for children under 6 years of age; MAOIs; narrow-angle glaucoma.
Precautions: Pregnancy; cardiovascular diseases, metabolic-endocrine diseases such as diabetes
Adverse effects: Burning, stinging, sneezing, dryness, headache, drowsiness, weakness, tremors, lightheadness, insomnia, palpitations.
Nursing considerations: •*See under Oxymetazoline*.
Dose: Adult and children over 6 years, instil 2-4 drops of 0.1% solution in each nostril as needed, not exceeding 3 hourly.

OTC **Tetrahydrozoline** *(EDL 17.2.1a)*
Nasal drops, Tetrahydrozoline HCl 0.1%.

OTC **TYZINE**® *(Pfizer/Neimeth)*
Nasal-drops, Tetrahydrozoline HCl 0.1%; Odourless, tasteless, and non-irritating solution.
Pack - 15 ml.

XYLOMETAZOLINE

Therapeutic category: Vasoconstrictor for nasal decongestion.
Pharmacology: It acts by stimulatindg the alpha-adrenergic receptors in the arterioles of the nasal mucosa causing vasoconstriction. Onset of action is about 5-10 minutes and lasts for about 5-6 hours.
Indications: Colds of various types; to aid drainage of secretions in affections of the paranasal sinuses; as an adjuvant in otitis media; to facilitate rhinoscopy.
Contra-indications: Status post hypophysectomy or after surgical interventions in which the dura mater has been exposed. Narrow-angle glaucoma.
Precautions: Hypersensitivity to sympathomimetics, prolonged use e.g. in chronic colds.
Adverse effects: Occasionally burning sensation in the nose and throat; local irritation,

nausea, headache, dryness of the nasal mucosa.
Advice to patients: Do not exceed recommended dosage; do not use for more than 4 consecutive days.
Nursing considerations: •*See under Oxymetazoline*.
Dose: Adult and children over 7 years of age, 2-3 drops of 0.1% solution into each nostril 4 times daily.
Infants and children up to 6 years of age, 1-2 drops of 0.05% solution into each nostril 3 times daily.

OTC **Xylometazoline** *(EDL 17.2.1a)*
Nasal drops, Xylometazoline HCl 0.05%, 0.1%.

OTC **ENAPHRIN®** *(Afrab-Chem)*
Nasal drops, Xylometazoline HCl 0.05%, 0.1%; almost odourless, slight menthol odour.
Pack - 10 ml.
Pack - 10 ml.

OTC **OTRIVIN®** *(Oculus)*
Nasal drops, Xylometazoline HCl 0.1%
Pack - 10 ml.
Paediatric nasal drops, Xylometazoline HCl 0.05%.

XYLOMETAZOLINE plus ANTAZOLINE

Indications: Nasal congestion of allergic origin.
Dose: 2-3 drops or 1 spray into each nostril, 3-4 times daily.

POM **Xylometazoline plus Antazoline** *(EDL 17.2.1a)*
Nasal spray, Xylometazoline HCl 0.05%, antazoline sulphate 0.5%.

POM **OTRIVIN-ANTISTIN®** *(Novartis)*
Nasal drops and spray, Xylometazoline HCl 0.05%, antazoline sulphate 0.5%.
Pack - 10 ml.

MISCELLANEOUS PREPARATIONS

OTC **PENETROL®** *(BCN)*
Inhalant, Menthol 17.5%, cajuput oil 2.5%, lavender oil 8%, eucalyptus oil 7.5%, peppermint oil 0.2%.
Pack - 20 ml.
Indications: For the relief of catarrh, hay fever, nasal congestion.
Precautions: Asphyxiation in young children, spasm of the glottis.
Adverse effects: Hypersensitivity reactions including contact dermatitis.
Dose: Sprinkle a few drops on your handkerchief and inhale the vapour.

OTC **ROBB®** *(P.Z.)*
Inhalant, Menthol 42.5%, camphor 40%, eucalyptus oil 5%, methyl salipcylate 12.5%.
Indications: Relief of nasal congestion.
Dose: Insert tip of inhaler into end of nostril and breathe in deeply.

14.2.2 Systemic nasal decongestants

BROMPHENIRAMINE plus PHENYLEPHRINE plus PHENYLPROPANOLAMINE

Therapeutic category: Antiallergic and nasal decongestant.
Indications: Allergic manifestations of upper respiratory illness like common cold, seasonal allergies, rhinitis, sinusitis.
Advice to patients: See label 2 in Appendix 6.
Avoid alcohol; may cause drowsiness, may impair coordination or judgement.
Dose: Adult, 1 tab. morning and evening.
Tablets not recommended for children under 12 years.
Child (4-12 years), 5-10 ml; 2-4 years, 7.5 ml; 7 months - 2 years, 2.5 ml; 1-6 months, 1.25 ml. To be taken 3 -4 times daily.

POM **Brompheniramine plus Phenylephrine plus Phenylpropanolamine** *(EDL 17.2.1b)*
Tablet, Brompheniramine maleate 12 mg, phenylephrine HCl 15 mg, phenylpropanolamine HCl 15 mg.
Elixir, Brompheniramine maleate 4 mg, phenylephrine HCl 5 mg, phenylpropanolamine HCl 5 mg per 5 ml.
Elixir (Paediatric), Brompheniramine maleate 1 mg, phenylephrine HCl 2.5 mg, phenylpropanolamine HCl 5 mg per 5 ml.

POM **DIMOTAPP LA®** *(Wyeth/Delpitano)*
Tablet, Brompheniramine maleate 12 mg, phenylephrine HCl 15 mg, phenylpropanolamine HCl 15 mg; s-r brown s-c tab. marked 'AHR'.
Pack - 15; 500.

POM **DIMOTAPP®** *(Wyeth/Delpitano)*
Elixir, Brompheniramine maleate 4 mg, phenylephrine HCl 5 mg, phenylpropanolamine HCl 5 mg per 5 ml.
Pack - 60 ml; 120 ml; 1000 ml.
Paediatric elixir, Brompheniramine maleate 1 mg, phenylephrine HCl 2.5 mg, phenylpropanolamine HCl 2.5 mg per 5 ml.

CLEMASTINE

Therapeutic category: Anti-allergic
Indications: Allergic rhinopathies including hay fever.
Contra-indications, Precautions, etc: See Clemastine in Section 8.1
Advice to patients: See label 2 in Appendix 6. Avoid alcohol; may cause drowsiness, may impair coordination or judgement.
Dose: By mouth, Adult and Children over 12 years, 1 mg twice daily.

POM **Clemastine** *(EDL 17.2.1)*
Tablet, Clemastine (as hydrogen fumarate) 1 mg
Elixir, Clemastine (as hydrogen fumarate) 0.5 mg per 5 ml.

POM **TAVEGYL®** *(Novartis)*
See under Section 8.1

PHENYLEPHRINE plus DIMENHYDRINATE plus CAFFEINE

Indications**: Alleviates the symptoms of acute cold, such as blocked nose, excessive secretion, itching and swelling of the mucous membrane of the nose; allergic rhinitis.**
Contra-indications**: Hypersensitivity to any of the components; hypertension and other cardiovascular disorders; diabetes or over-active thyroid; raised I.O.P., enlarged prostate with urine retention, occlusion of the neck of the bladder; children below 12 years.**
Precautions**: Elderly; pregnancy, breast-feeding.**
Interactions**: Sedatives, hypnotics, alcohol.**
Adverse effects**: Dry mouth, drowsiness, nervousness; nausea, vomiting, hot sensations, headache, dizziness, confusion, agitation, changes in pulse rate.**
Advice to patients**: Avoid alcohol; ability to drive or operate machinery may be impaired.**
Dose**: Adult and child above 12 years, by mouth, 1 capsule in the morning and evening.**

OTC RHINOCAP® ***(Supreme)***
***Capsule*, Phenylephrine HCl 20 mg, dimenhydrinate 10 mg, caffeine 25 mg. Pack - 10.**

PHENYLPROPANOLAMINE

Therapeutic category: Sympathomimetic nasal decongestant.
Indications: Congestion in the nasal cavity and paranasal sinuses associated with the common cold, sinusitis and influenza.
Contra-indications, Precautions, etc: See the combination with diphenylpyraline.
Advice to patients: See label 2 in Appendix 6. See also under Pseudoephedrine plus Triprolidine.
Dose: Adult, 1 cap. 12 hourly.
Child (under 12 years): not recommended except under expert advice.

OTC **Phenylpropanolamine** *(EDL 17.2.1b)*
Tablet, Phenylpropanolamine HCl 50 mg.

OTC **CONTAC 12®** *(GSK)*
Capsule, Phenylpropanolamine HCl 50 mg. 50 mg - 8.

PHENYLPROPANOLAMINE plus DIPHENYLPYRALINE

Therapeutic category: Sympathomimetic/ antihistamine
Pharmacology: A combination of a nasal and sinus decongestant and an antihistamine (H_1-receptor antagonist).
Indications: Congestion and hypersecretion in the nasal cavity and paranasal sinuses associated with common cold, allergic rhinitis, acute and chronic rhinitis, sinusitis and influenza.
Contra-indications: Hypertension, severe heart disease, hyperthyroidism, hypersensitivity to phenylpropanolamine
Precautions: In patients with organic heart disease, angina pectoris, prostatic hypertrophy or glaucoma.
Interactions: MAOIs, tricyclics, alcohol.
Adverse effects: Dry mouth, blurred vision, urinary hesitancy or retention, palpitation, drowsiness, dizziness.
Advice to patients: See label 2 in Appendix 6. See also under Pseudoephedrine plus Triprolidine.
Dose: Adult, 1 cap. 12 hourly
Elderly: Use with great caution.
Child (under 12 years): Cap. not recommended.
Child (2-5 years): 2.5 ml up to 4 times daily; 6 -12 years, 5 ml up to 4 times daily.

OTC **Phenylpropanolamine plus Diphenylpyraline** *(EDL 17.2.1b)*
Spansule, Phenylpropanolamine HCl 50 mg, diphenylpyraline 5 mg.
Syrup, Phenylpropanolamine HCl 12.5 mg, diphenylpyraline 1.5 mg per 5 ml.

OTC **ESKORNADE**® *(GSK)*
Spansule, Phenylpropanolamine HCl 50 mg, diphenylpyraline HCl 5 mg; clear/grey s-r cap. with red, white and grey pellets.
Pack - 12.
Syrup, Phenylpropanolamine HCl 12.5 mg, diphenylpyraline HCl 1.5 mg per 5 ml.

PHENYLPROPANOLAMINE plus CHLORPHENIRAMINE plus PARACETAMOL

Indications**: Symptomatic relief of pain, fever and nasal congestion associated with allergic rhinitis, hay fever, sensitivity reactions, urticaria and common cold.**
Contra-indications**: Hypersensitivity to any of the components; nursing mothers, children below 6 years, hypertensive patients.**
Precautions**: May cause drowsiness thereby affecting mental alertness and ability to perform hazardous tasks; avoid alcoholic beverages; cardiovascular disorder, diabetes mellitus, hypertension, hyperthyroidism, renal and hepatic function impairment; pregnancy.**
Interactions**: TCAs and other CNS depressants, MAOIs, general anaesthetics, other sympathominetics and hepatic enzyme– inducing agents.**
Adverse effects**: Drowsiness; dryness of mouth, nose and throat; GI disturbances.**
Dose**: By mouth, Adult, 2 tabs 3-4 times daily.**
Child (above 6 years), 1 tab 3-4 times daily; do not exceed 50 mg Phenylpropanolamine daily.

OTC PARCLORPHEN® ***(Hovid)***
Tablet**, Phenypropanolamine HCL 12.5 mg, chlorpheniramine maleate 2 mg, paracetamol 300 mg; f-c tab.**
Pack – 100; 1000.

OTC **KATA**® *(Jawa)*
Tablet, Paracetamol 500 mg, phenylpropanolamine HCl 25 mg, chlorpheniramine maleate 2 mg.

Paracetamol + Chlorpheniramine
OTC **COL-COL**® *(Justeen)*
Tablet, Paracetamol 500 mg, Chlorpheniramine maleate 2 mg.
Pack – 4 x 25's.

Paracetamol + Chlorpheniramine + Ascorbic acid
OTC FLU-J® ***(Juhel)***
Tablet**, Paracetamol 500 mg, chlorpheniramine maleate 2 mg, ascorbic acid 25 mg.**
Pack – 200; 500.
Indications: For symptomatic relief of fever, headache and nasal congestion associated with influenza and common cold, including allergic rhinitis.
Dose: Adults: 2 tabs. 2-3 times daily; up to a max. 6 tabs. daily.
Child (2-6 years): ½ tab. 3 times daily.
Syrup, Paracetamol 120 mg, Chlorpheniramine maleate 2 mg, Ascorbic acid 25 mg per 5 ml.
Pack – 100 ml.

PHENYLPROPANOLAMINEplus CHLORPHENIRAMINE plus CAFFEINE plus PARACETAMOL

Indications: For symptomatic relief of fever, headache, nasal congestion and rhinitis associated with influenza and common cold.
Precautions: Avoid driving a motor vehicle or operating machinery while taking this drug.
Dose: By mouth, Adult, 1 tab. 3-4 times daily; Child (6-12 years), ½ tab. 3-4 times daily; 2-6 years, ¼ tab. 3-4 times daily.

OTC CAEPRAMIN® ***(Vital)***
Tablet**, Paracetamol 500 mg, caffeine 30 mg, phenylpropanolamine HCl 25 mg, chlorpheniramine maleate 2 mg; pink scored tab. marked 'CAEPRAMIN'.**
Pack - 50 x 4.

OTC TRAC® ***(Sam)***
Tablet**, Paracetamol 500 mg, caffeine 30 mg, phenylpropanolamine HCl 25 mg, chlorpheniramine maleate 2 mg.**
Pack - 50 x 4.

OTC UBARCOLD® ***(St. Michael)***
Tablet**, Paracetamol 500 mg, caffeine 30 mg, phenylpropanolamine HCl 25 mg, chlorpheniramine maleate 2 mg.**

PSEUDOEPHEDRINE

Therapeutic category: Oral vasoconstrictor for nasal decongestion.
Indications: Symptomatic relief from nasal stuffiness due to colds, from irritation and inflammation of the nose and throat due to hay fever and other conditions of allergic origin and from nasal catarrh due to irritation of the vasomotor nerves.
Contra-indications: Severe hypertension or severe coronary artery disease; patients receiving MAOIs.
Precautions: Hypertension; hyper-thyroidism;

enlargement of the prostate; persons over 65 years of age; pregnancy, breast-feeding.
Interactions:
•MAOIs (avoid co-administration), antihypertensives, digitalis, tricyclic anti-depressants, aluminium hydroxide.
Adverse effects: Occasionally dryness of mouth, loss of appetite, restlessness, insomnia, acceleration of the pulse, palpitation.
Advice to patients: Do not exceed recommended dosage and do not use for more than 3 - 5 days; may cause wakefulness or nervousness; take last dose 4-6 hours before bedtime; do not crush sustained release product; consult pharmacist or physician before using.
Nursing considerations: •Do not crush extended release drug product.
•Give chewing gum or sips of water to relieve dry mouth.
•Elderly patients should be counseled about the proper use of OTC cough and cold preparations.
•Advise patient to avoid activities requiring mental alertness as drowsiness or dizziness may occur.
Dose: Adult and children over 12 years of age, One cap. 12 hourly preferably morning and evening.
Not for long-term treatment.

OTC **OTRINOL®** *(Novartis)*
Capsule, Pseudoephedrine HCl 120 mg; s-r cap. 120 mg - 10.

PSEUDOEPHEDRINE plus TRIPROLIDINE

Therapeutic category: Nasal decongestant
Indications: Non-specific nasal congestions; nasal allergic conditions, common cold, Hay fever, allergic and vasomotor rhinitis, aerotitis (otitis barotrauma).
Precautions: Cardiovascular disorders including hypertension; road users.
Interactions: MAOIs (contra-indicated), other sympathomimetic agents, CNS depressants, alcohol.
Adverse effects: Insomnia due to pseudo-ephedrine; drowsiness due to triprolidine; skin eruptions.
Advice to patients: See label 2 in Appendix 6. Do not take drug within 2 hours of bedtime; because it can cause insomnia; take hard chewing gum or frequent sips of water to relieve dry mouth; do not crush extended-release dosage forms; avoid concurrent use of alcohol and other CNS depressants; notify physician if confusion, restlessness or hypotension occurs.
Dose: Adult and children over 12 years, 1 tab. or 10 ml 3 times daily; 6-12 years, 5 ml 3 times daily; 2-5 years, 2.5 ml 3 times daily.

OTC **Pseudoephedrine plus Triprolidine** *(EDL 17.2.1)*
Tablet, Pseudoephedrine HCl 60 mg, triprolidine HCl 2.5 mg.
Syrup, Pseudoephedrine HCl 30 mg, triprolidine HCl 1.25 mg per 5 ml.

OTC **ACTID®** *(Ranbaxy)*
Syrup, Triprolidine HCl 1.25 mg, pseudoephe-drine HCl 30 mg.
Pack - 100 ml.

OTC **ACTIFED®** *(GSK)*
Tablet, Triprolidine HCl 2.5 mg, pseudoephedrine HCl 60 mg; white scored tab. marked 'WELLCOME M2A'.
Pack - 20; 100.
Syrup, Triprolidine HCl 1.25 mg, pseudoephedrine HCl 30 mg per 5 ml.
Pack - 100 ml

OTC **ACTIHIST®** *(Hovid)*
Tablet, Triprolidine HCl 2.5 mg, pseudoephedrine HCl 60 mg.
Pack - 1000.

OTC **SINUFED®** *(SKG)*
Tablet, Triprolidine HCl 2.5 mg, pseudoephedrine HCl 60 mg; white scored tab. marked 'SKG C3A'.
Pack - 20; 100.
Syrup, Triprolidine HCl 1.25 mg, pseudoephedrine HCl 30 mg per 5 ml.
Pack - 100 ml

PSEUDOEPHEDRINE plus IBUPROFEN

Therapeutic category: Analgesic/Nasal Decongestant.
Indications: Temporary relief of symptoms associated with the common cold, sinusitis or flu, including nasal congestion, headache, fever, body aches and pains.
Contra-indications, Precautions, etc: See Ibuprofen in section 2.1 and Pseudoephedrine above.
Advice to patients: Take with food or milk if occasional mild heartburn, upset stomach or stomach pain occurs; consult your physician if symptoms persist; do not take more than 6 caplets in 24 hours. If abdominal pain, heartburn, nausea or vomiting, bloating, diarrhoea or constipation, ringing or buzzing in the ears, nervousness, sleeplessness, dizziness, any change in vision, fluid retention, itching, skin rashes or other adverse reactions occur, discontinue use immediately and contact your physician.

Dose: By mouth, Adult and child above 12 years, 1 caplet every 4-6 hours; may take 2 caplets at once if necessary but not exceeding 6 caplets in 24 hours.
Not recommended for children below 12 years.

POM **ADVIL®** *(Matbeny)*
Caplet, Pseudoephedrine HCl 30 mg, Ibuprofen 200 mg.
Pack - 10.

14.2.3 Preparations for the cauterisation of nose

SILVER NITRATE
Indications: Cauterisation of the nose.
Nursing considerations: Avoid contact with clothing and unaffected areas, since discolouration may occur.

POM **Silver Nitrate** *(EDL 17.2.2)*
Solution, Silver nitrate 0.5%; freshly prepared.
Sticks or crystals.

14.3 Throat drugs

Drug preparations are used locally for oral antisepsis and to relieve pain and inflammation in such conditions as tonsillitis, mouth ulcers and infections, pharyngitis, glossitis and other related inflammatory conditions. Corticosteroids in lozenges or paste are most effective particularly if used in the prodromal phase of aphthous ulcers.
Oral antiseptic lozenges like dequalinium, domiphen bromide and amylmetacresol plus dichlorobenzyl alcohol do have beneficial actions in mouth and throat infections but may sometimes irritate and cause sore tongue and sore lips. Topical antibiotic formulations for the treatment of infections and inflammatory conditions of the respiratory tract include fusafungine which is used as spray in sinusitis, rhinitis, coryza, pharyngitis, tonsillitis and other related conditions for oral hygiene. Glycerine, thymol, menthol, camphor and eucalyptus are used in different formulations either as mouthwashes or as tablets or lozenges.

AMYLMETACRESOL plus DICHLOROBENZYL ALCOHOL

Indications: Oral antiseptics
Precautions: May cause sore tongue and lips.

OTC **Amylmetacresol plus Dichlorobenzyl Alcohol** *(EDL 17.3.1)*
Lozenges, Amylmetacresol 0.6 mg, dichlorobenzyl alcohol 1.2 mg.

DEQUALINIUM

Indications: For rapid relief of pain, soreness and inflammation associated with common mouth infections such as Vincent's angina, tonsillitis, sore throat, stomatitis, pharyngitis, aphthous ulcer, thrush, glossitis; also for prevention and treatment of infections following tooth extractions.
Advice to patients: See Label 24 in Appendix 6.
Dose: Initially, one Lozenge to be sucked slowly 2-3 hourly; decrease the time interval between doses when infection subsides.

OTC **Dequalinium** *(EDL 17.3.1)*
Lozenges, Dequalinium HCl 0.25 mg.

OTC **DEQUADIN®** *(Evans)*
Lozenges, Dequalinium Chloride 250 mcg; mottled orange coloured pleasantly tasting flat/pain tab.
250 mcg - 20; 250.
Paint, Dequalinium Chloride 0.5% w/v; clear bright hygroscopic solution.
Pack - 10 ml.
Indications: Oral thrush; prevention and treatment of infections of gums, oral cavity and following tooth extraction; ulcers of oral cavity; general mouth antiseptic.
Dose: Apply by means of a cotton wool or cotton bud to the sites of infection every 3 hours; do not swallow saliva for a few moments after each application and for young child, hold its mouth open for a few moments.

DOMIPHEN BROMIDE

Therapeutic category: Antiseptic lozenge
Indications: Prevention and treatment of sore throats and husky voice (laryngitis); oral hygiene.
Dose: One lozenge to be sucked every 2 or 3 hours.

OTC **Domiphen Bromide** *(EDL 17.3.1)*
Lozenges, Domiphen bromide 0.5 mg.

OTC **BRADOSOL®** *(Novartis)*
Lozenges, Domiphen bromide 0.5 mg; white lozenge marked 'BRADOSOL' and 'CIBA'.

FUSAFUNGINE

Therapeutic category: Topical antibiotic /anti-inflammatory.

Indications: Treatment of infections and infammatory conditions of the respiratory tract: sinusitis, rhinitis and coryza, pharyngitis and tonsillitis, post-tonsillectomy states, laryngitis, tracheitis, bronchitis.
Contra-indications: Fusafungine hypersensitivity; children under 30 months old.
Precautions: Prolonged treatment exceeding 10 days.
Adverse effects: Rare and usually transient bucco-pharyngeal irritation usually not requiring cessation of treatment; sneezing.
Dose: Usually 4 metered doses in the mouth and/or each nostril 4 times daily.

POM **Fusafungine** *(EDL 17.3.1)*
Aerosol spray, Fusafungine 25 mg per 10 ml.

GLYCERINE plus THYMOL

Indications: Oral hygiene,

OTC **Glycerine plus Thymol** *(EDL 17.3.1)*
Mouth-wash, Glycerin 10%, thymol 0.05%

OTC **Glycerine plus Thymol** *(Afrab-chem)*
Mouth-wash, Glycerol 10%, thymol 0.05%; clear red solution.
Pack - 200 ml.

OTC **Moko Glycerine Borax** *(New Healthway)*
Mouth wash, Glycerine 88%, Borax decahydrate 12%.

Pack - 50 ml.

HEXETIDINE

Indications: Oral hygiene
Dose: Use 15 ml undiluted 2-3 times daily

OTC **Hexetidine** *(EDL 17.3.1)*
Mouth wash or gargle, Hexetidine 0.1%

OTC **HEXEDENE®** *(Pharma-Deko)*
Mouth-wash, Hexetidine 0.1%; clear red solution.

MENTHOL plus ASCORBIC ACID plus CITRIC ACID

Indications: Oral hygiene.
Dose: Dissolve one solution tablet or lozenge under the tongue 3 times daily.

OTC **Menthol plus Ascorbic Acid plus Citric Acid** *(EDL 17.3.1)*
Lozenges, Menthol 0.0900%, Ascorbic acid 2.9412%, Citric acid 0.8332%

MENTHOL plus EUCALYPTUS OIL plus CAMPHOR plus THYMOL

Indications: Nasal obstruction in acute rhinitis or sinusitis
Precautions: Infants less than one month of age.
Dose: Dissolve one lozenge under the tongue 3 times daily.

OTC **Menthol plus Eucalyptus Oil plus Camphor plus Thymol** *(EDL 17.3.1)*
Lozenges, Menthol 0.207%, Eucalyptus oil 0.069%, Camphor 0.0007%, thymol 0.007%.

NEOMYCIN plus BACITRACIN plus AMYLOCAINE plus MENTHOL

Indications: Sore throat, tonsillitis, gingivitis, seasonal mouth and throat infections, treatment of germ carriers.
Contra-indication: Hypersensitivity to any component of the preparation.
Precautions: Not recommended for children under 3 years of age, pregnant women, diabetic patients; avoid long-term use since it may result in growth of non-susceptible organism. If itching, burning, inflammation or other signs of sensitivity occur, patients should be advised to discontinue this preparation and consult a physician.
Adverse effects: Because of local anesthetic effect, taste of food may be disturbed.
Dose: Allow one lozenge to be dissolved slowly in the mouth; 8-10 lozenges (or more if necessary) daily.

OTC **MYBACIN®** *(Didachons)*
Lozenge, Neomycin sulphate equiv. to Neomycin base 2.5 mg, Bacitracin zinc 100.0 units, Amylocaine HCI 0.5 mg. *Excipients* - Sodium cyclamate, PVP K-90 (povidone), Menthol, Peppermint oil, Calcium Stearate, Sucrose qs. to 1.0 g.
Pack – 10's (in aluminium satchets); 40's and 140's (in boxes).

THYMOL

Indications: Sore throat and general oral hygiene
Dose: Suck 1-2 tablets or throat lozenges 2-3 times daily.

OTC **Thymol** *(EDL 17.3.1)*
Tablet, Thymol 2 mg.

OTC **BREACOL®** *(GSK)*
Tablet, Thymol 2 mg; chocolate brown tab. 2 mg - 10.

15. Dermatological drugs

RETURN

15.1 Anti-infective skin preparations
15.1.1 Antibacterial preparations
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15.2 Anti-inflammatory and antipruritic drugs
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15.9 Hair growth stimulants
15.10 Topical circulatory preparations

The skin is frequently exposed to hazards from the environment which explains the varieties of skin infections and disorders that plague man. However, the skin is highly amenable to treatment by local application as there is intimate contact between the drug and target tissue with a minimum of systemic effects. In burns and excoriated skin surfaces, systemic effects may create some problems due to enhanced absorption. Similarly, it may be difficult to control the quantity of drug applied to the area concerned and lack of patient compliance may be a problem.

For topical application, dermatological drugs are usually formulated as ointments, creams, lotions or sprays. In these formulations, the vehicle and the active ingredients are both important to the success of treatment. The vehicle may affect the degree of skin hydration, have mild anti-inflammatory effect and the penetration of active drug in the preparation. The other additives may be a source of skin sensitization particularly of eczamatous skin. This should be considered during treatment. The serious skin disorders encountered include bacterial and fungal infections for which appropriate formulations are used. Serious inflammatory conditions are also encountered.

15.1 Anti-infective skin preparations

15.1.1 Antibacterial preparations
15.1.2 Antifungal preparations
15.1.3 Scabicides and pediculicides
15.1.4 Antiviral preparations

Topical anti-infective preparations for the treatment of skin infections include Bacitracin plus Neomycin cream, a broad-spectrum formulation widely used for skin and mucous membrane bacterial infections. Various antifungal and antiviral preparations are also used for suspected fungal and viral infections respectively. They should be applied topically in a controlled manner and with accurate diagnosis to ensure effectiveness and avoid systemic toxicities. Skin irritation and sensitization may be problematic in some individuals.

15.1.1 Antibacterial preparations

Staphylococcal infections of the skin such as impetigo, folliculitis, and furunculi and streptococcal infections such as cellulitis and erysipelas are very common where the climate is hot and humid, where standards of hygiene are compromised, and in immunodeficient patients.

In all skin infections, an important part of treatment is cleansing and thorough drying. Washing with soap and water will often help to prevent infection. Light localized infections can often be treated effectively with an antiseptic solution such as **chlorhexidine** (section 16.3). Superficial crusts should be gently washed with soap and water or a weak solution of **aluminium acetate** (section 15.3) or a 0.01% solution of **potassium permanganate**. Infected burns should be treated with **silver sulfadiazine**, which is bactericidal against both Gram-positive and Gram-negative organisms.

An ointment containing 2% **mupirocin**, which is active against Gram-positive bacteria, is of value, particularly in impetigo. To prevent the development of resistance, mupirocin should not be used for more than 10 days. Topical preparations containing **neomycin** and **bacitracin** are also widely used but these carry a risk of sensitization particularly with continued or repeated use.

Topical use of preparations containing antimicrobials which are widely used systemically should be avoided. These include penicillins, sulfonamides, streptomycin and gentamicin, which should be reserved for the systemic treatment of infections because of the possibility of inducing sensitivity and favouring the emergence of resistant organisms. Only widespread superficial or deep-seated infections associated with fever require treatment with a systemic antibiotic (sections 9.1.1 and 9.1.2). Whenever possible, the choice of an antimicrobial should be based on the results of sensitivity tests.

ACRIFLAVINE

Indications: Treatment of infected wounds or burns; skin disinfection.

OTC **Acriflavine** *(EDL 14.1)*
Lotion, Proflavine hemisulphate 0.1%.

BENZYLPENICILLIN

Synonym: Penicillin G; Crystalline Penicillin.
Therapeutic category: Penicillin Antibiotic.
Indications: Local treatment of topical infections of the skin including infected wounds, impetigo, abscess, intertrigo, secondary infected eczema, burns, furunculi.
Contra-indications: Hypersensitivity to penicillin
Adverse effects: Allergic reactions such as exanthema, rash or urticaria may occur at the site of application (usually disappear on cessation of therapy).
Administration: Apply in a thin layer to the affected area 2-3 times daily. Cover with a sterile dressing to avoid contamination of the affected area.

POM **Penicillin** *(Daily Need)*
Ointment, Penicillin potassium BP 10,000 IU per g.
Pack - 20 g.

POM **Penicillin** *(Doyin)*
Ointment, Benzylpenicillin potassium 10,000 i.u. per g
Pack - 20 g (in tube).

POM **Penicillin** *(Drugfield)*
Ointment, Benzylpenicillin.
Pack - 20 g.

GENTAMICIN

Therapeutic category**: Aminoglycoside, broad spectrum bactericidal antibiotic.**
Indications**: Primary skin infections; infected burns and wounds and other secondary skin infections.**
Contra-indications**: Hypersensitivity to gentamicin.**
Precautions**: Prolonged treatment may cause overgrowth of nonsusceptible micro-organisms including fungi; if irritation, hypersensitivity or significant infection occurs, discontinue therapy.**
Adverse effects**: Irritation of skin, erythema, itching, smarting; allergic sensitization (discontinue treatment).**
Nursing considerations: •Cleanse affected area with soap and water before application; apply enough medication to completely cover lesions, after drying.
•Teach patient to aply carefully under asepsis to avoid further infection.
•Avoid use on large skin lesions or over a wide area because of possible systemic toxic effects.
•Prolonged use may result in overgrowth of nonsusceptible organisms.
•Instruct patient not to use in eyes or external ear, if ear drum is perforated.
•Advise patient to avoid the use of OTC creams, ointment or lotions unless on doctor's prescription
•Observe for allergic reactions e.g. burning, stinging, swelling, redness, rash.
Administration**: Cream or Ointment, apply a thin layer to the affected skin area 3-4 times daily.**

POM GENTADERM® ***(Fill Pharma)***
***Cream*, Gentamicin (as Sulfate) 1 mg per g.**
Pack - 20 g.

POM GENTALEK® ***(Taylek)***
***Cream or Ointment*, Gentamicin sulfate 1 mg per g.**
Pack -15 g.

POM **Gentamicin** *(Drufgield)*
Ointment, Gentamicin.
Pack - 15 g.

METHYLROSANILINIUM CHLORIDE

Methylrosanilinium chloride is a representative topical anti-infective drug. Various drugs can serve as alternatives.

Synonym: Gentian violet; Crystal violet.

Indications: Superficial fungal and bacterial infections.

Contra-indications: Excoriated or ulcerated lesions, broken skin, mucous membranes.

Adverse effects: Severe irritation (discontinue treatment); temporary staining of skin, permanent staining of fabrics; animal carcinogenicity (restricted use in some countries).

Advice to patients: Drug stains skin and clothing purple; do not apply to ulcerative lesion; keep affected area clean, dry and exposed to air to prevent spread of infection.

Nursing considerations: •Apply carefully to the lesion only; avoid undue staining of the skin.
•Do not use occlusive dressings.

Administration: *Skin infections*, apply 2 or 3 times daily for 2–3 days.

POM **Methylrosanilinium chloride** *(WMF 13.2)*
Cutaneous solution, Methylrosanilinium chloride 0.5%
Tincture, Methylrosanilinium chloride 0.5%

OTC **Methylrosanilinium chloride** *(EDL 14.1)*
Solution or Tincture, Methylrosanilinium chloride 1%.

OTC **MOKO GENTIAN VIOLET®** *(New Healthway)*
Solution, Gentian violet 5 mg per ml.
Pack - 60 ml.

NEOMYCIN plus BACITRACIN

Bacitracin is a representative topical antibacterial. Various drugs can serve as alternatives.

Therapeutic category: Topical antibiotic.

Indications: Superficial bacterial infections of the skin due to staphylococci and streptococci.

Precautions: Avoid application to substantial areas of skin or to broken skin (risk of significant systemic absorption); overgrowth of resistant organisms on prolonged use.

Adverse effects: Sensitization, especially to neomycin, causing reddening and scaling; anaphylaxis reported rarely; systemic absorption leading to irreversible ototoxicity, particularly in children, the elderly, and in renal impairment.

Nursing considerations: •Cleanse lesion with soap and water before application; cover lesion completely with medication.
•Teach patient to wash hands before and after each application.
•Observe skin for redness, burning, stinging or swelling.
•Do not use for more than 1 week unless directed by physician.

Administration: *Bacterial skin infections*, adult and child over 2 years apply thin layer 3 times daily.

Note: **Aerosol powder** - Prior to use, shake the aerosol container vigorously and spray the powder to the affected area from a distance of 20-25 cm. After use clean the valve by turning the aerosol container upside down and blow the valve by short pressing.

POM **Neomycin plus Bacitracin** *(WMF 13.2)*
Ointment, Neomycin sulfate 5 mg, bacitracin zinc 500 units/g.

POM **Bacitracin plus Neomycin** *(EDL 14.1)*
Ointment or Cream, Neomycin sulphate 5 mg, bacitracin zinc 500 units per g; in 5 g, 30 g tubes.
Powder, Neomycin sulphate 5 mg, bacitracin zinc 250 units per g.
Spray, Neomycin sulphate 165,000 units, bacitracin 12, 500 units.

POM **BANEDIF®** *(Afrab-Chem)*
Powder, Neomycin sulphate 5 mg, bacitracin zinc 250 units per g.
Spray, Neomycin sulphate 165,000 units, bacitracin 12, 500 units.

POM **BIVACYN®** *(Taylek)*
Powder, Neomycin sulphate 3,500 l.U. (5 mg), bacitracin 250 I.U. per g.
Pack - 5 g.
Spray(Aerosol Powder), Neomycin sulphate 165,000 l.U., bacitracin 12,500 l.U. per 150 ml.
Pack-150 ml.

POM **CICATRIN®** *(SKG)*
Powder, Neomycin sulphate 3,300 units, bacitracin zinc 250 units, L-cysteine 2 mg, dl-threonine 1 mg, glycine 10 mg per g.
Pack - 5 g.

POM **NEOBACIN®** *(Drugfield)*
Powder, Neomycin sulphate, zinc bacitracin.
Pack - 5 g

MUPIROCIN

Therapeutic category: Topical antibiotic
Pharmacology: Mupirocin is a topical broad spectrum antibiotic for the treatment of bacteria skin infections. It is active against staphylococci, including methicillin-resistant strains. It is also active against many Gram-negative bacteria as a result of the high concentrations achieved after topical administration. Mupirocin penetrates intact human skin but the rate of absorption is low and the absorbed drug is rapidly metabolised and excreted as inactive metabolite, monic acid.
Indications: Topical treatment of skin infections such as impetigo, folliculitis, infected dermatosis e.g infected eczema, infected traumatic lesions e.g insect bites and minor wounds and burns; to prevent bacterial infection of small wounds, cuts and abrasions.
Contra-indications: Not recommended for ophthalmic or intra-nasal use.
Precautions: When used on the face, avoid contact with the eyes. Discontinue treatment if sensitisation reaction or severe local irritation occurs; pregnancy, breast-feeding.
Adverse effects: Localised itching, a burning sensation, erythema, stinging and dryness; rarely cutaneous sensitisation reactions.
Advice to patients: For topical use only; do not apply into the eye; discontinue if rash, itching, or irritation occurs; improvement should be seen in 5 days; do not use for treatment of pressure sores in elderly.
Administration: Apply three times a day for up to ten days. Duration of treatment should not be extended beyond ten days. Discard the remaining ointment after treatment.

POM **BACTROBAN®** *(GSK)*
Ointment, Mupirocin 2%; sterile ointment in a white, transluscent, water soluble, polyethylene glycol base.

POVIDONE-IODINE

Indications: An antiseptic for the treatment of contaminated wounds; bacteria, fungi and protozoa infections like boils, furunculosis, tinea infestations, cutaneous candidiasis.

OTC **WOSAN®***(Jawa)*
Ointment, Povidone-iodine 5%.
Pack - 20 g tube.
Solution, Povidone-iodine 5%.
Pack - 40 ml; 100 ml; 2 l.

POTASSIUM PERMANGANATE

Indications: Wet dressings to assist healing of suppurating superficial wounds, tropical ulcers, tinea pedis, pemphigus, impetigo.
Contra-indications: Avoid occlusive dressings.
Precautions: Irritant to mucous membranes.
Adverse effects: Local irritation; skin and fabrics stained brown.
Administration: *Suppurating superficial wounds and tropical ulcers*, wet dressings of 1:10 000 (0.01%) solution, changed 2 or 3 times daily; tropical ulcers also require treatment for 2–4 weeks with procaine benzylpenicillin (section 9.1.1.1).
Tinea pedis, soak severe weeping lesions in 1:10 000 (0.01%) solution every 8 hours
Pemphigus, soak compresses in 1:10 000 (0.01%) solution and apply every 4 hours
Impetigo, superficial crusts should be gently separated with a 1:10 000 (0.01%) solution.

POM **Potassium permanganate** *(WMF 13.2)*
Cutaneous solution, Potassium permanganate 1:10 000 (0.01% solution)
NOTE: POTASSIUM PERMANGANATE IS SOMETIMES SUPPLIED AS AN AQUEOUS STOCK SOLUTION OF 1 IN 1000 (0.1%) FOR DILUTION BEFORE USE.

SILVER SULFADIAZINE

Therapeutic category: Topical antibacterial.
Indications: Prophylaxis and treatment of infection in burns.
Contra-indications: Hypersensitivity to sulfonamides; pregnancy (Appendix 2); neonates.
Precautions: Renal or hepatic impairment; G6PD deficiency; breastfeeding (Appendix 3).
Adverse effects: Allergic reactions include rashes, burning and itching; argyria and sulfonamide-induced systemic toxicity, including blood disorders following application to large areas or prolonged use; transient leukopenia reported.
Advice to patients: For external use only; bathe daily to aid in debridement (if not contraindicated); apply liberally to burned areas; notify physician if condition persists or worsens.

Nursing considerations: •Cleanse the affected area with soap & water to remove debris before each application if necessary.
•Completely cover burns with enough medication at all times, using aseptic technique. If needed, give an analgesic before application.
•Inspect patient's skin daily and notify doctor if there is excessive pain or burning.
•Evaluate therapeutic response viz development of granulation tissue.
•Encourage patient to bathe daily, if possible.

Administration: *Infection in burns*, apply using aseptic technique daily (more frequently if volume of exudate is large) whilst there is a possibility of infection, or until healing is complete.

POM **Silver sulfadiazine** *(WMF 13.2)*
Cream, Silver sulfadiazine 1%.

POM **Silver Sulfadiazine** *(EDL 14.1)*
Cream, Silver sulfadiazine 1%

POM **DERMAZIN®** *(Taylek)*
Cream, Silver sulfadiazine 1% in a hydrophilic base.
Pack - 25 g; 50 g.
Administration: Cleanse the burn and apply with a sterile spatula or a gloved hand to cover the burnt area once daily; may be reapplied daily in severe burn wounds. Before each reapplication, wash the burn in shower or with an antiseptic solution. Duration of treatment depends on the injury ranging from several days to one month at most.

POM **SILVEROL®** *(Dizpharm)*
Cream, Silver sulfadiazine 1%
Pack - 400 g.

15.1.2 Antifungal preparations

RINGWORM

Benzoic acid and **methylrosanilinium chloride** (gentian violet) solution are inexpensive and effective fungistatic compounds for the treatment of dermatophyte infections such as ringworm. Minor skin lesions due to ringworm can be cleared with repeated applications of **compound benzoic acid** ointment (Whitfield ointment), which combines the fungistatic action of benzoic acid with the keratolytic action of salicylic acid. However, the most effective topical treatment for dermatophyte infections is a cream containing an imidazole such as **miconazole**, which is effective for long-established lesions but is more expensive than compound benzoic acid ointment. Extensive and generalized infections of the skin, nails and scalp should be treated systemically for several weeks with **griseofulvin** or **fluconazole** (see section 9.2).

Scalp ringworm (tinea capitis) typically appears as a patch of scaling alopecia, or a swollen inflammatory area (tinea kerion). Mild forms may remit spontaneously at puberty. Inflamed lesions should be treated systemically with **griseofulvin**. Application of **miconazole** cream may accelerate healing of scaly lesions.

Ringworm on the body (tinea corporis) can also be cleared with **compound benzoic acid** ointment or a topical imidazole such as **miconazole**. In resistant cases a 4-week course of oral **griseofulvin** is required.

Foot ringworm (tinea pedis or athlete's foot) is usually treated topically. **Compound benzoic acid** ointment should be applied twice daily to all infected areas and all toe clefts for at least 4 weeks. Systemic therapy with **griseofulvin** or **fluconazole** may be required if the foot is extensively infected. Tinea pedis commonly recurs and may be treated with miconazole cream. Severe weeping lesions respond to frequent soaking in solutions of 1:10 000 **potassium permanganate**, and systemic antifungals may also be needed.

Nail infections (onychomycosis, tinea unguium) are difficult to treat; fingernails may require 6 months treatment with oral **griseofulvin** and toenails may require 12 months or more of this treatment. Approximately 60% of nail infections either do not respond or relapse after treatment with griseofulvin.

Ringworm of the groin (tinea cruris) is usually limited to the skin of the inner thigh in contact with the scrotum. Flexural eczema, often superinfected with candida or bacteria, occurs in the same site. The latter is frequently treated with combined antifungal/corticosteroid preparations, but must not be treated with a corticosteroid alone, which will worsen the condition. An imidazole cream such as **miconazole** applied daily for 2 weeks is usually effective. Lesions unresponsive to topical preparations can usually be cleared with a 4-week course of **griseofulvin**.

CANDIDOSIS

Candida can infect the oral cavity, the vagina or the skin. Cutaneous lesions tend to occur in patients with diabetes mellitus and some chronic debilitating conditions, including hypoparathyroidism and various congenital disorders of the immune system. The most severe infections of candida are now seen in patients with HIV infection.

Cutaneous candidosis usually responds to **miconazole** cream as a twice daily application. Chronic candida paronychia, which can result ultimately in nail dystrophy, is more difficult to treat. Treatment should be based on determination of the underlying cause and its reduction or elimination; hands and folds of the nail must be kept dry and daily application of an imidazole cream for several months may be required, ensuring penetration of the cleft between the nail plate and the swollen skin around the nail.

PITYRIASIS VERSICOLOR

Pityriasis (tinea) versicolor is caused by a commensal yeast. Application of **sodium thiosulfate** twice daily for 4 weeks is usually effective although areas of depigmentation on darker skins remain after completion of treatment. Relapses can be frequent, however, probably because much of the infected area may appear normal and be left untreated. Better results have been reported with topical applications of **miconazole** or **selenium sulfide**.

BENZOIC ACID/BUCLOSAMIDE plus SALICYLIC ACID

Indications: Mild dermatophyte infections, particularly tinea pedis and tinea corporis.
Adverse effects: Occasionally localized, mild inflammatory reaction.
Administration: *Fungal skin infections*, apply twice daily until the infected skin is shed (usually at least 4 weeks).

POM **Benzoic acid plus Salicylic acid** *(WMF 13.1)*
Ointment, Benzoic acid 6%, salicylic acid 3%.

OTC **Benzoic acid/Buclosamide plus Salicylic acid** *(EDL 14.6)*
Ointment or Cream, Salicylic acid 2-5%, benzoic acid or buclosamide 4-10%.

OTC **DERMOL®** *(Jawa)*
Ointment, Benzoic acid 6%, salicylic acid 3%, precipitated sulphur 5%, menthol crystals 1.5%, titanium dioxide 8%.
Pack - 15 g tube.
Indications: Athlete's foot, skin itch, prickly heat, ringworm, eczema, skin rash, burning skin, acne, etc.
Administration: Wash the affected parts of the skin gently with warm water and soap and dry. Apply the ointment on the affected parts twice daily, in the morning and evening.

OTC **NIXODERM®** *(Johnson Wax)*
Ointment, Benzoic acid 6%, Salicylic acid 2.5%, Sulphur 4.6%, titanium oxide 10%.
Pack - 17.7 g in a metal jar; Box of 17.7 g x 24.
Indications: Skin troubles such as eczema, pimples, rashes, peeling and scaling conditions.

OTC **MIRADERM®** *(Mirapharm)*
Ointment, Benzoic acid 6%, Salicylic acid 3%, 18%.

OTC **MAXADERM®** *(Therapeutics)*
Ointment, Benzoic acid 6%, salicylic acid 3%.
Pack - 15 g tube; 30 g; 60 g.

OTC **VITADERM®** *(Strides Vital)*
Ointment, Benzoic acid 6%, salicylic acid 3%, sulphur 4.5%; white coloured cream.
Pack - 30 g.

OTC **Whitfield's Ointment** *(Drugfield)*
Ointment, Salicylic acid, benzoic acid
Pack - 20 g.

OTC **Whitfield's Ointment** *(Leady-pharma)*
Ointment, Benzoic acid 6%, salicylic acid 3%.

MESULPHEN plus SULPHUR

Therapeutic category: Antifungal/keratolytic.
Indications: Parasitic skin infections such as scabies, ringworm. Also pyoderma, seborrhoid eczema, secondary infections of acne vulgaris, pruritus.
Contra-indications: Hypersensitivity to any of the ingredients.

OTC **Mesulphen plus Sulphur** *(EDL 14.1)*
Ointment, Mesulphen 64%, Sulphur 10-20%.

OTC **MITIGAL®** *(Gemini)*

Ointment, Sulphur 20%, mesulphen 64%.
Pack - 15 g.

OTC **Moko Sulphur** *(New Healthway)*
Ointment, Precipitated sulphur 25 g.

OTC **Sulphur** *(Daily Need)*
Ointment, Sulphur.

OTC **Sulphur** *(Drugfield)*
Ointment, Sulphur.
Pack - 25 g.
Indications: Treatment of ringworm, acne, scabies.
Administration: Apply thinly to the affected areas 2-3 times daily.

BIFONAZOLE

Therapeutic category: Broad spectrum antifungal with fungicidal activity.
Pharmacology: Bifonazole is a broad spectrum antifungal reliably active against dermatophytes, yeasts, moulds and other fungi such as *Malassezia furfur*; further, it is effective against *Corynebacterium minutissimum*. Its *in vitro* activity against dermatophytes (e.g Trichophyton spp) is primarily fungicidal where as, that against yeasts is primarily fungistatic.
Indications: Mycoses of the skin caused by dermatophytes, yeasts, moulds and other fungi such as *Malassezia furfur* and infections due to *Corynebacterium minutissimum*.
Infections of this type may be e.g. mycoses affecting feet and hands (athlete's foot, tinea manuum), mycoses involving skin and skin folds (tinea corporis, tinea cruris). Pityriasis versicolor; *Candida balanitis*; Erythrasma.
Contra-indications: Hypersensitivity to bifonazole.
Dose: Unless otherwise prescribed, Micogem cream is used once daily, at best before retiring. It is applied thinly to the skin areas affected and rubbed into the skin. Usually only a small amount of cream (line of about ½ cm) will suffice for the treatment of an area of the size of the palm. For hygenic support of treatment it is advisable to wash and thoroughly dry the skin area affected before applying the cream.
Note: To achieve a lasting cure, treatment with micogem cream should not be stopped when the acute inflammatory symptoms and signs have subsided but, depending on the type of disease, be continued for the periods listed below:
Mycoses of the foot, body, interdigital mycoses (between the toes), 3 weeks;
Mycoses affecting body, hands and skin folds, 2-3 weeks;
Pityriasis versicolor, erythrasma, 2 weeks;
Superficial candidosis of the skin, 2 weeks.

POM **MYCOGEM®** *(Gemini)*
Cream, Bifonazole 0.15 g per 15 g.
Pack - 15 g (tube).

CLOTRIMAZOLE

Therapeutic category: Imidazole antifungal.
Indications: Dermatomycoses due to dermatophytes and candida species; other fungal skin diseases showing secondary infection with these fungi.
Advice to patients: May cause irritation to the skin; avoid contact with eyes; notify physician if condition worsens or persists, or itching or burning occurs.
Nursing considerations: •Cleanse affected area with soap and water, dry well before each application; completely cover lesions with enough medication; do not use occlusive dressings; teach patient to wash hands before and after each application.
•Tell patient to continue using drug until full treatment period even if symptoms may have improved.
•Instruct patient to avoid OTC creams, lotions and ointments unless on prescription.
•Evaluate signs of allergy viz burning, swelling, stinging, redness; advise patient to notify physician if no improvement is observed.

POM **Clotrimazole** *(EDL 14.6)*
Cream or Ointment, Clotrimazole 1%.
Spray aerosol, Clotrimazole 1%.
Powder, Clotrimazole 1%.

POM **Clotrimazole plus Azidamfenicol** *(EDL 14.6)*
Ointment or Cream, Clotrimazole 1%, azidamfenicol 1%.

POM **CLOTRIDERM®** *(Fill Pharma)*
Cream, Clotrimazole B.P. 1% w/w.
Pack - 20 g (in tube).
Dose: Apply thinly to the affected parts and gently massage 2-3 times daily. Duration of treatment could be up to 2-4 weeks depending on the extent and site of the disease.

POM **CLOTRIMAX®** *(SKG)*
Cream, Clotrimazole 1%, in a water-miscible base.
Pack - 20 g.

POM **MYCOTEN**® *(Drugfield)*
Cream, Clotrimazole 1%
Pack - 20 g.
Solution, Clotrimazole 2%
Pack - 25 ml.
Powder, Clotrimazole 1%
Pack - 10 g.

POM **SABRESTEN**® *(Gemini)*
Cream, Clotrimazole 1%, in a water-miscible base.
Pack - 10 g; 20 g.
Dose: Apply thinly 2-3 times daily to the diseases sites and rubb in. Duration of treatment depends on the extent and localisation of the disease:
Dermatomycoses, 3-4 weeks;
Candida vulvitis and candida balanitis, 1-2 weeks;
Erythrasma and pityriasis versicolor, approx. 3 weeks.
Note: In fungi infection of the feet, to prevent relapses, treatment should be continued for about 2 weeks beyond the disapperance of all signs of disease. After washing, the feet should be thoroughly dried (spaces between the toes). Sabresten cream is odourless, can be washed off and does not stain.

POM **YTACAN**® *(Strides Vital)*
Cream, Clotrimazole 1%.
Pack - 30 g.

Clotrimazole + Zinc Oxide + Ichthammol +Menthol
POM **TRIBOTAN**® *(Fill Pharma)*
Ointment, Clotrimazole, Zinc oxide, Ichthammol, Menthol.
Pack - 20 g (in tube).
Pharmacology: Tribotan is useful for the treatment of skin infections caused by various species of pathogenic dermatophyte, yeasts, and other isolates. Clotrimazole exhibits fungistatic activity against isolates of *Trichophyton mentagrophytes*. *Epidermophyton floccusum* and Candida spp. including *Candida albicans*. Strains of fungi having resistance to clotrimazole are rare. Only a single isolate of *Candida guilliermondi* has been reported to have primary resistance to clotrimazole. Zinc Oxide and ichthamol are used in combination to treat other skin infections such as chronic eczema. The bacteriostatic property of Ichthamol makes it useful in treating other varieties of skin disorders. Menthol when applied to the skin has a soothing effect, which helps in relieving the discomfort of itching and skin irritation.
Indications: Treatment of superficial inflammation occurring in moist skin-folds of inner thighs, waist, buttocks, underside of breasts and armpits; all dermatomycoses due to fungal species such as Trichophyton species, yeast (Candida species), mould and other fungi; skin rashes; eczema and slight excoriation; pruritus and urticaria of the skin; other skin disorders.
Contra-indications: Hypersensitivity to any of the constituents.
Precautions: Discontinue if irritation occurs; use the medication for full duration of treatment even when symptoms have improved. Avoid sources of infection, or re-infection. Even when symptoms have improved, do not discontinue the use of the medication before full duration of treatment. Not for ophthalmic use.
Adverse effects: Erythema, stinging, blistering, peeling, edema, burning and general irritation of the skin could be reported in connection with the use of Tribotan.
Advice to patients: Use the medication for full treatment time even when symptoms have improved. Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling or oozing) indicative of possible sensitization. Avoid sources of infection or re-infection.
Dose: Gently massage sufficient Tribotan into the affected and surrounding skin areas twice a day (morning and evening). Clinical improvement with relief usually occurs within the first week of treatment.

POM **BABY TRIBOTAN**® *(Fill Pharma)*
Cream, Clotrimazole, Boric acid, Ichthammol.
Pack - 20 g (in tube).
Indications: Prevention and treatment of baby nappy rashes and superficial inflammation occurring as a result of moisture and humidity in body areas; Heat rashes on baby's skin; Itching, discoloration, blemishes, eczema and other skin disorders peculiar to babies and young children.
Administration: Apply sufficient cream unto buttocks area during every nappy change. For other affected areas, apply sufficient cream unto area 2-3 times daily or as often as you bathe the baby.
See also under Tribotan® for Adult above.

ECONAZOLE

Therapeutic category: Imidazole antifungal
Pharmacology: Econazole is an imidazole antifungal agent closely related to miconazole and with similar antifungal and antibacterial

properties
Indications: Fungal infections of the skin such as candidiasis, pityriasis versicolor and tinea.
Advice to patients: See under clotrimazole.
Nursing considerations: •*See under Clotrimazole.*
Dose: Apply 1-2 times daily up to a minimum of 10 days after symptoms subside.

POM **Econazole** *(EDL 14.6)*
Spray solution, Econazole 1%

POM MITEKOL® ***(Taylek)***
***Cream*, Econazole nitrate 1%**
Pack - 30 g (in tube).
***Powder*, Econazole nitrate 1%**
Pack - 30 g (in box).

ISOCONAZOLE

Indications: Broad spectrum antimycotic for the following skin conditions: superficial mycoses caused by dermatophytes; yeast and yeast-like fungi particularly *Candida albicans;* moulds e.g. Tinea species, Candidosis, Pityriasis versicolor, Paronychia candidimycetica.
Precautions: Avoid contact with eyes.
Adverse effects: Skin irritation; allergic reactions.
Dose: *Superficial dermatomycoses*, apply once daily for 2-3 weeks or longer.
Vulvo-vaginal mycoses, apply twice daily for 1 week. Treat sexual partner concurrently.

POM **TRAVOGEN®** *(CHI/Schering)*
Cream/Ointment, Isoconazole nitrate 1%.
Pack - 20 g tube.

KETOCONAZOLE

Therapeutic category: Synthetic broad-spectrum antifungal agent.
Indications: Dermatophyte infections of the skin, cutaneous candidosis, tinea(ptyriasis) versicolor,seborrheic dermatitis, dandruff.
Precautions: Avoid contact with eyes; irritation may occur when used after a prolonged therapy with topical corticosteroids(gradually withdraw the steroid therapy).
Adverse effects: Irritation, burning sensation.
Nursing considerations: •*See under Clotrimazole.*
Dose: Cream, *Dermatophyte skin infections and tinea versicolor* apply once daily to the affected areas for at least until a few days after disappearance of all symptoms; *Serborrhoeic dermatitis,* apply 1-2 times daily depending on severity of infection as above.
Shampoo, wash the affected areas of the skin with the shampoo:
Treatment, *Seborrhoeic dermatitis and dandruff,* twice weekly for 2-4 weeks; *Pityriasis versicolor,* once daily for 5 days.
Prophylaxis, *Seborrhoeic dermatitis and dandruff,* once every 1-2 weeks.
The shampoo should be left on the skin for 3-5 minutes before rinsing.

POM NIZORAL® ***(Janssen-Cilag)***
Cream, Ketoconazole 2%; in a water-miscible base.
Pack - 15 g (in tubes).
Shampoo, Ketoconazole 2%
Pack - 60 ml (in plastic containers).

POM **NITOZOL®** *(Pharmabox)*
Cream, Ketoconazole USP 20 mg per g; milky white topical cream.
Pack – 20 g.

MICONAZOLE

Miconazole is a representative topical antifungal. Various drugs can serve as alternatives.
Therapeutic category: Imidazole antifungal.
Indications: Superficial fungal infections due to dermatophytes and yeasts, and secondary infections caused by Gram-positive cocci, including ringworm, intertrigo, candida napkin rash, paronychia, and pityriasis versicolor.
Adverse effects: Occasional local irritation and burning, also contact dermatitis; discontinue if sensitization occurs.
Advice to patients: See under clotrimazole.
Nursing considerations: •*See under Clotrimazole*.
Administration: *Skin infections*, apply twice daily to clean dry lesions, continuing for at least 10 days after the condition has cleared.
Nail infections, apply 1–2 times daily.

POM **Miconazole** *(WMF 13.1)*
Cream, Miconazole nitrate 2%
Ointment, Miconazole nitrate 2%

POM **Miconazole** *(EDL 14.6)*
Cream or Powder, Miconazole nitrate 2%

POM **DAKTARIN®** *(Janssen-Cilag)*
Cream, Miconazole nitrate 2%; in a water-miscible base.
Pack – 15 g (in tube).
Powder, Miconazole nitrate 2%
Pack – 20 g (in a shaker)
Tincture, Miconazole 2%; alcoholic solution.
Pack – 30 ml (in a bottle with brush)

Administration: Apply 2 times daily, to the lesion and spread it out with the brush.
For feet infections, powder the feet with Daktarin powder during and after treatment especially between the toes and also possibly the socks and shoes.
Note: Hygienic measures such as washing the lesions or infected areas daily, changing and disinfecting socks and shoes are recommended. Clean the treated nail once weekly with a piece of cotton with pure acetone (no nail remover) since dust and fibres of clothes may colour the nail black. Do not apply to open lesions.

POM **FUNGUSOL**® *(Afrab-chem)*
Lotion, Miconazole nitrate 2%.
Pack - 50 ml.
Powder, Miconazole nitrate 2%.
Pack - 20 g.
Ointment, Miconazole nitrate 2%.
Pack - 20 g.
Dose**: *Candida infections, tinea cruris and corporis,* apply twice daily (morning and evening) to the affected areas for 2 weeks.**
***Tinea pedis,* apply twice daily as above for one month.**
***Tinea versicolor,* apply once daily.**

POM **MICOZOL**® *(Drugfield)*
Cream, Miconazole nitrate 2%
Pack - 20 g
Lotion, Miconazole nitrate 2%
Pack - 50 ml.

POM **MYCOHEAL**® *(Supreme)*
Cream, Miconazole nitrate 2%
Pack - 30 g

POM **TINAZOL**® *(Hovid)*
Cream, Miconazole nitrate 2%; in a water-miscible base.
Pack - 15 g (in tube)

With Metronidazole
POM **ITCHCARE**® *(Vitabiotics)*
Cream, Miconazole nitrate 2.0%, metronidazole 2.0%.
Pack - 60 ml

MICONAZOLE plus HYDROCORTISONE

Therapeutic category: Antimycotic, antibacterial, anti-inflammatory agent.
Indications**: Mycotic infections of the skin associated with inflammation, pruritus and allergy; bacterial infections due to staphylococci and streptococci; eczematous skin diseases that require "protective" treatment.**
Contra-indications: Tuberculous skin affection, herpes simplex, vaccinia, all forms of varicella.
Precautions: Pregnancy and infants especially if the medication is to be applied to extensive surface areas or under occlusive dressing.
Administration: Apply 1-2 times daily; rub into the affected areas gently until completely absorbed. Continue treatment until lesion has disappeared.

POM **DAKTACORT**® *(Janssen-Cilag)*
Cream, Miconazole nitrate 2%, hydrocortisone 1%.
Pack - 15 g (in tube).

NYSTATIN

Therapeutic category: Antifungal Agent, topical.
Indications: Localized forms of candidiasis, infant eczema, pruritus and vulvae.
Adverse effects: Contact dermatitis.
Advice to patients: Discontinue and report to physician if irritation occurs; do not stop treatment even if you are feeling better; use only on the skin.
Nursing considerations: •Cleanse affected area with soap and water, and dry well before application.
•Do not use occlusive dressings.
•Cream is recommended for intertrigous areas; powder for very moist areas; ointment for dry areas.
•Tell patient to continue using drug until full treatment period.
Dose: Apply 2-4 times daily; continue treatment for 7 days after lesions have healed.

POM **Nystatin** *(EDL 14.6)*
Ointment or Cream, Nystatin 100,000 units per g.

SELENIUM SULFIDE

Selenium sulfide is a complementary drug for use in rare disorders or in exceptional circumstances.
Indications: Pityriasis versicolor (lotion), seborrhoeic dermatitis (detergent-based suspension).
Contra-indications: Children under 5 years.
Precautions: Do not apply to damaged skin (risk of systemic toxicity); avoid contact with eyes; do not use within 48 hours of applying preparations for hair colouring, straightening, or permanent waving.

Adverse effects: Local irritation, hair discoloration or loss; absorption may result in systemic toxicity including tremors, weakness, lethargy, pain in lower abdomen, occasional vomiting (symptoms usually resolve within 10 days).
Advice to patients: For external use only; notify physician if condition persists or worsens; avoid contact with eyes; thoroughly rinse after application; discontinue use and notify physician if rash or irritation occurs.
Administration: *Pityriasis versicolor*, apply lotion with a small amount of water to the entire affected area and rinse off after 10 minutes, repeat once daily for 7–14 days; or apply undiluted lotion at bedtime and rinse off the following morning, repeat after 3 and 6 days.
Seborrhoeic dermatitis, massage 5–10 ml of shampoo into wet hair and leave for 2–3 minutes before rinsing thoroughly; repeat twice weekly for 2 weeks, then once weekly for 2 weeks, thereafter only when needed.
NOTE: TO MINIMIZE ABSORPTION, RINSE HAIR THOROUGHLY AFTER USE AND REMOVE ALL TRACES FROM SKIN (INCLUDING NAILS).

POM **Selenium sulfide** *(WMF 13.1)*
Lotion, Selenium sulfide 2.5% [not included on WHO Model List].
Detergent-based suspension (Shampoo), Selenium sulfide 2.5%.

POM **Selenium Sulfide** *(EDL 14.6)*
Shampoo, Selenium sulfide 2.5%.

SODIUM THIOSULFATE

Indications: Pityriasis versicolor; cyanide poisoning (section 19.2.7).
Administration: *Pityriasis versicolor*, apply twice daily for 4 weeks.

POM **Sodium thiosulfate** *(WMF 13.1)*
Cutaneous solution, Sodium thiosulfate 15%.

TERBINAFINE

Therapeutic category: Allylamine antifungal
Pharmacology: A broad spectrum antifungal which at low concentrations is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity agianst yeasts is fungicidal or fungistatic, depending on the species. Less than 5% of terbinafine is absorbed after topical application to humans; systemic exposure is thus very slight.
Indications: Fungal infections of the skin and nails caused by dermatophytes; yeast infections of the skin caused by the genus candida; pityriasis (tinea) versicolor.
Precautions: Avoid contact with eyes; children.
Adverse effects: Occasionally redness, itching or stinging at the site of application.
Advice to patients: For external use only; not for oral, ophthalmic, or intravaginal use; if irritation or sensitivity occurs, discontinue use and notify physician.
Administration: Apply once or twice daily to the affected skin and sorrounding area in a thin layer and rub in lightly; for 1-2 weeks in *tinea corporis or cruris*, 2-4 weeks in *tinea pedis*, 1-2 weeks in *cutaneous candidiasis*, 2 weeks in *pityriasis versicolor.*
Note: Cleanse and dry the affected areas thoroughly prior to application.

POM **LAMISIL®** *(Oculus)*
Cream, Terbinafine (as HCl) 1%.

TIOCONAZOLE

Therapeutic category: Antifungal
Pharmacology: Tioconazole is a broad spectrum antifungal agent which also has antibacterial activity against several Gram-positive organisms including staphylococcus and streptococcus spp.
Indications: Topical treatment of dermal infections due to susceptible fungi (dermatophytes and yeasts) and in those conditions complicated by infection with susceptible gram-positive bacteria.
Precautions: 1st trimester of pregnancy.
Advice to patients: See under clotrimazole.
Nursing considerations: •*See under Clotrimazole*.
Administration: Apply to the affected and sorrounding skin area 1-2 times daily.

POM **Tioconazole** *(EDL 14.6)*
Cream or Powder, Tioconazole 1%.

POM **BETROSIL®** *(Drugfield)*
Cream, Tioconazole 1%.
Pack - 20 g.

POM **TROSYD®** *(Neimeth)*
Cream, Tioconazole 1%; in tube.
Powder, Tioconazole 1%; in plastic bottle.
Pack - 20 g.

TOLNAFTATE

Therapeutic category: Antifungal Agent,

Topical.

Indications: Treatment of tinea pedis, tinea cruris ,tinea manuum, tinea versicolor infections.

Contra-indications: Hypersensitivity to tolnaftate ;nail and scalp infections.

Precautions: Keep from eyes; if no improvement within 4 weeks,discontinue treatment. Usually not effective alone for the treatment of infections involving hair follicles or nails.

Adverse effects: Pruritus, contact dermatitis, irritation, stinging.

Advice to patients**: Avoid contact with eyes; apply to clean dry area; consult the physician if a skin irritation develops or if the skin infection worsens or does not improve after 10 days of therapy; does not stain skin or clothing.**

Nursing considerations: •Wash and dry the affected area before each application; apply only a small quantity of medication as directed; ensure the area is not wet with the solution after the application.

•Tell patient to continue using medication until full treatment period.

•Itching, burning, and soreness are usually relieved within 24-72 hours.

•Discontinue medication and report to doctor if condition worsens.

Administration: Wash and dry the affected area; apply 1-3 drops of solution and rub into the affected areas 2-3 times per day for 2-4 weeks.

POM **TINADERM®** *(Supreme)*
Solution(topical), Tolnafte 1%.
Pack - 10 ml.

With Betamethasone plus Gentamicin
POM **QUADRIDERM®** *(Supreme)*
Cream, Tolnaftate, betamethasone, gentamicin, iodochlorhydroxyquin.
Pack - 15 g.

15.1.3 Scabicides and pediculicides

SCABIES

Scabies is caused by a mite, *Sarcoptes scabiei*, that burrows into the skin. It is readily transmitted from person to person, therefore the entire household must be treated at the same time to prevent reinfection. It is not necessary to take a bath before treatment with an acaricide, but all clothing and bedding should be washed to prevent reinfection.

Benzyl benzoate is an inexpensive scabicide. It must be applied to all skin surfaces, from the scalp to the soles of the feet, avoiding contact with the eyes; it is too irritant for use on children. **Permethrin** is less irritant and more effective than benzyl benzoate, but also more expensive; it may be used on children. Young infants can be treated with a cream containing precipitated **sulfur** 6–10% applied once daily for one week.

PEDICULOSIS

Pediculosis of the head and body is caused by *Pediculus humanus capitis* and *Pediculus humanus corporis* respectively; pubic lice (crab lice) infestations are caused by *Pthirus pubis*, which may also affect the eye lashes and brows. All are transmitted by person to person contact, and may also contaminate clothing and bedding. All members of the affected household (and sexual contacts) must be treated at the same time, and clothing and bedding should be washed or exposed to the air; in head lice infestations, hair brushes and combs should also be disinfected.

Head and body lice are readily treated with **permethrin**; **malathion** is effective against pubic lice. **Benzyl benzoate** may be used for all lice infestations.

BENZYL BENZOATE

Benzyl benzoate is a representative parasiticide. Various drugs can serve as alternatives.

Indications: Scabies; head, body and pubic lice.

Precautions: Do not use on inflamed or broken skin; avoid contact with eyes and mucous membranes; not recommended for children; breastfeeding (withhold during treatment).

Adverse effects: Local irritation, particularly in children.

Nursing considerations: •For topical use only; do not apply to raw or inflamed skin, or face; avoid contact with eyes. Flush with water if there is accidental contact with eyes.

•Instruct patient to discontinue and report to physician if skin irritation or hypersensitivity occurs.

•Clothing and bedding should be washed off drug and then sterilized by boiling, dry cleaning or applying very hot iron to kill the scabies mite.

•Reassure patient that itching may take several weeks to stop.

•Topical corticosteroids may be prescribed if dermatitis develops from scratching.

•Avoid application to children's hands as they will put hands in their mouths.

•Benzyl benzoate is preferred to lindane in treating children and pregnant or nursing mothers.

Administration: *Scabies*, ADULT, apply from neck down at night for 2 nights; on each occasion wash off after at least 24 hours.
Pediculosis, ADULT, apply to affected area and wash off 24 hours later; further applications possibly needed after 7 and 14 days.

OTC **Benzyl benzoate** *(WMF 13.6)*
Lotion (Cutaneous suspension), Benzyl benzoate 25%.

OTC **Benzyl Benzoate** *(EDL 14.8)*
Emulsion, Benzyl benzoate 25%.

OTC **BELL'S BENZYL BENZOATE®** *(De-Sears)*
Application, Benzyl benzoate 25%; a white semi-liquid emulsion.
Pack - 100 ml.
Administration: *Scabies*, After a hot bath and drying, apply to the whole body except the head and face; a second application may be necessary within 5 days of the first. Alternatively, apply to the whole body except the head and face, 3 times at 12-hourly intervals. The patient should have a hot bath 12 hours after the last application and change to clean clothes and sheets.
Pediculosis, Coat the affected region with the application followed by a wash 24 hours later with soap and water; this procedure may be repeated 2-3 times in severe cases.The patient should be examined a week after to confirm disinfestation
Note: Benzyl benzoate application can be diluted with an equal quantity of water for older children and with three parts of water for babies.

OTC **Benzyl Benzoate** *(Leady)*
Application, Benzyl benzoate 25%.

OTC **Moko Benzyl Benzoate** *(New Healthway)*
Emulsion, Benzyl benzoate 28%.
Pack - 100 ml

POM **SCABCARE®** *(Vitabiotics)*
Cream, Benzyl Benzoate
Pack - 100 ml

CROTAMITON

Therapeutic category: Antipruritic; Ascaricide; Pediculicide.

Indications: Pruritus of varying origin, e.g. essential pruritus; senile pruritus; anogenital pruritus; pruritus associated with allergies, jaundice or diabetes mellitus; pruritus due to insect bites and stings; scabies (infestation of the skin by mites); *Pediculosis capitis* (infestation by head lice).
Contra-indications: Hypersensitivity to crotamiton or the excipients.
Precautions: Avoid contact with the conjunctiva (in case of accidental contact, the eyes should be bathed with water). Not recommended for acutely inflammed, weeping skin conditions due to the danger of systemic absorption. Pregnancy (particularly during the first trimester); breast-feeding (avoid applying around the nipples).
Adverse effects: Irritation of the skin or contact allergy (discontinue).
Administration: *Pruritus*, apply to the affected area 2-3 timed daily untill the itching stops.
Scabies, apply morning and evening to the entire body surface (excluding the face and scalp) for 3-5 days depending on response.
Child: Never apply more than once daily.
Pediculosis capitis, apply to the whole of the scalp and hair after thorough washing and drying; a second course of treatment may be required on the 8th day if lice or their eggs are not completely removed.
Method of Application: **Scabies -** After a warm bath, the skin is well dried and then rub into the entire body surface (excluding the face and scalp) until no traces of the cream or lotion is visible on the face. Special attention should be paid to sites that are more susceptible to infestation by the mites such as interdigital spaces, wrists, axillae, and genitalia. On completion of treatment, a cleansing bath should be taken, followed by a change of bed-linen and underclothing.
Pediculosis capitis - 1st day - Wash the hair thoroughly with warm water and shampoo, and dry it well. Apply the lotion lightly to the whole of the scalp and hair, particularly the back of the head and the area around the ears. Avoid contact with the eyes. Allow the hair to dry on its own and it should not be washed for 24 hours.
2nd to 7th day - Wash the hair thoroughly once daily with warm water and shampoo. Then, using a fine-tooth comb that has been dipped in vineger, comb the hair while it is still wet so as to remove the nits.
8th day - Carefully examine the hair and scalp;

a repeat course of therapy will be required if the lice, their larvae, or fresh nits are not completely removed.

POM **EURAX®** *(Oculus)*
Cream, Crotamiton 10%
Pack - 20 g; 60 g.
Lotion, Crotamiton 10%
Pack - 50 ml.

DICOPHANE

Indications: Scabies, Pediculosis.
Precautions: Avoid contact with eyes.
Administration: Apply thoroughly to the affected parts.

OTC **Dicophane** *(EDL 14.8)*
Lotion, Dicophane 1-2 %.
Dusting powder, Dicophane 5-10%.

LINDANE

Indications: Pediculosis, Scabies
Precautions: Avoid contact with eyes
Adverse effects: Rarely skin irritations.
Nursing considerations: •For topical use only; do not apply to raw or inflamed skin, or face; avoid contact with eyes. Flush with water if there is accidental contact with eyes.
•Instruct patient to discontinue drug, wash it off skin and report to physician if skin irritation or hypersensitivity occurs.
•Warn patient to avoid inhaling vapours, and not to apply lotion after a hot soapy bath.
•Clothing and bedding should be washed off drug and then sterilized by boiling, dry cleaning or applying very hot iron.
•Combs and brushes may be washed with lindane shampoo and then thoroughly rinsed with water.
•Topical corticosteroids or oral antihistamines may be prescribed for itching.
•Prophylactic treatment may be administered to members of patient's family, using lotion and shampoo to decrease spread of infection; treat sexual partner simultaneously.
•Instruct patient to notify physician if condition worsens.
Administration: *Pediculosis*, rub 0.1-2% application into hair and scalp; *Scabies*, apply 1% lotion over the whole body.

OTC **Lindane** *(EDL 14.8)*
Cream, Lindane 1%
Lotion, Lindane 0.5-1%
Shampoo, Lindane 2%

MONOSULFIRAM

Therapeutic category: Parasiticide
Indications: Scabies
Precautions: Avoid contact with eyes
Interactions: Alcohol

OTC **Monosulfiram** *(EDL 14.8)*
Solution, Monosulfiram 25%; for dilution.
Soap, Monosulfiram 5%.

OTC **TETMOSOL®** *(Jagal)*
Soap, Monosulfiram 5%; yellow perfumed soap.
Pack - 75 g.

PERMETHRIN

Indications: Scabies; head and body lice.
Precautions: Do not use on inflamed or broken skin; avoid contact with eyes; breastfeeding (withhold during treatment).
Adverse effects: Local irritation; rarely rashes and oedema.
Administration: *Scabies and body lice*, apply cream over whole body and wash off after 8–12 hours.
Head lice, apply lotion to clean damp hair and rinse off after 10 minutes.

POM **Permethrin** *(WMF 13.6)*
Cream, Permethrin 5%.
Lotion (Cutaneous suspension), Permethrin 1%.

15.1.4 Antiviral Preparations

Aciclovir cream is indicated for the treatment of initial and recurrent labial and genital herpes simplex infections. However, systemic treatment is necessary for buccal or vaginal infection and herpes zoster (shingles) infection. **Idoxuridine** is used less frequently for herpetic infections of the skin since acyclovir is more effective. Herpes simplex seems to respond to frequent applications if started early and continued for 3 to 4 days.

ACICLOVIR

Indications: Topical treatment of herpes viral infections.
Adverse effects: Transient burning and stinging, rash, pruritus.
Nursing considerations: •Wear finger cot or rubber gloves when applying cream or ointment for self-protection.
•For use on skin only; don't apply to the eye.
•Ensure ointment covers all the lesions.
•Inform patient that he may transmit the virus even during treatment; he should avoid sexual intercourse when lesions are present.
•Explain to patient that aciclovir is not a cure.
Dose: Adult and child: apply to all lesions every

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3 hours while awake, 6 times daily for one week.

POM **Acyclovir** *(EDL 6.12)*
Cream, Aciclovir 5%.

POM **ACRON®** *(Pharmabox)*
Cream, Aciclovir USP 50 mg per g; milky white topical cream.
Pack - 10 g tube.

POM **LOVIR®** *(Ranbaxy)*
Cream, Aciclovir 5%.
Pack - 5 g; 10 g (in tubes).

POM **VACRAX®** *(Alpha)*
Cream, Aciclovir 5%; in a white soluble cream base.
Pack - Tubes of 5 g and 10 g.

POM **VIREST®** *(Hovid)*
Cream, Aciclovir 5%; white opaque cream.
Pack - 5 g; 10 g (in tubes).

POM **ZOVIRAX®** *(GSK)*
Cream, Aciclovir 5%.

IDOXURIDINE

Indications: Severe herpetic infections of the skin.
Precautions: Pregnancy, breast-feeding; solution in DMS should not be used close to the eyes.
Adverse effects: Stinging on application.
Administration: Apply to the affected area 4 times daily for 3-4 days.

POM **Idoxuridine** *(EDL 6.12)*
Application, Idoxuridine 5% in dimethyl-sulphoxide.

15.2 Anti-inflammatory and antipruritic drugs

CONTACT DERMATITIS

Contact dermatitis can result from an allergic or irritant skin reaction. Removal of the substance provoking the reaction is the first step in treating this condition. Mild cases of contact dermatitis can be treated with topical **hydrocortisone** which suppresses inflammation. A short course of oral prednisolone or a topical corticosteroid such as **betamethasone** should be considered for more severe cases and for suppression of severe acute reactions associated with blistering, exudation and oedema. Soaking in clean water or mild saline solution is recommended in the acute stages of severe dermatitis.

PRURITUS

Pruritus or itching is a common symptom of many skin diseases. However, contact with certain substances, conditions that dry the skin, stress, and extremes of temperature may also be a cause. Thus, an important part of treatment is to eliminate or minimize the reason for the irritation.

Corticosteroids, such as hydrocortisone or betamethasone applied topically, can give relief. Soothing baths or the application of an emollient cream may also be helpful; the value of calamine lotion is uncertain. Systemic antihistamines, such as oral chlorphenamine (section 8.1), may relieve generalized pruritus.

ATOPIC DERMATITIS

Atopic dermatitis (or eczema) is a common skin disorder, which mainly occurs in infants and children; it is associated with intense itching, with areas of red skin. Pruritus may be partially relieved by applying astringent **aluminium acetate** (section 15.3) lotion to exudative lesions and emollients to lichenified plaques. Topical **hydrocortisone** should be applied in short courses of 1–2 weeks to treat even mild areas of involvement. The use of **betamethasone** should be considered in the treatment of persistent localized dermatitis in adults. Topical antihistamines are not effective and should be avoided because of the risk of sensitization. However, a sedative antihistamine can be given at night to calm pruritus and facilitate sleep (section 8.1). A secondary infection, often involving *Staphylococcus aureus*, may be responsible for exacerbations; in such cases, an oral antibiotic such as erythromycin can be given for 7–10 days (section 9.1.2.4).

SEBORRHOEIC DERMATITIS

Use of a keratolytic shampoo and exposure to ultraviolet light reduce both the inflammation and the scaling resulting from seborrhoeic dermatitis of the scalp (dandruff). The shampoo should be massaged into the scalp, immediately rinsed off and then reapplied until a foam is produced, leaving the second application in contact with the scalp for at least 5

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minutes. **Selenium sulfide**, which has both antifungal and keratolytic properties, is widely used in many proprietary shampoos. A combination of sulfur and salicylic acid, which has an additional antimicrobial action, is also effective.

ICHTHYOSIS

In ichthyosis, emollients such as aqueous creams and emulsifying creams should be applied daily (or more frequently in severe cases) to affected skin. The addition of a keratolytic, such as **salicylic acid** 5% can be helpful.

LICHEN PLANUS

Lichen planus is a chronic, papular, pruritic skin eruption that occurs typically in middle age and later life; the condition is often mild and may need no treatment. In more severe cases, when the underlying cause cannot be identified, a topical corticosteroid offers the only prospect of remission.

PITYRIASIS ROSEA

In pityriasis rosea, a common self-limiting dermatosis that is probably of infective origin, **calamine lotion** helps to relieve pruritus in most cases. If it does not, topical application of **hydrocortisone** in a concentration not exceeding 1% is worth trying.

CALAMINE

Calamine is a representative topical antipruritic. Various drugs can serve as alternatives.

Indications: Mild pruritus.

Administration: *Mild pruritus*, apply liberally 3–4 times daily.

OTC **Calamine** *(WMF 13.3)*

Lotion (Cutaneous suspension), Calamine 8% (USP), 15% (BP).

See also section 15.3 (Astringents) for Calamine plus Zinc oxide preparations.

Corticosteroids

BETAMETHASONE

Betamethasone (as valerate) 0.1% is a representative potent topical corticosteroid. Various drugs can serve as alternatives.

Indications: Severe inflammatory skin conditions inluding contact dermatitis, atopic dermatitis (eczema), seborrhoeic dermatitis, lichen planus, psoriasis of the scalp, hands and feet, intractable pruritus.

Contra-indications: Untreated skin infections or broken skin, rosacea, acne, perioral dermatitis.

Precautions: Children (avoid prolonged use); adrenal suppression if used on a large area of the body or for a long time, particularly with an occlusive dressing or on broken skin; avoid use on the face for more than 7 days; secondary infection requires treatment with an appropriate antimicrobial.

Adverse effects: Exacerbation of local infection; local atrophic changes particularly on the face and in skinfolds, characterized by thinning of the dermis, depigmentation, dilatation of superficial blood vessels and formation of striae; perioral dermatitis; acne at site of application; suppression of the hypothalamic-pituitary-adrenal axis with prolonged or widespread use (particularly under occlusion)

Advice to patients: Apply sparingly to affected areas and gently rub in until it disappears; not for use on broken skin; do not apply to wet skin unless directed; do not apply to face or inguinal areas; discontinue use and notify physician if skin irritation or ulceration occurs.

Nursing considerations: •Wash the skin gently; rub medication in gently to prevent damage to skin, leaving a thin coat. If the area is hairy, part the hair and apply directly to lesion.

•Avoid application near eyes, mucous membranes or in ear canal; do not apply on broken skin or in areas of infection.

•Inform patient that the gel may cause mild, transient stinging especially if used on or near excoriated skin due to alcohol content of vehicle.

•Prolonged or excessive use as well as occlusive dressings can enhance systemic absorption.

•Teach patient to stop drug and inform physician if he develops signs of systemic absorption, skin irritation or ulceration, hypersensitivity, or infection.

•Avoid use of plastic pants or diapers that are tight-fitting on treated areas in young children to minimize systemic absorption.

•It is important not to put occlusive dressing for a long time; it should be avoided in infections or with weeping or exudative lesions. Guaze dressings are preferable.

•Treatment should be continued for a few days after clearing of lesions to prevent recurrence.

Administration: *Inflammatory skin conditions*, ADULT and CHILD over 2 years of age, apply small quantity to the affected area 1–2 times daily until improvement occurs, then less frequently.

POM **Betamethasone** *(WMF 13.3)*

Cream, Betamethasone (as valerate) 0.1%

Ointment, Betamethasone (as valerate) 0.1%.

POM **Betamethasone** *(EDL 14.2)*
Cream or Ointment, Betamethasone valerate 0.1%

POM **Betamethasone** *(Drugfield)*
Cream, Betamethasone.
Pack - 20 g.

POM **BETNOVATE®** *(GSK)*
Cream, Betamethasone (as valerate ester) 0.1%; white water-miscible cream in tubes,
Pack - 15 g; 30 g; 100 g.
Ointment, Betamethasone (as valerate ester) 0.1%, white, paraffin-based ointment.
Lotion, Betamethasone (as valerate ester) 0.1%; white translucent aqueous fluid in bottles.
Pack - 20 ml.

POM **DIPROSONE®** *(Supreme)*
Cream, Betamethasone (as dipropionate) 0.05%; in a water-washable paraben-free base.
Pack - 15 g; 30 g (in tube).

POM **TEMPROSONE®** *(Orange Drugs)*
Cream, Betamethasone (as dipropionate) 0.05%; in a water-washable cream base.
Pack - 30 g (in tube).

BETAMETHASONE plus CLIOQUINOL

Therapeutic category: Corticosteroid/ antibacterial
Pharmacology: Betamethasone valerate is an active topical corticosteroid which produces a rapid response in those inflammatory dermatoses that are normally responsive to topical corticosteroid therapy, and is often effective in the less responsive conditions such as psoriasis.
Clioquinol is an anti–infective agent which has both antibacterial and anticandidal activity.
Indications: Inflammatory skin conditions where secondary bacterial and/or fungal infection is present, suspected, or likely to occur such as in eczema, psoriasis, neurodermatoses, seborrheic dermatitis, contact sensitivity reactions; also in secondarily infected insect bites and anal and genital intertrigo.
Contra-indications, Precautions, etc: see under Betamethasone.
Advice to patients: Seeunder Betamethasone
Administration: Small quantity applied to the affected area 2-3 times daily until improvement occurs; then, once daily or less for maintenance.

POM **BETNOVATE–C®** *(GSK)*
Cream, Betamethasone (as the valerate ester) 0.1%, clioquinol 3%; smooth, straw-coloured water-miscible cream.
Ointment, Betamethazone (as the valerate ester) 0.1%, clioquinol 3%; white or pale, straw-coloured paraffin based ointment.

BETAMETHASONE plus NEOMYCIN

Therapeutic category: Corticosteroid/ antibacterial
Pharmacology: Betamethasone valerate is an active topical corticosteroid used in inflammatory dermatoses. Neomycin sulphate is a broad spectrum bactericidal antibiotic effective against the majority of bacteria commonly associated with skin infections.
Indications: Severe inflammatory skin disorders as for betamethasone but where prophylaxis against secondary bacterial infection is required.
Contra-indications, Precautions, etc: See under Betamethasone.
Advice to patients: See under Betamethasone.
Administration: Small quantity applied to the affected area 2-3 times daily until improvement occurs; then, once daily or less for maintenance.

POM **Betamethasone plus Neomycin** *(EDL 14.2)*
Cream, Ointment or Lotion, Betamethasone valerate 0.25%, Neomycin sulphate 0.25-0.5%.

POM **Betamethasone plus Neomycin** *(Drugfield)*
Cream, Betamethasone, neomycin.
Pack - 20 g.

POM **BETNOVATE-N®** *(GSK)*
Cream, Betamethasone (as valerate ester) 0.1%, neomycin sulphate 0.5%; smooth white water miscible cream in tubes.
Pack - 15 g; 30 g.
Ointment, Betamethasone (as valerate ester) 0.1%, neomycin sulphate 0.5%; white paraffin-based ointment in tubes.
Pack -15 g; 30 g.
Lotion, Betamethasone (as valerate ester) 0.1%, neomycin sulphate 0.5%; white aqueous translucent fluid in bottles
Pack - 20 ml.

POM **DERMESONE-N®** *(Supreme)*
Cream or ointment, Betamethasone 0.1%, neomycin 0.5%.

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POM **NEO-BETASONE®** *(Hovid)*
Cream, Betamethasone (as 17-valerate) 0.1%, neomycin sulphate 0.5%.
Pack -15 g.

CLOBETASOL

Therapeutic category: Corticosteroid
Pharmacology: Clobetasol propionate is a very active topical corticosteroid which is of particular value when used in short courses for the treatment of more resistant dermatoses.
Indications: Psoriasis, recalcitrant eczemas, lichen planus, discoid lupus erythematosus.
Contra-indications, Precautions, etc: See under Betamethasone.
Advice to patients: Apply sparingly in light film; rub in lightly; do not use tight-fitting diapers or plastic pants on children being treated in the diapper area; use only as prescribed and for no longer than the period prescribed; avoid contact with eye; notify physician if condition being treated persists or worsens; do not use on open wounds.
Nursing considerations: •Warn patient not to use for longer than 14 consecutive days because drug is a very potent and fluoridated corticosteroid.
•Not recommended for children under 12 years.
•Avoid use of occlusive dressings; do not bandage, cover or wrap the treated area of skin.
•*See also under Betamethasone*.
Administration: Apply sparingly 1-2 times daily until improvement occurs; up to 4 weeks.

POM **Clobetasol** *(EDL 14.2)*
Cream or Ointment, Clobetasol propionate 0.05%.

POM **DERMOVATE®** *(GSK)*
Ointment, Clobetasol propionate 0.05%; white paraffin-based ointment.
Pack -25 g; 100 g.
Scalp application, Clobetasol propionate 0.05%, isopropyl alcohol 50%; transparent, slightly gelled solution.

POM **TEMPOVATE®** *(Orange Drugs)*
Cream, Clobetasol propionate 0.05%; white water-miscible cream.
Pack - 25 g (in tube).

CLOBETASONE

Therapeutic category: Topical corticosteroid
Indications: Eczema and dermatitis of all types including atopic eczema, photodermatitis, otitis externa, primary irritant and allergic dermatitis(including napkin rash), intertrigo, prurigo nodularis, seborrhoeic dermatitis and insect bite reactions.
Contra-indications, Precautions, etc: See under Betamethasone.
Advice to patients: See under Clobetasol.
Administration: Apply sparingly to the affected area up to 4 times daily until improvement occurs, reducing according to response.

POM **EUMOVATE®** *(GSK)*
Cream, Clobetasone butyrate 2.05%; white emolient water-miscible cream.
Ointment, Clobetasone butyrate 2.05%; white paraffin-based ointment.

CLOTRIMAZOLE plus AZIDAMFENICOL plus DEXAMETHASONE

Therapeutic category: Anti-eczematous
Pharmacology: A combination of the anti-inflammatory and antipruritic effects of dexamethasone, the antimycotic/antibacterial activity of clotrimazole and the antibacterial activity of azidamfenicol.
Indications: Inflammation and infection of the skin particularly those caused by fungi and/or bacteria such as various forms of eczema, intertrigo, non-specific pruritus, neurodermatitis ,pyodermia, pustular dermatitis.
Contra-indications: Tuberculosis of the skin, viral infections of the skin.
Precautions: Pregnancy, infants, long term and extensive use.
Adverse effects: Skin irritation, dryness of skin.
Advice to patients: See under Betamethasone.
Administration: Apply sparingly twice daily, continuing several days after the disappearance of symptoms.

POM **Clotrimazole plus Azidamfenicol plus Dexamethasone** *(EDL 14.6)*
Ointment or Cream, Clotrimazole 1%, azidamfenicol 1%, dexamethasone 0.1-0.5%.

POM **BIOCOTEN®** *(Drugfield)*
Cream, Dexamethasone, gentamicin, clotrimazole
Pack - 20 g.
Indications: Inflammation and infection of the skin caused by fungi and/or bacteria such as contact dermatitis, eczema, intertrigo, non-specific pruritus, pastular neurodermatitis, folliculitis, pastular dermatitis, secondary infection of burns and injuries.

Administration: Apply sufficient quantity to the affected skin area twice daily.

POM **DEMA®** *(Pharmabox)*
Cream, Clotrimazole 10 mg, Betamethasone dipropionate 0.64 mg, Gentamicin sulfate 1 mg per g; milky white topical cream.
Pack – 15 g; 20 g; 450 g.
Indications: Allergic inflammatory skin disease (acute & chronic eczema, contact dermatitis, atopic dermatitis, seborrheic dermatitis, chronic simple lichen, intertrigo, exfoliative dermatitis, pustular urticaria, psoriasis, pruritus vulvae, pruritus and dermatitis solaris); Skin mycosis (athlete's foot, trichophytia etc.); Tinea versicolor; Bite by insect; Alopecia areata; First degree burn; Skin disease by secondary infections.
Administration: Gently massage cream into the affected surrounding skin areas one or several times daily.

POM **KEMI®** *(Jawa)*
Cream, Clotrimazole 0.15%, beclomethasone dipropionate 0.00375%.
Pack - 15 g tube.
Indications: Fungal infections of the skin like Tinea capitis, Tinea pedis, Tinea corporis, Tinea versicolor.
Administration: Gently massage into the affected skin area twice daily, in the morning and in the evening.

POM **VECUTEN®** *(Gemini)*
Cream, Dexamethasone 6 mg, clotrimazole 150 mg, neomycin sulphate 96.8 mg per 15 g.
Pack - 15 g in tube.

CROTAMITON

See under Section 15.1.3

DEXAMETHASONE plus NEOMYCIN

Therapeutic category**: Anti-inflammatory/ antiallergic/antibiotic**
Indications**: Primary inflammation of the skin including pyoderma; allergic dermatoses including dermatitis, eczema, pruritus.**
Contra-indications**: Skin turberculosis, vaccination, varicella; see also under betamethasone.**
Administration**: Apply as a thin layer to the affected area 1-3 times daily.**

POM BIVACYN-N® ***(Taylek)***
***Cream or Ointment*, Dexamethasone 0.1%, Neomycin sulphate o.5%.**
Pack - 15; 20 g (in tubes).

DIFLUCORTOLONE

Indications: All dermatoses in which corticoids are indicated; Psoriasis vulgaris; first degree burn; insect bite; dyshidrosis; contact dermatitis.
Contra-indications, Precautions, etc: See under Betamethasone.
Administration: Apply thinly 1-2 times daily for up to 4 weeks.

POM **NERISONE®** *(CHI/Schering)*
Cream or Ointment, Diflucortolone valerate 0.1%.
Pack - 15 g tube.

POM **NERISONE C®** *(CHI/Schering)*
Cream, Diflucortolone valerate 0.1%, chlorquinadol 1%.
Pack - 15 g tube.
Indications: Steroid-responsive dermatoses complicated by bacteria or monilial infection.

DIFLUCORTOLONE plus ISOCONAZOLE

Indications: Combination of corticosteroid and antimycotic topical preparation indicated in initial or interim treatment of dermatomycoses accompanied by inflammatory or eczematous skin conditions.
Contra-indications, Precautions, etc: See under Betamethasone.
Administration: Apply thinly 1-2 times daily; not exceeding 15 days, then change over to isoconazole cream alone.

POM **TRAVOCORT®** *(CHI/Schering)*
Cream, Diflucortolone valerate 1 mg, isoconazole nitrate 10 mg per g.
Pack - 15 g tube.

FLUOCINOLONE

Therapeutic category: Corticosteroid.
Pharmacology: Fluocinolone is a synthetic glucocorticoid used topically in the treatment of various skin disorders.
Indications: Local inflammatory, pruritic and allergic conditions of the skin and mucosa such as atopic dermatoses (e.g. eczema), contact dermatitis, psoriasis in all its forms; intertrigo, otitis externa.
Precautions: Infants and adolescent girls when extensive or prolonged treatment is envisaged.
Advice to patients: See under Clobetasol.
Administration: Apply a small quantity to the

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affected area 2-3 times daily.

POM **Fluocinolone** *(EDL 14.2)*
Cream or Ointment, Fluocinolone acetonide 0.025%.

POM **SYNALAR®** *(Reals)*
Cream and Ointment, Fluocinolone acetonide 0.025% w/w; both white.
Pack - 15 g tube

With Clioquinol
POM **SYNALAR C®** *(Reals)*
Cream and Ointment, Fluocinolone acetonide 0.025%, clioquinol 3%
Pack - 15 g (in tube).

HALOMETASONE plus TRICLOSAN

Therapeutic category: Topical corticosteroid /Broad-spectrum antimicrobial.
Indications: Secondarily infected, corticosteroid-responsive skin diseases such as eczema; acutely inflammed dermatomycosis and superficial forms of pyoderma.
Contra-indications: Viral skin infections, tuberculosis of the skin, syphilitic skin infections; application to the ulcerated areas and to the eye; perioral dermatitis, rosacea, acne vulgaris.
Precautions: Avoid long-term therapy and discontinue if no improvement occurs within a week; children, pregnancy, lactation.
Adverse effects: Local irritation; rarely erythema, dryness, skin atrophy, contact allergy; discontinue treatment if severe irritation or sensitisation develops; skin pigmentation may occur on prolonged therapy.
Administration: Apply 1-2 times daily in a thin film, avoid occlusive dressings.

POM **SICORTEN PLUS®** *(Novartis)*
Cream, Halometasone 0.05%, triclosan 1%.
Pack - 10 g.

HYDROCORTISONE

Hydrocortisone acetate is a representative mild topical corticosteroid. Various drugs can serve as alternatives.
Indications: Contact dermatitis, atopic dermatitis (eczema), lichen planus; intractable pruritus and phototoxic reactions, including polymorphic light eruptions and actinic prurigo; short-term treatment of psoriasis of the face and flexures.
Contra-indications: Untreated skin infections or broken skin; rosacea, acne, perioral dermatitis.
Precautions: Children (avoid prolonged use); occlusive dressings increase penetration into keratinized lesions (use occlusive dressings only at night and for no longer than 2 days; avoid use on weeping lesions); secondary infection requires treatment with an appropriate antimicrobial.
Adverse effects: Exacerbation of local infection; atrophic changes (see under Betamethasone) less likely with mild corticosteroids, but infants and children particularly susceptible.
Advice to patients: See label 28 in Appendix 6. See also under Betamethasone.
Administration: *Inflammatory skin conditions*, apply a small quantity to the affected area 1–2 times daily until improvement occurs, then less frequently.

POM **Hydrocortisone** *(WMF 13.3)*
Cream, Hydrocortisone acetate 1%
Ointment, Hydrocortisone acetate 1%

POM **Hydrocortisone** *(EDL 14.2)*
Cream, Ointment, Hydrocortisone acetate 1%.

POM **CORTISONE®** *(Hovid)*
Ointment, Hydrocortisone 1%.
Pack - 15 g.

POM **Hydrocortisone** *(Drugfield)*
Cream, Hydrocortisone.
Pack - 15 g.

HYDROCORTISONE plus NEOMYCIN

Indications: Inflammatory dermatoses with secondary bacterial infection.
Advice to patients: See under Betametha sone.
Administration: Apply sparingly 2-3 times daily.

POM **Hydrocortisone plus Neomycin** *(EDL 14.2)*
Ointment or Cream, Hydrocortisone 0.5-1%, neomycin 0.25-0.5%.

HYDROCORTISONE plus OXYTETRACYCLINE

Therapeutic category: Anti-inflammatory/ anti-infective.
Pharmacology: Oxytetracycline is a potent broad spectrum antibiotic whereas hydrocortisone has anti-inflammatory, antipruritic and vasoconstrictive actions.
Indications: Cutaneous infections; atopic

dermatitis; contact dermatitis; nonspecific pruritus of the anus, vulva, and scrotum.
Contra-indications: Acute herpes simplex, tuberculosis of the skin, fungal diseases of the skin, hypersensitivity to the drug.
Precautions: Discontinue if irritation occurs; over-growth of nonsusceptible organisms; pregnancy.
Adverse effects: Local irritations such as burning, itching, dryness, allergic contact dermatitis.
Advice to patients: See under Betametha sone.
Administration: Apply a small amount to the affected skin areas 2-4 times daily.

POM **TERRA-CORTRIL**® *(Pfizer)*
Ointment, Oxytetracycline (as HCl) 30 mg, hydrocortisone 10 mg per g.
Pack - 5 g.

METHYLPREDNISOLONE

Pharmacology: Topical methylprednisolone is effective in suppressing inflammatory and allergic skin reactions as well as reactions associated with increased cellular regeneration, leading to regression of the objective symptoms (erythemia, oedema, thickening of the skin, coarseness of the skin surface) and the subjective complaints (itching, burning, pain).
Indications: Endogenous eczema (atopic dermatitis, neurodermatitis); contact eczema; degenerative, dyshidrotic, or vulgar eczema; eczema in children.
Contra-indications: Tuberculous or syphilitic processes in the affected area; viral diseases (e.g. vaccinia, chicken-pox, shingles); rosacea.
Precautions: Pregnant and lactating women; avoid large- area or prolonged use; skin diseases involving bacterial and/or fungal infection may require additional therapy; avoid contact with eyes when applying to the face; ointment should be used instead of cream if excessive skin drying occurs during prolonged use.
Adverse effects: Local skin reactions such as itching, burning, erythema or vesiculation. Rarely folliculitis, increased growth of body hair (hypertrichosis), perioral dermatitis, allergic skin reactions.
Advice to patients: See under Betamethasone.
Administration: Apply thinly to the affected area once daily. Not exceeding 12 weeks in adults and 4 weeks in children.

POM **ADVANTAN**® *(CHI/Schering)*
Cream, Methylprednisolone aceponate 0.1%.
Pack - 15 g (tube).
Recommended for acute and weeping stages of eczema, for very greasy skin and for use on exposed or hairy parts of the body.

Ointment, Methylprednisolone aceponate 0.1%.
Pack - 15 g (tube).
Recommended for skin conditions which are neither weeping nor very dry; it makes the skin slightly greasy without retaining warmth and fluid.

PANTHENOL

Indications: To support wound healing and epithelization.
Administration: Apply thinly to the affected area 1-3 times daily.

POM **Panthenol** *(EDL 14.2)*
Cream or Ointment, Panthenol 2-5%.

POM **BEPANTHEN**® *(Swipha)*
Cream, Panthenol 5%; white non-sticky odourless cream.
Pack - 30 g.

15.3 Astringents

Aluminum acetate is a topical astringent used as an antiseptic for various skin conditions including suppurating superficial wounds and tropical ulcers, and the lesions produced by pemphigus and impetigo. **Potassium permanganate** (section 15.1.1) may be used in the same way.

ALUMINIUM DIACETATE

Indications: Wet dressings to assist healing of suppurating superficial wounds, tropical ulcers and eczematous skin lesions; removal of adherent crusts.
Precautions: Avoid use of plastic or rubber occlusive dressings.
Administration: *Suppurating superficial wounds and tropical ulcers*, apply dressings soaked in 0.65% solution for 30–120 minutes daily, changing dressings every 5–15 minutes; tropical ulcers also require treatment with procaine benzylpenicillin for 2–4 weeks (section 9.1.1.1).
Pemphigus, apply dressings soaked in 5% solution every 4 hours.
Impetigo, apply dressings soaked in 0.65% solution until superficial crusts can be separated.
Dilution of Aluminium Acetate Solution 13%: Dilute 1 in 20 with water for 0.65% solution; dilute 1 in 2.6 with water for 5%.

OTC **Aluminium diacetate** *(WMF 13.4)*

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Solution for dilution (Concentrate for cutaneous solution), Aluminium acetate 13%.

OTC **Aluminium Diacetate** *(EDL 14.3)*
Solution, Aluminium diacetate 13%

CALAMINE plus ZINC OXIDE

Indications: Relieves the discomfort due to rashes, stings, insect bites, and other similar skin conditions such as measles; pruritus.

Administration: Apply to the to the affected parts with the help of cotton wool or any suitable applicator

OTC **Calamine plus Zinc Oxide** *(EDL 14.3)*
Lotion and Plaster.

OTC **Calamine Lotion** *(BCN)*
Lotion, Calamine 15.0 g, zinc oxide 5.0 g phenol 0.42 g, bentonite 3.0 g, sodium citrate 0.5 g, glycerol 6.3 g; thick pink coloured suspension.
Pack - 100 ml.

OTC **Calamine Lotion** *(Evans)*
Lotion, Calamine 15.0 g, zinc oxide 5.0 g, phenol 0.43 g, bentonite 3.0 g, sodium citrate 0.5 g, glycerol 6.3 g; thick pink coloured suspension.
Pack - 100 ml.

OTC **Calamine Lotion** *(Leady)*
Lotion, Calamine Lotion B.P.

OTC **Galways Calamine Lotion** *(SKG)*
Lotion, Calamine 15.0 g, zinc oxide 5.0 g, liquified phenol 0.5 ml, bentonite 3.0 g, sodium citrate 0.5 g, glycerol 5.0 ml; thick pink coloured suspension.
Pack - 100 ml.

OTC **Moko Calamine** *(New Healthway)*
Lotion, Calamine 15 g, zinc oxide 5 g, bentonite 3 g, phenol 0.5 ml per 100 ml; thick pink coloured suspension.

15.4 Preparations for acne

15.4.1 Topical preparations for acne
15.4.2 Oral preparations for acne

Acne vulgaris

Acne is a disorder of the pilosebaceous follicles and typically first appears during puberty when androgenic stimulation triggers excessive production of sebum. *Mild acne* is characterized by comedones and a few pustules which heal without scarring, and usually responds to topical therapy alone. In *moderate acne*, where there are more extensive pustules causing mild scarring, oral antibiotics such as a tetracycline or erythromycin (section 9.1.2.4) are commonly used. In *severe acne*, widespread pustules are accompanied by nodular abscesses and cysts, requiring treatment with estrogens, antiandrogens, or retinoids. Since scarring of the skin resulting from severe nodular acne causes major distress, acne should always be treated as soon as possible. Exposure to substances suspected of causing or aggravating the condition should be avoided. Systemic treatment must be continued for several months before a response can be anticipated. During this time, topical preparations should be applied to the affected areas to prevent the development of new lesions.

Benzoyl peroxide is a keratolytic drug with bacteriostatic activity against *Propionibacterium acnes*; treatment is usually started at a lower strength and increased as tolerance develops to the initial irritant reaction.

Preparations containing **sulfur,** which is bactericidal and promotes desquamation, are often used, and may be combined with salicylic acid, which is a keratolytic agent.

Topical antibiotics such as clindamycin are widely used in inflammatory acne. However, treatment must be maintained for 2 to 3 months before any benefit is seen and this prolonged course carries the risk of selection and spread of antibiotic-resistant organisms.

15.4.1 Topical preparations for acne

BENZOYL PEROXIDE

Indications: Mild to moderate acne and as an adjunct to oral therapy in more severe cases.

Precautions: Avoid contact with eyes, mouth, and mucous membranes; avoid use of occlusive dressings; avoid excessive exposure to sunlight.

Adverse effects: Initial irritation common but subsides with continued use; rarely, contact sensitivity occurs, occasionally even 1 application can cause severe irritation; may bleach fabrics, hair and skin.

Advice to patients: Shake lotion before using;

cleanse and make sure skin is dry before applying; drug may bleach hair or clothing; may be worn under water based makeup. Improvement should occur within 2 weeks; keep away from eyes, mouth, mucous membranes;. if excessive dryness or peeling occurs, reduce dose, frequency or concentration; if excessive stinging or burning occurs, remove with mild soap and water; resume use the next day; if excessive redness or irritation occurs, discontinue use. Avoid excessive sunlight, sun lamps, or other topical medications unless directed by a physician.

Nursing considerations: •Observe for signs of systemic infection; granulation may indicate effectiveness.

Administration: *Acne*, initially apply to clean skin on alternate days, increasing frequency to 1–2 times daily as tolerance to irritant effect develops.

OTC **Benzoyl peroxide** *(WMF 13.5)*
Cream, Benzoyl peroxide 5%.
Lotion (Cutaneous suspension), Benzoyl peroxide 5%.

OTC **Benzoyl peroxide** *(EDL 14.4)*
Cream or Gel, Benzoyl Peroxide 2.5%, 5%, 10%.

METHYLPREDNISOLONE plus NEOMYCIN plus SULPHUR plus ALUMINIUM CHLOROHYDROXIDE

Pharmacology: Methylprednisolone acetate acts on inflammatory manifestations. Neomycin sulfate exerts an antibacterial effect and avoids the development of cutaneous superinfections. Aluminium chlorohydroxide hydrate causes lesions to dry. Sulfur has keratolytic and antifungal properties.

Indications: Treatment of acne vulgaris, acne rosacea and seborrhoeic dermatitis; control of skin irritation and eruptions that often occur after shaving.

Contra-indications: Hypersensitivity to any of the components of the preparation. Local application is contraindicated in tuberculosis of the skin, herpes simplex, vaccinia, varicella, and in other cutaneous infections for which an effective antibiotic or chemotherapeutic agent is not available for simultaneous application.

Precautions: Because of the potential hazard of nephrotoxicity and ototoxicity, prolonged use of large amounts of this product should be avoided in the treatment of skin infections following extensive burns, trophic ulceration and other conditions where absorption of neomycin is possible. Because of the concern of nephrotoxicity and ototoxicity associated with neomycin, this combination product should not be used over a wide area or for extended periods of time.

This preparation is usually well tolerated. However, neomycin may occasionally induce sensitivity reactions. If signs of irritation or sensitivity should develop, application should be discontinued. If extensive areas are treated or if the occlusive technique is used, the possibility exists of increased absorption of the corticoid and suitable precautions should be taken. The safety of the use of topical steroid preparations during pregnancy has not been fully established. Therefore, they should not be used unnecessarily during pregnancy, on extended areas, in large amounts, or for prolonged periods of time.

This product should not be put in the eyes or, if the ear drum is perforated, in the external ear canal.

Note: The prolonged use of antibiotic containing preparations may result in overgrowth of non-susceptible organisms, particularly fungi. If new infections appear during treatment, appropriate therapy should be instituted.

Adverse effects: When steroid preparations are used for long periods in intertriginous areas or under occlusive dressing, localized atrophy and striae may occur. Other local adverse reactions associated with topically applied corticoids either with or without occlusive dressings include: burning sensations, itching, irritation, dryness, folliculitis, secondary infection, atrophy of the skin, acneiform eruption and hypopigmentation. Ototoxicity and nephrotoxicity have been reported following absorption of topically applied neomycin. According to current medical literature there has been an increase in the prevalence of neomycin hypersensitivity.

Administration: After careful cleansing of the affected skin to minimize the possibility of introducing infection, a small amount is applied and rubbed gently into the involved areas. Application should be made initially 1-2 times daily. Once control is achieved, the frequency of application should be reduced to the minimum necessary to avoid relapses.

POM **NEO-MEDROL®** *(Pharmacia)*
Lotion, Methylprednisolone acetate, Neomycin sulfate, Aluminium chlorohydroxide hydrate, Sulfur (as dispersible form).
Pack - 25 ml.

POM **NEO-PRESOL**® *(Drugfield)*
Lotion, Methylprednisolone acetate, neomycin sulphate, sulphur, aluminium chlorohydroxide
Pack - 25 ml.

TRETINOIN

Synonym: Vitamin A acid; Retinoic acid.
Therapeutic category: Anti-acne
Indications: Tretinoin is a vitamin A derivative used topically in the treatment of acne vulgaris in which comedones, papules, and pustules predominate.
Contra-indications: Acute eczema, rosacea, acute inflammation of the skin; avoid contact with eyes, mouth and mucous membranes; pregnancy, breast-feeding.
Precautions: Avoid direct sunlight and u.v. light (sunscreen or protective clothing may be used if exposure to sun is unavoidable); avoid use in severe acne involving large areas; do not use together with benzoyl peroxide or medicated cosmetics.
Interactions: Keratolytics
Adverse effects: Excessive redness of skin, oedema, blisters or crusts.
Advice to patients: Thoroughly wash hands after applying; avoid hydration of skin immediately before applying; minimize exposure to sunlight; avoid washing face more frequently than 2-3 times daily; if severe irritation occurs, discontinue medication temporarily and adjust dose when irritation subsides; avoid using topical preparations with high alcoholic content during treatment period such as shaving lotion; do not exceed prescribed dose.
Nursing considerations: •Cleanse area thoroughly before application.
•Advise patient to wash face with a mild soap no more than 2-3 times daily; avoid strong or medicated cosmetics, soaps, or other topical products containing alcohol or astringents.
•Do not apply to normal skin, eyes, nose, other mucous membranes.
•Observe for signs of hypersensitivity, blistering, excessive dryness.
•Explain to patient that drug is not a cure but relieves symptoms; therapeutic effect may take up to 6 weeks.
Administration: Apply 1-2 times daily
See lit. for details.

POM **Tretinoin** *(EDL 14.4)*
Cream, Tretinoin 0.05%
Gel, Tretinoin 0.025%.

POM **RETIN-A**® *(Janssen-Cilag)*
Cream, Tretinoin 0.05%
Pack - 30 g
Gel, Tretinoin 0.025%
Pack - 30 g.

TRICLOSAN

Indications: Skin disinfection; acne (with sulphur).

OTC **Triclosan** *(EDL 14.4)*
Soap, Triclosan 0.75%

OTC **Triclosan plus Sulphur** *(EDL 14.4)*
Cream, Triclosan 0.05-0.2%, precipitated Sulphur 2-5%.

15.4.2 Oral preparations for acne

CYPROTERONE plus ETHINYLOESTRADIOL

Indications: Androgen-dependent skin diseases in women such as acne, androgenic alopecia, mild forms of hirsutism.
Contra-indications, Precautions, etc.: See under Laevonorgestrel plus Ethinylestradiol in Section 11.3.1.
Dose: 1 tablet daily for 21 days starting on 1st day of menstrual cycle and repeated after a 7-day interval, usually for several months; withdraw when acne or hirsutism completely resolved (repeat courses may be given if recurrence).

POM **DIANE 35**® *(CHI/Schering)*
Tablet, Ethinyloestradiol 0.035 mg, cyproterone acetate 2 mg.
Pack - 21.

15.5 Preparations for psoriasis

Psoriasis, which affects people of all ages in all countries, is one of the most common chronic dermatoses in industrialized countries, and is characterized by epidermal thickening and scaling. Considerable local variations in its prevalence have been variously attributed to genetic, climatic, nutritional and ecological factors. Various biological events may trigger psoriasis, such as streptococcal or viral infection, an emotional crisis or pregnancy. Occasionally psoriasis may be provoked or exacerbated by drugs such as ACE inhibitors, beta-adrenoceptor antagonists (beta-blockers), chloroquine, lithium, and non-steroidal anti-inflammatory drugs.

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Psoriasis vulgaris (chronic plaque psoriasis) is the most common form of the condition, usually affecting extensor surfaces of the limbs and the scalp. Guttate psoriasis, commonly seen in children, is often caused by a streptococcal infection; lesions may disappear following antimicrobial treatment. The condition is also known to resolve spontaneously but more commonly transforms into chronic plaque psoriasis. No treatment is known to assure remission, although sunlight often clears lesions.

Dithranol restores the normal rate of epidermal cell proliferation and keratinization, and localized psoriasis vulgaris can frequently be cleared by daily applications for a period of 2 to 4 weeks. A short contact method of application causes little, if any, irritation or staining of normal skin, and is particularly useful for outpatient management. There is a risk of severe conjunctivitis if dithranol enters the eye.

Crude coal tar is also effective in the treatment of psoriasis. Some preparations additionally contain salicylic acid as a keratolytic. Good results are often obtained when daily applications or baths are combined with exposure to ultraviolet light or sunlight.

Emollients containing low concentrations of **salicylic acid** (1–2%) are a useful adjunct to treatment, particularly where there is thick scaling. A preparation containing **urea** 10%, which has moisturizing, keratolytic and antimitotic properties, may prove more effective than an emollient.

Topical corticosteroids have a limited role in psoriasis. A mild corticosteroid such as hydrocortisone may be used on the face and flexures, whereas a potent corticosteroid such as betamethasone is most appropriate for the scalp, hands and feet. However, when extensive areas of the body surface are involved or when there is erythrodermic psoriasis, sufficient may be absorbed to cause adrenal suppression; also rebound often occurs after stopping treatment, resulting in a more unstable form of psoriasis.

COAL TAR

Indications: Chronic psoriasis, either alone or in combination with exposure to ultraviolet light.

Contra-indications: Inflamed, broken or infected skin.

Precautions: Skin protection possibly required to reduce photosensitivity reactions.

Adverse effects: Irritation, photosensitivity reactions; rarely hypersensitivity; skin, hair and fabrics discoloured.

Administration: *Psoriasis*, apply 1–4 times daily, preferably starting with lower strength preparation.
Coal tar bath, use 100 ml in bath of tepid water and soak for 10–20 minutes; use once daily to once every 3 days for at least 10 baths; often alternated with ultraviolet (UVB) rays, allowing at least 24 hours between exposure and treatment with coal tar

POM **Coal tar** *(WMF 13.5)*
Solution (Cutaneous solution), Coal tar 5%

POM **Coal tar** *(EDL 14.7)*
Solution or Cream, Coal tar 1-10%.

DITHRANOL

Indications: Moderately severe psoriasis.

Contra-indications: Hypersensitivity; avoid use on face, acute eruptions, excessively inflamed areas.

Precautions: Irritant—avoid contact with eyes and healthy skin.

Adverse effects: Local irritation; discontinue use if excessive erythema or spread of lesions; conjunctivitis following contact with eyes; staining of skin, hair, and fabrics.

Administration: *Psoriasis*, initiate under medical supervision: starting with 0.1%, carefully apply to lesions only, leave in contact for 30 minutes, then wash off thoroughly; repeat application daily, gradually increasing strength to 2% and contact time to 60 minutes at weekly intervals; wash hands thoroughly after use.

POM **Dithranol** *(WMF 13.5)*
Ointment, Dithranol 0.1–2%.

POM **Dithranol** *(EDL 14.7)*
Ointment, Dithranol 0.1-2%.

OLIVE OIL

Indications: Externally, Olive oil is emollient and soothing to inflammed surfaces and is employed to soften the skin and crusts in

eczema and psoriasis.

OTC **BELL'S OLIVE OIL**® *(De-Sears)*
Liquid, Olive Oil BP 1973; a pale yellow or greenish-yellow oil.
Pack - 70 ml; 150 ml.

UREA

Indications: Hydrating agent and keratolytic for dry, scaling and itching skin conditions.
Precautions: Avoid application to face or broken skin; avoid contact with eyes.
Adverse effects: Transient stinging and local irritation.
Administration: *Dry, scaling skin disorders*, apply twice daily, preferably to damp skin.

POM **Urea** *(WMF 13.5)*
Cream, Urea 10%
Ointment, Urea 10%

15.6 Preparations for actinic keratosis

The lesions of actinic keratosis are distributed primarily over sun-exposed areas. Horny growths, which are often covered by light brown scales, are usually asymptomatic but can be disfiguring. They respond to light cautery and cryosurgery or topical application of **fluorouracil** over a three-week period. Simple emollients may be satisfactory for people with many lesions.

FLUOROURACIL

Indications: Actinic keratosis; genital warts unresponsive to podophyllum resin; malignant disease (section 12.1.3).
Contra-indications: Haemorrhagic ulcerated tissue.
Precautions: Avoid mucous membranes and eyes; since UV light intensifies the inflammatory reaction, avoid prolonged exposure to sunlight.
Adverse effects: Local inflammatory and allergic reactions; rarely erythema multiforme; photosensitivity reactions during and for up to 2 months after treatment.
Administration: *Actinic keratosis, genital warts*, apply thinly 1–2 times daily until marked inflammatory response occurs (usually 3–4 weeks); healing may require further 2 months after completion of treatment.

NOTE: AVOID USE OF METAL APPLICATOR

POM **Fluorouracil** *(WMF 13.5)*
Cream, Fluorouracil 5%

15.7 Preparations for warts

Warts most commonly affect the hands, feet (plantar warts, verrucas), and anogenital region (condylomata acuminata); all are caused by the human papilloma virus. They may regress spontaneously at any time within months or years of their first appearance; however, particularly in immunosuppressed patients, they may spread and be difficult to cure. Many common, plane and plantar warts can reasonably be left untreated, but painful or unsightly lesions generally respond to application of preparations containing **salicylic acid**. Where available, cryotherapy using liquid nitrogen applied with a cotton-tip or a spray is highly effective; however, freezing the skin can produce temporary or permanent depigmentation (particularly on dark skin), and should be used with caution.

Anogenital warts are usually transmitted by sexual contact; they should always be treated, although they frequently recur, because of the increased risk of cervical cancer. **Podophyllum resin**, a caustic antimitotic agent, may be applied to small external lesions. The risk of extensive local necrosis and of systemic toxicity exclude the use of podophyllum resin on larger surfaces. When available podophyllotoxin is a less toxic alternative. Where podophyllum is contraindicated or ineffective surgical removal, electrocautery, cryosurgery and laser therapy are possible options. Topical application of **fluorouracil** has been reported to be of value in resistant cases but the treatment is expensive and efficacy is still under investigation.

PODOPHYLLUM RESIN

An example of an application to treat warts. Various drugs can serve as alternatives.
Indications: External anogenital warts; plantar warts.
Contra-indications: Pregnancy (Appendix 2); breastfeeding; children.
Precautions: Avoid use on large areas, mucous membranes; irritant to eyes; avoid contact with normal skin.

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Adverse effects: Systemic effects resulting from cutaneous absorption include nausea, vomiting, abdominal pain and diarrhoea; also transient leukopenia and thrombocytopenia; renal failure; delayed neurotoxicity including visual and auditory hallucinations, delusions, disorientation, confusion and delirium following excessive application.

Nursing considerations: •Shake well before using; solution should be washed off within 1-4 hours for genital and perianal warts, and within 1-2 hours for accessible meatal warts.

•Use protective occlusive dressing around warts to prevent contact with unaffected skin.

Administration: NOTE: MEDICAL SUPERVISION REQUIRED.

Warts, adult apply carefully to warts, avoiding contact with normal tissue; rinse off after 1–4 hours; may be repeated at weekly intervals but no more than 4 times in all; only few warts to be treated at any one time.

POM **Podophyllum resin** *(WMF 13.5)*
Solution (Cutaneous solution), Podophyllum resin 10–25%.

POM **Podophyllum resin** *(EDL 14.7)*
Solution, Podophyllum 10-25%.

SALICYLIC ACID

Indications: Hyperkeratotic conditions.

Contra-indications: Broken or inflamed skin; children under 2 years.

Precautions: Diabetes mellitus or if peripheral blood circulation impaired; avoid contact with eyes, mouth, and mucous membranes; avoid application to large areas.

Adverse effects: Local irritation, dermatitis; salicylism on excessive application or treatment of large areas, particularly in children.

Advice to patients: When applying in concentrations more than 10%, protect surrounding tissue with petrolatum; do not use on open skin, avoid contact with eyes, mouth, and other mucous membranes.

Nursing considerations: •For warts, before applying product, soak area in warm water for 5 minutes; dry thoroughly, then apply medication.

Administration: *Hyperkeratotic skin disorders*, apply once daily, starting with lower strength preparations; gradually increase strength until satisfactory response obtained.

POM **Salicylic acid** *(WMF 13.5)*
Topical solution (Cutaneous solution), Salicylic acid 5%.
Ointment, Salicylic acid 1–6% [not included on WHO Model List].

POM **Salicylic acid** *(EDL 14.7)*
Collodion or Ointment, Salicylic acid 12%, 25% respectively.

15.8 Ultraviolet blocking agents

Exposure of skin to sunlight is beneficial in moderation since ultraviolet light is vital for the synthesis of vitamin D. Excessive exposure is hazardous, however, particularly in light-skinned persons who tan poorly, and in patients with pathological or drug-induced photosensitivity. Photodamage is first evident as acute sunburn and, in the longer term, as premature ageing of the skin. Excessive exposure to sunlight predisposes to the development of malignant and pre-malignant skin lesions including actinic keratosis, squamous cell carcinoma, basal cell carcinoma and malignant melanoma, and also exacerbates cutaneous porphyrias, systemic lupus erythematosus, rosacea, and possible herpes labialis.

The best protection is to reduce exposure and thereby avoid sunburn either by the use of protective clothing or, when this is not practicable, by regular use of sunscreen products with a sun protection factor (SPF) rating of at least 15.

The major categories of chemical sunscreens include cinnamates, which are UVB absorbers, and dibenzoylmethanes, which are UVA absorbers. Physical sunscreens, such as titanium dioxide, are opaque and reflect ultraviolet light. Many sunscreen products combine sunscreens from different groups in order to widen the range of protection. An example of a broad-spectrum topical sun protection product which protects from both UVA and UVB contains octinoxate 3%, avobenzone 2%, and titanium dioxide 2%, formulated in an acrylate polymer or an oily basis.

AMINOBENZOIC ACID

Indications: Sun screening agent.

Administration: To be applied to the whole body.

POM **Amino Benzoic Acid** *(EDL 14.9)*

RETURN

Lotion, Cream or Paste, Aminobenzoic acid 5%

TITANIUM DIOXIDE

Indications: Sunscreening agent
Administration: To be applied to the whole body

OTC **Titanium Dioxide** (*EDL 14.9)*
Cream or Paste, Titanium dioxide 20-25%.

15.9 Hair growth stimulants

MINOXIDIL

Therapeutic category: Hair Growth stimulant; vaso-dilator
Pharmacology: Topical minoxidil solution stimulates hair growth in individuals with androgenetic alopecia, expressed in males as baldness of the vertex of the scalp and in females as diffuse hair loss or thinning of the frontoparietal areas. The mechanism by which minoxidil stimulates hair growth is not known but like minoxidil some other arterial dilating drugs also stimulate hair growth when given systemically.
Indications: Treatment of androgenetic alopecia, expressed in males as baldness of the vertex of the scalp and in females as diffuse hair loss or thinning of the frontoparietal areas. At least four months of twice daily applications are generally required before evidence of hair growth can be expected.
Contra-indications: Hypersensitivity to minoxidil or any other component of the preparation.
Precautions: Local abrasion or dermatitis of the scalp may increase absorption and hence increase the risk of side effects; patients with history of or existing heart disease should be advised of potential serious adverse effects; observe patients for tachycardia and fluid retention; patients should be monitored for increased heart rate and weight gain or other systemic effects (discontinue use if systemic effects occur); avoid use in pregnancy, lactation and children below 18 years of age; avoid contact with eyes and any irritated skin areas.
Interactions: •Avoid co-administration with other topical agents including topical corticosteroids, retinoids, and petrolatum or agents that are known to enhance cutaneous drug absorption.
•Avoid co-administration with guanethidine.
Adverse effects: Most commonly itching and other skin irritations of the treated area of the scalp.
Advice to patients: Discontinue and contact your doctor if you have palpitations; rapid weight gain of 2.5kg or more; swelling or puffiness of hands, face, ankles, or stomach; dizziness, lightheadedness, or fainting; burred vision, new or worsening pain in the chest, arm, or shoulder; signs of severe indigestion; severe scalp irritation. Avoid contact with eyes and any irritated skin areas.
Administration: Wash the hair and scalp using a mild shampoo, and dry.
Apply 1ml solution as a thin film twice daily at 12 hour intervals, to the centre of the bald areas and spread to cover the entire affected area; 4 months of therapy or longer may be necessary for hair regrowth.
Note: The total daily dosage should not exceed 2ml. If finger tips are used to facilitate drug applications, hands should be washed afterwards. Apply the drug only when the hair and scalp are thoroughly dry. Do not use a hair dryer to speed the drying of the solution on the scalp. Blowing air on the scalp may decrease its effectiveness. Do not apply other medications to your hair while using topical minoxidil solution. It may only be used by males, ages 18-65, for the treatment of male pattern baldness.

POM **APO-GAIN®** *(Lahams)*
Solution, Minoxidil 2%; clear, colourless to slightly yellow solution.
Pack - 60 ml.

15.10 Topical circulatory preparations

HEPARINOID plus HYALURONIDASE

Indications: Sprains, haematoma, venipuncture, thrombophlebitis, superficial thrombosis, vericose ulcer, haemorrhoids to soft scar tissues.
Contra-indications: Open or infected wounds.
Precautions: Hypersensitivity to heparin.
Administration: Haemorrhoids, apply morning and night and after defecation; others, apply sufficient quantity 2-3 times daily.

POM **Heparinoid plus Hyaluronidase** *(EDL 11.2)*
Ointment, Hyaluronidase 15,000 units per 100 mg, heparinoid equivalent to 5000 units of heparin.

16. Disinfectants and antiseptics

RETURN

16.1 Aldehydes
16.2 Cationic surfactants
16.3 Chlorhexidine salts
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16.7 Iodine
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16.10 Potassium permanganate
16.11 Alcohol

ANTISEPTICS

An antiseptic is a type of disinfectant, which destroys or inhibits growth of micro-organisms on living tissues without causing injurious effects when applied to surfaces of the body or to exposed tissues. Some antiseptics are applied to the unbroken skin or mucous membranes, to burns and to open wounds to prevent sepsis by removing or excluding microbes from these areas. Iodine has been modified for use as an antiseptic. The iodophore, **polyvidone-iodine**, is effective against bacteria, fungi, viruses, protozoa, cysts and spores and significantly reduces surgical wound infections. The solution of polyvidone-iodine releases iodine on contact with the skin. **Chlorhexidine** has a wide spectrum of bactericidal and bacteriostatic activity and is effective against both Gram-positive and Gram-negative bacteria although it is less effective against some species of *Pseudomonas* and *Proteus* and relatively inactive against mycobacteria. It is not active against bacterial spores. Chlorhexidine is incompatible with soaps and other anionic materials, such as bicarbonates, chlorides, and phosphates, forming salts of low solubility which may precipitate out of solution. **Ethanol** has bactericidal activity and is used to disinfect skin prior to injection, venepuncture or surgical procedures.

DISINFECTANTS

A disinfectant is a chemical agent, which destroys or inhibits growth of pathogenic micro-organisms in the non-sporing or vegetative state. Disinfectants do not necessarily kill all organisms but reduce them to a level, which does not harm health or the quality of perishable goods. Disinfectants are applied to inanimate objects and materials such as instruments and surfaces to control and prevent infection. They may also be used to disinfect skin and other tissues prior to surgery (see also Antiseptics, above).

Disinfection of water can be either physical or chemical. Physical methods include boiling, filtration and ultraviolet irradiation. Chemical methods include the addition of **chlorine releasing compounds**, such as sodium hypochlorite solution, chloramine T powder, or sodium dichloroisocyanurate (NaDCC) powder or tablets. Where water is not disinfected at source it may be disinfected by boiling or by chemical means for drinking., cleaning teeth and food preparation.

Chlorine is a hazardous substance. It is highly corrosive in concentrated solution and splashes can cause burns and damage the eyes. Appropriate precautions must be taken when concentrated chlorine solutions or powders are handled.

The chlorinated phenolic compound, **chloroxylenol**, is effective against a wide range of Gram-positive bacteria. It is less effective against staphylococci and Gram-negative bacteria; it is often ineffective against *Pseudomonas* spp. and inactive against spores.

The aldehyde bactericidal disinfectant, **glutaral**, is strongly active against both Gram-positive and Gram-negative bacteria. It is active against the

tuberculosis bacillus, fungi such as *Candida albicans*, and viruses such as HIV and hepatitis B. A 2% w/v aqueous alkaline (buffered to pH 8) glutaral solution can be used to sterilize heat-sensitive pre-cleansed instruments and other equipment.

16.1 Aldehydes

FORMALDEHYDE SOLUTION

Indications and Administration: Preservation of pathological specimens, 10% solution in saline; treatment of skin warts, 3% solution; treatment of sweating of the feet, 1 part of formaldehyde solution in 3 parts of glycerol or 5 to 10 parts of alcohol; etc.
Adverse effects: Irritant to eyes, nose and repiratory tract; concentrated solutions may cause skin whitening and hardening; contact dermatitis and sensitivity reactions.

OTC **Formaldehyde** *(EDL 10)*
Solution, Formaldehyde 1.5-10%

GLUTARAL

Indications: Disinfection and sterilization of instruments and surfaces.
Precautions: Minimize occupational exposure by adequate skin protection and measures to avoid inhalation of vapour.
Adverse effects: (Occupational exposure) nausea, headache, airway obstruction, asthma, rhinitis, eye irritation and dermatitis and skin discoloration.
Administration: *Disinfection of clean instruments*, immerse in undiluted solution for 10–20 minutes; up to 2 hours may be required for certain instruments (for example bronchoscopes with possible mycobacterial contamination); rinse with sterile water or alcohol after disinfection.
Sterilization of clean instruments, immerse in undiluted solution for up to 10 hours; rinse with sterile water or alcohol after disinfection.

OTC **Glutaral** *(WMF 15.1)*
Solution, Glutaral 2% aqueous alkaline (pH 8) solution.

OTC **Glutaraldehyde** *(EDL 10)*
Solution, Glutaraldehyde 2% in a buffered base

16.2 Cationic surfactants

CETRIMIDE

Indications and Administration: As aqueous solution or creams for the pre-operative cleansing of the skin and for cleansing wounds; as aqueous solutions for cleansing contaminated utensils and as preservatives.
Precautions: Avoid contact with eyes as well as prolonged and repeated applications to the skin.
Adverse effects: Skin irritation and hypersensitivity especially on prolonged or repeated applications.

OTC **Cetrimide** *(EDL 10)*
Solution, Cetrimide 1% (dilute); 20-40% (strong).

OTC **SAVLON®** *(Bolar)*
Solution (Hospital concentrate), Chlorhexidine gluconate 1.5%, cetrimide 15%; clear deep orange solution.
To be used diluted 1 in 100 (1%) to 1 in 30 with water for skin disinfection and wound cleansing, and diluted 1 in 30 in alcohol 70% for pre-operative skin preparation.

16.3 Chlorhexidine salts.

CHLORHEXIDINE

Chlorhexidine gluconate is a representative disinfectant and antiseptic. Various agents can serve as alternatives.
Indications: Antiseptic; disinfection of clean instruments.
Precautions: Aqueous solutions—susceptible to microbial contamination—use sterilized preparation or freshly prepared solution and avoid contamination during storage or dilution; instruments with cemented glass components (avoid preparations containing surface active agents); irritant—avoid contact with middle ear, eyes, brain and meninges; not for use in body cavities; alcoholic solutions not suitable before diathermy; syringes and needles treated with chlorhexidine (rinse thoroughly with sterile water or saline before use); inactivated by cork (use glass, plastic or rubber closures); alcohol based solutions are flammable.
Adverse effects: Occasional skin sensitivity and irritation.
Administration: *Antiseptic (pre-operative skin disinfection and hand washing)*,

RETURN

use 0.5% solution in alcohol (70%).
Antiseptic (wounds, burns and other skin damage), apply 0.05% aqueous solution.
Disinfection of clean instruments, immerse for at least 30 minutes in 0.05% solution containing sodium nitrite 0.1% (to inhibit metal corrosion).
Emergency disinfection of clean instruments, immerse for 2 minutes in 0.5% solution in alcohol (70%).

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

OTC **Chlorhexidine** *(WMF 15.1)*
Solution (Concentrate for solution), Chlorhexidine gluconate 5%.

OTC **Chlorhexidine** *(EDL 10)*
Solution, Chlorhexidine gluconate 5%; for dilution

OTC **Chlorhexidine plus Cetrimide** *(EDL 10)*
Solution., Chlohexidine gluconate 1.5%, cetrimide 15%; for dilution.

OTC **GATTOL®** *(Gateway)*
Solution, Chlorhexidine 1.5%, cetrimide 1.5%.
Pack - 4 litres.
Solution (concentrated), Chlorhexidine 3%, cetrimide 3%.
Pack - 4 litres.

OTC **HIBISCRUB®** *(Bolar)*
Solution,Chlorhexidine gluconate 4%; red perfumed detergent solution.

OTC **HIBITANE®** *(Reals)*
Cream, Chlorhexidine gluconate 1%; white water-miscible cream.
An antimicrobial preparation designed for application to broken skin surfaces; may also be applied to the hands by hospital staff as a barrier against bacterial infection.

OTC **HIBITANE 5% CONCENTRATE®** *(Reals)*
Solution, Chlorhexidine gluconate 5%; clear red perfurmed aqueous solution.
Recommended dilutions and uses:

Method of Preparation	Concentration	Use
10ml made up to 1 litre with water (1 in 100)	1 in 2000 (0.05%) Aqueous of sterile instrument	Swabbing in obstetrics, Wounds&burns. Storage
10ml with 15ml water made up to 100ml with 95% alcohol (1 in 10)	1 in 200 (0.05%) in 70% alcohol	Pre–operative skin disinfection. Emergency instrument disinfection (2 minutes' immersion) excluding endoscopes containing cemented glass components.

16.4 Chlorine and its compounds

CHLORINE RELEASING COMPOUNDS

Chlorine releasing compounds are representative disinfectants. Various agents can serve as alternatives.

Indications: Disinfection of surfaces, equipment, water.
Contra-indications: Avoid exposure of product to flame; activity diminished in presence of organic material and increasing pH (can cause release of toxic chlorine gas).
Adverse effects: Irritation and burning sensation on skin.
Administration: *Surface disinfection (minor contamination)*, apply solutions containing 1000 parts per million.
Instrument disinfection, soak in solution containing 1000 parts per million for a minimum of 15 minutes; to avoid corrosion do not soak for more than 30 minutes; rinse with sterile water.

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

OTC **Chlorine releasing compounds** *(WMF 15.1)*
Powder for solution, Chlorine releasing compound, 1 g available chlorine/litre (1000 parts per million; 0.1%).

CHLORINATED LIME plus BORIC ACID (EUSOL)

Indications: Disinfectant lotion and wet dressing, but not recommended for wound irrigation since it may cause irritation of the tissues.
Precautions: Bleaches fabric; avoid use in broken skin.

OTC **Chlorinated Lime plus Boric Acid** *(EDL 10)*
Solution, chlorinated lime 1.25%, boric acid 1.25%; to be freshly prepared.

SODIUM HYPOCHLORITE

See under Chlorine releasing compounds above

OTC **Sodium Hypochlorite** *(EDL 10)*
Solution, Different preparations with available chlorine from 1 to 10%

OTC **PAROZONE®** *(NGC)*
Solution, Sodium hypochlorite 3.5%.
Pack - 500 ml; 1 L.

16.5 Dyes

METHYLROSANILINIUM

Synonym: Gentian Violet; Crystal Violet
Indications and Administration: Treatment of candidal infections of the mouth, boils, chronic ulcers, and mycotic skin affections, 0.5% aqueous solution applied topically; pre-operative skin disinfection, 0.5% crystal violet plus 0.5% brilliant green.

OTC **Moko Gentian Violet** *(New Healthway)*
Solution, Gentian violet 5 mg per ml.
Pack - 60 ml.

16.6 Hydrogen peroxide

HYDROGEN PEROXIDE

Indications: Disinfectant and deodorant. For cleansing of wounds, 6% solution; Mouth-Wash in the treatment of acute stomatitis and as a deodorant gargle, 1.5% solution.
Precautions: Large or deep wounds; bleaches fabric.

OTC **Hydrogen Peroxide** *(EDL–10)*
Solution, Hydrogen peroxide 6% (20 volumes).

OTC **Hydrogen Peroxide** *(Morison)*
Solution, Hydrogen peroxide 6% (20 volumes); clear colourless solution.
Pack - 100 ml; 200 ml.

16.7 Iodine

IODINE

Indications and Administration: Used as weak iodine solution or as a 2% solution. Solution of iodine in 75% industrial methylated spirit for the disinfection of unbroken skin. May also be used for treatment of small wounds and abraisions but wound healing may be delayed.
Precautions: Avoid occlusive dressings; may interfere with tests of thyroid function; broken skin.

OTC **Iodine** *(EDL 10)*
Solutions, Different preparations.

OTC **Moko Iodine Tincture** *(New Healthway)*
Solution, Iodine 2.5%. potassium iodide 2.5%.
Pack - 15 ml.

POLYVIDONE-IODINE

Polyvidone-iodine is a representative antiseptic. Various agents can serve as alternatives.
Indications: Antiseptic; skin disinfection
Contra-indications: Avoid regular or prolonged use in patients with thyroid disorders or those taking lithium; avoid regular use in neonates; avoid in very low birthweight infants.
Precautions: Pregnancy (Appendix 2); breastfeeding (Appendix 3); broken skin (see below); renal impairment (Appendix 4)
LARGE OPEN WOUNDS: THE APPLICATION OF POLYVIDONE-IODINE TO LARGE WOUNDS OR SEVERE BURNS MAY PRODUCE SYSTEMIC ADVERSE EFFECTS SUCH AS METABOLIC ACIDOSIS, HYPERNATRAEMIA, AND IMPAIRMENT OF RENAL FUNCTION.
Adverse effects: Irritation of skin and mucous membranes; may interfere with thyroid function tests; systemic effects (see under Precautions).
Administration: *Pre- and post-operative skin disinfection*, ADULT and CHILD apply undiluted (see also Contraindications above).
Antiseptic (minor wounds and burns), ADULT and CHILD apply twice daily (see also Contraindications above).

POM **Polyvidone-iodine** *(WMF 15.1)*
Cutaneous solution, Polyvidone-iodine 10%.

16.8 Methylated spirits

METHYLATED SPIRITS

Indications: Skin disinfection before injection
Precautions: Flammable; avoid broken skin.

OTC **Methylated Spirit** *(EDL 10)*
Solutions.

OTC **Methylated Spirit** *(Leady-pharma)*
Liquid, Methylated Spirit.

OTC **Moko Methylated Spirit** *(New Healthway)*
Solution, Isopropyl alcohol 95%; clear colourless volatile liquid.
Pack - 200 ml.

16.9 Phenols and related substances

CHLOROXYLENOL

Chloroxylenol is a representative disinfectant and antiseptic. Various agents can serve as alternatives.
Indications: Antiseptic; disinfection of instruments and surfaces.
Precautions: Aqueous solutions should be

freshly prepared; appropriate measures required to prevent contamination during storage or dilution.

Adverse effects: Skin sensitivity reported.

Administration: *Antiseptic (wounds and other skin damage)*, apply a 1 in 20 dilution of 5% concentrate in water. *Disinfection of instruments*, use a 1 in 20 dilution of 5% concentrate in alcohol (70%).

DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Chloroxylenol** *(WMF15.1)*
Solution (Concentrate for solution), Chloroxylenol 5%.

OTC **Chloroxylenol** *(EDL 20)*
Solution, Chloroxylenol 5%; for dilution.

OTC **DETTOL**® *(Reckitt Benckiser)*.
Solution, Chloroxylenol 4.8%

OTC **MORIGAD ANTISEPTIC**® *(Morison)*
Solution, Chloroxylenol 5%; golden brown aqueous solution which forms a dense white emulsion on dilution with water.
Pack - 250 ml; 500 ml; 4 L.
Recommended dilutions and uses:

Method of Preparation	Dilutions	Uses
One capful to 1 litre of water	1 in 100	Cuts, bites, burns, stings & abraisions
One capful to linen, 1 litre of water	1 in 100	Soaking soiled handkerchiefs
One capful to 1 litre of water	1 in 100	For general household Use.

OTC **ROBERT ANTISEPTIC**® *(P.Z.)*
Solution, Chloroxylenol.

DICHLOROXYLENOL plus CHLOROPHENOL

Indications: A powerful germicide for disinfecting drains, lavatories, hospitals and linen.

Precautions: Avoid contact of undiuted solution with the skin and eyes and when contact occurs, wash off immediately with plenty of water. Avoid mixing solution with other chemicals.

OTC **Dichloroxylenol plus chlorophenol** *(EDL 10)*
Soap solution

OTC **MORIGAD GERMICIDE**® *(Morison)*
Soap solution, Dichloroxylenol plus chlorophenol with total phenol content of 30-35%; greyish white emulsion.

Recommended dilutions and uses:

Method od Preparation	Dilutions	Uses
10ml added to one litre of water	1 in 100	Animal husbandary, sinks, etc.
10ml added to three litres of water	1 in 300	Lavatories, hospital use for equipment & linen material.
10ml added to six litres of water	1 in 600	For general disinfection

OTC **SAFE GUARD**® *(NGC)*
Solution, Dichlorometaxylenol, terpineol
Pack - 500 ml.

OTC **XENNOL**® *(De-Sears)*
Solution, Chlorinated Phenols 1.2 %.
Pack- 500 ml.
Uses/Dilutions:(1) Cuts, Bites, Abrasions And Insect Stings: Bathe with 30 ml to half a litre of water. Cover with a clean, dry dressing.
(2) Personal Hygiene: One or two capfuls in the bath is hygienic and refreshing. Dandruff: Wash hair with 45 ml to half a litre of water. Then shampoo as normal.
(3)Household Cleaning And Laundry: Add 30 ml to each litre of water.
(4) Toilets, Sinks And Drains: Use undiluted.

CRESOL AND SOAP SOLUTION (SAPONATED CRESOL)

Indications: General disinfectant for hospital and domestic uses.

Precautions: Dilute solutions may be irritant to the skin. Avoid skin contact with undiluted solution.

OTC **Saponated Cresol** *(EDL 10)*
Solution, Cresol and soap solution.

OTC **IZAL**® *(GSK)*
Solution, Saponated cresol with phenol content of 27%; viscous milky-white liquid with characteristic choking odour.
Pack - 150 ml; 5 L.
Recommended dilutions and uses:

Method of Preparation	Uses
10 drops in a large cupful of water	Cuts, sores and insect bites
1 in 200 solution	Disinfection of sinks, drains and lavatories, wash down with hot solution
1 in 200 solution (soak for 1 hour) or 1 in 600 solution (soak for 12 hours)	Infected linen
A little izal solution in the bath water	Personal protection
3 or 4 drops in a large cupful of water	Prickly heat and craw–craw

OTC **MORIGAD LYSOL**® *(Morison)*
Solution, Cresol and soap solution B.P.; almost colourless to pale brownish-yellow liquid.
Pack - 4 L.

To be used diluted (1 in 100 solution) for the disinfection of hospital floors, sanitary wares and morgues

TRICHLOROPHENOL

Indications: For all first aid uses and personal hygiene and minor ailments such as cuts, bites, stings, minor burns and scalds, etc. The ointment is also indicated for haemorrhoids.

OTC **Tricholorophenol** *(EDL 10)*
Cream, Oitnment or liquid, Mixture of halogenated phenolic bodies and salicyclic acid.

OTC **TCP®** *(Pfizer/Neimeth)*
Liquid, Aqueous solution of halogenated phenolic bodies plus salicyclic acid.
Pack - 100 ml; 240 ml; 4 L.
Cream or Oitnment, Halogenated phenolic bodies and salicylic acid in a suitable base.
Pack - 15 g; 30 g.

Recommended Uses and Directions for use:

Preparations	Uses	Direction
TCP Lquid	Cuts, grazes, bites stings, minor burns and scalds	Apply freely,and if necessary, cover with a dry surgical dressing
	Boils, spot, skin irritations, pimples, rashes, sunburn.	Dab every 4 hours and allow to dry
	Colds, sore throats, influenza	At first signs, gargle with the liquid diluted with about 5 parts of water or spray the throat with slightly diluted TCP. Repeat morning and night.
	Mouth wash	Use daily, diluted with about 5 parts of water, after meals.
	Gum troubles and mouth ulcers	Apply undiluted three times daily and consult your dentist.
	Bruises, sprains	Apply lint dressing soaked TCP liquid diluted 3 parts of water. Dab again at intervals
	Sore eyes, styes	Bath with an eye–bath of tepid water containing a few drops of TCP liquid.
TCP Cream	Cuts, scratches small wounds, etc.	First wash the affected area, then apply freely on guaze dressing
	Bites, stings, minor burns, etc.	Smooth on gently and cover with dry guaze
TCP Ointment	Haemorrhoids	Apply liberally morning and evening
	Pruritus, first aid uses, spots, rashes	First clean the affected area and apply freely on dry guaze.

16.10 Potassium permanganate

POTASSIUM PERMANGANATE

Indications and Administration: Disinfectant and deodorant for use as cleansing application to ulcers or abscesses , 1 in 1000 solution; and as wet dressings and in baths in eczematous conditions and acute dermatoses, 1 in 1000 solution.
Precautions: Irritant to mucous membranes; stains skin and clothing.
Adverse effects: Repeated use of dilute solutions may cause corosive burns. Crystals and concentrated solutions are caustic

OTC **Potassium Permanganate** *(EDL 10)*
Solution, Potassium permanganate 0.1%; to be freshly prepared.

16.11 Alcohol

ETHANOL

Ethanol is a representative disinfectant. Various agents can serve as alternatives.
Indications: Disinfection of skin prior to injection, venepuncture or surgical procedures.
Precautions: Flammable; avoid broken skin; patients have suffered severe burns when diathermy has been preceded by application of alcoholic skin disinfectants.
Adverse effects: Skin dryness and irritation with frequent application.
Administration: *Disinfection of skin*, apply undiluted solution.

OTC **Ethanol** *(WMF 15.1)*
Cutaneous solution, Ethanol 70%.

17. Immunological products and vaccines

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17.1 Vaccines (Active immunity)
17.1.1 Vaccines for universal immunization
17.1.1.1 BCG vaccine (dried)
17.1.1.2 Diphtheria, pertussis and tetanus vaccines
17.1.1.3 Hepatitis B vaccine
17.1.1.4 Measles vaccines
17.1.1.5 Poliomyelitis vaccines
17.1.2 Vaccines for specific groups of individuals
17.1.2.1 Influenza vaccine
17.1.2.2 Meningococcal polysaccharide vaccine
17.1.2.3 Mumps vaccine
17.1.2.4 Rabies vaccine (inactivated)
17.1.2.5 Rubella vaccine
17.1.2.6 Typhoid vaccine
17.1.2.7 Yellow fever vaccine
17.1.3 Other vaccines
17.2 Sera and immunoglobulins (Passive immunity)
17.2.1 Anti-D immunoglobulin (human)
17.2.2 Antitetanus immunoglobulin (human)
17.2.3 Diphtheria antitoxin
17.2.4 Rabies immunoglobulin (human)
17.2.5 Antivenom sera
17.2.6 Others
17.3 Diagnostic agents

Active immunity

Active immunity may be induced by the administration of micro-organisms or their products which act as antigens to induce antibodies to confer a protective immune response in the host. Vaccination may consist of (a) a **live attenuated** form of a virus or bacteria, (b) **inactivated** preparations of the virus or bacteria, or (c) **extracts of** or **detoxified exotoxins**. Live attenuated vaccines usually confer immunity with a single dose which is of long duration. Inactivated vaccines may require a series of injections in the first instance to produce an adequate antibody response and in most cases, require reinforcing (booster) doses. The duration of immunity varies from months to many years. Extracts of or detoxified exotoxins require a primary series of injections followed by reinforcing doses.

Passive immunity

Passive immunity is conferred by injecting preparations made from the plasma of immune individuals with adequate levels of antibody to the disease for which protection is sought. Treatment has to be given soon after exposure to be effective. This immunity lasts only a few weeks but passive immunization can be repeated where necessary.

17.1 Vaccines (Active immunity)

17.1.1 Vaccines for universal immunization
17.1.2 Vaccines for specific groups of individuals
17.1.3 Other vaccines

Vaccines

All vaccines should comply with the WHO requirements for biological substances. Vaccines may consist of a live attenuated form of a virus (for example, rubella or measles) or bacteria (for example, BCG vaccine); an inactivated preparation of a virus (for example, influenza vaccine) or bacteria; an extract of or detoxified exotoxin produced by a micro-organism (for example, tetanus vaccine).

CONTRAINDICATIONS AND PRECAUTIONS

Recipients of any vaccine should be observed for an adverse reaction. Anaphylaxis though rare, can occur and epinephrine (adrenaline) must always be immediately available whenever immunization is given. If a serious adverse event (including anaphylaxis, collapse, shock, encephalitis, encephalopathy, or non-febrile convulsion) occurs following a dose of any vaccine, a subsequent dose should not be given. In the case of a severe reaction to Diphtheria, Pertussis, and Tetanus vaccine, the pertussis component should be omitted and the vaccination completed with Diphtheria and Tetanus vaccine.

Immunization should be postponed in acute illness which may limit the response to immunization, but minor infections without fever or systemic upset are not contraindications. A definite reaction to a preceding dose is a definite contraindication.

If alcohol or other disinfecting agent is used to wipe the injection site it must be allowed to evaporate, otherwise inactivation of a live vaccine may occur.

The intramuscular route must not be used in patients with bleeding disorders such as haemophilia or thrombocytopenia.

Some viral vaccines contain small quantities of antibacterials such as polymyxin B or neomycin; such vaccines may need to be withheld from individuals who are extremely sensitive to the antibacterial. Some vaccines are prepared using hens' eggs and a history of anaphylaxis to egg ingestion is a contraindication to the use of such vaccines; caution is required if such vaccines are used in persons with less severe hypersensitivity to egg.

When two live virus vaccines are required (and are not available as a combined preparation) they should be given *either* simultaneously at different sites using separate syringes *or* with an interval of at least 3 weeks. Live virus vaccines should normally be given *either at least 2–3 weeks before or at least 3 months after* the administration of immunoglobulin.

Live vaccines should not be routinely administered to pregnant women because of the possible harm to the fetus but where there is significant risk of exposure, the need for immunization may outweigh any possible risk to the fetus.

Live vaccines should not be given to anyone with malignant disease such as leukaemia or lymphomas or other tumours of the reticulo-endothelial system. Live vaccines should not be given to individuals with an impaired immune response caused by disease, radiotherapy or drug treatment (for example, high doses of corticosteroids).

However, the WHO recommends that immunocompromized individuals who are HIV-positive should, under certain circumstances, be given some live vaccines. *Asymptomatic* and *symptomatic* HIV-positive children and women of child-bearing age should receive diphtheria, pertussis, tetanus, hepatitis B and oral poliomyelitis vaccines (included in the Expanded Programme on Immunization (EPI)). Because of the risk of early and severe measles infection, infants should receive an extra dose of measles vaccine at 6 months of age with the EPI dose as soon after 9 months of age as possible. Individuals with *symptomatic* HIV infection must **not** be given either BCG or yellow fever vaccines. MMR vaccine should not be given to severely immunocompromized children with HIV infection. Individuals with *asymptomatic* HIV infection should only be given BCG or yellow fever vaccines where the prevalence of tuberculosis or yellow fever, respectively, is high. National policies on immunization of HIV-positive individuals may vary.

ADVERSE REACTIONS

Local reactions including inflammation and lymphangitis may occur. Sterile abscess may develop at the injection site; fever, headache, malaise starting a few hours after injection and lasting for 1–2 days may occur. Hypersensitivity reactions can occur including rarely, anaphylaxis.

Further information on vaccines

Handling: For vaccines and antisera products, refrigerated storage is usually required so that they are not denatured and there by rendered ineffective. Most vaccines must be stored at 2-8°C and not allowed to freeze. Vaccines should be protected from light. Opened multidose vials not fully used should be discarded within an hour if no preservative is present (most live virus vaccines) or within3

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hours or at the end of a session (when vaccines containing a preservative are used but also including oral poliomyelitis vaccine). The leaving of needles in the vials must be discouraged.

Vaccines that are best kept frozen (-15 to -25°C) include Oral Polio Vaccine (OPV), BCG and Measles lyophilised powder.

Administration Of Vaccines: The sites of I.M./I.V. vaccination are

i) Adult: The deltoid region of the arm
ii) Young children and babies: The anterolateral thigh.

Note: Intragluteal administration of vaccines is discouraged.

IMMUNIZATION SCHEDULE

The updated NPI (*National Programme on Immunization*) schedule should be obtained through the Primary Healthcare Department of the Federal Ministry of Health, Abuja.

NPI Immunization and Vitamin A Administration Schedule

Time of Aministration	Vaccine/Micronutrient
At Birth	BCG, OPV**0**, Hepatitis B**1**
6 weeks of Age	DPT**1**, OPV**1**, Hepatitis B**2**
10 weeks of Age	DPT**2**, OPV**2**
14 weeks of Age	DPT**3**, OPV**3**
9 months	Hepatitis B**3**, Measles, Yellow Fever and Vitamin A
18 months	DPT & OPV Boosters; (Measles: A reinforcing dose of Measles may also be given).

The Updated Private Immunization Schedule also includes:

Vaccine	Timeof Administration
Hib-Haemophillus influenza type b	At 6, 10 & 14 weeks of age with DTP and OPV.Booster at 18 months.
MMR-Measles, Mumps & Rubella	From 15 months upwards (usually at 18 months or 4 - 6 years).
Typhoid Fever Vaccine	From 2 years of age.
Pneumococcal Vaccine (For At-Risk groups e.g. sickle cell disease).	From 2 years of age.
CSM - Cerebrospinal Meningitis A+C (Supplemental Immunization)	From 2 years of age (in meningitis belt)

(SOURCE: Paediatric Association of Nigeria)

Immunization and Vitamin A Administration Schedule for Women of Child bearing Age

Time of Administration	Micronutrient/Vaccine	Protection Duration
Soon after delivery	Vitamin A to Mother	
At 6 weeks after delivery	Vitamin A to Mother	
First Contact	T.T.1	None
4 weeks after T.T.1	T.T.2	3 years
6 months after T.T.2 OR during subsequent pregnancy.	T.T.3	5 years
At least 1 year after T.T.3 OR during subsequent pregnancy.	T.T.4	10 years
At least 1 year after T.T.4 OR during subsequent pregnancy	T.T.5	For life

(SOURCE: NPI).

17.1.1 Vaccines for universal immunization

17.1.1.1 BCG vaccine (dried)
17.1.1.2 Diphtheria, pertussis and tetanus vaccines
17.1.1.3 Hepatitis B vaccine
17.1.1.4 Measles vaccines
17.1.1.5 Poliomyelitis vaccines

IMMUNIZATION SCHEDULE RECOMMENDED BY WHO

Scheme A
Recommended in countries where perinatal transmission of hepatitis B virus is frequent (for example, countries in south-east Asia)

Age	Vaccines
Birth	BCG; Poliomyelitis, oral (1st); Hepatitis B (1st)
6 weeks	Diphtheria, pertussis, tetanus (1st); Haemophilus influenzae (type b)[1] (1st); Poliomyelitis, oral (2nd); Hepatitis B (2nd)
10 weeks	Diphtheria, pertussis, tetanus (2nd); Haemophilus influenzae (type b)[1] (2nd); Poliomyelitis, oral (3rd)
14 weeks	Diphtheria, pertussis, tetanus (3rd); Haemophilus influenzae (type b)[1] (3rd); Poliomyelitis, oral (4th); Hepatitis B (3rd)
9 months	Yellow fever (in countries where yellow fever poses a risk); Measles

Scheme B
Recommended in countries where perinatal transmission of hepatitis B virus is less frequent (for example, countries in sub-Saharan Africa)

Schedule as Scheme A, but hepatitis B (1st) given at 6 weeks and hepatitis B (2nd) given at 10 weeks

[1]Haemophilus influenzae (type b) vaccine not included on WHO Model List

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The WHO Expanded Programme on Immunization (EPI) currently recommends that all countries immunize against diphtheria, hepatitis B, measles, poliomyelitis, pertussis, tetanus and that countries with a high incidence of tuberculosis infections should immunize against tuberculosis. Immunization against yellow fever is recommended in endemic countries. Routine vaccination against *Haemophilus influenzae* type b infection is also recommended in some countries. In geographical regions where the burden of disease is unclear, efforts should be made to evaluate the magnitude of the problem.

17.1.1.1 BCG vaccine (dried)

Where tuberculosis remains highly prevalent, routine immunization of infants within the first year of life with BCG vaccine, derived from bacillus Calmette-Guérin (an attenuated strain of *Mycobacterium bovis*), is highly cost-effective. This has been estimated, in several settings, to reduce the incidence of meningeal and miliary tuberculosis in early childhood by 50 to 90%. However, estimates of its effectiveness in older children have differed greatly from region to region and because efficacy against pulmonary tuberculosis is doubtful, the mainstay of the tuberculosis control programme is case-finding and treatment.

BCG VACCINE

BCG vaccine should comply with the recommendations published in the report of the WHO Expert Committee on Biological Standardization, WHO Technical Report Series, No. 745, 1987 and Amendment 1987, WHO Technical Report Series No. 771, 1988.

Indications: Active immunization against tuberculosis; see also section 9.1.4.

Contra-indications: See introductory notes; generalized oedema; antimycobacterial treatment.

Precautions: Pregnancy (Appendix 2); eczema, scabies—vaccine site must be lesion-free; **interactions**: Appendix 1.

Adverse effects: See introductory notes; lymphadenitis and keloid formation; osteitis and localized necrotic ulceration; rarely, disseminated BCG infection in immunodeficient patients; rarely anaphylaxis.

Advice to patients: A nodule may be palpable at the injection site for a few weeks.

Nursing considerations: •Administer by I.M. injection in the vastus lateralis muscle in infants. •Teach mother to give paracetamol syrup to reduce or prevent fever.

Dose: Note: National immunization schedules may vary.

Immunization against tuberculosis, by intradermal injection, INFANTS up to 3 months, 0.05 ml; ADULT and CHILD over 3 months, 0.1 ml.

Reconstitution And Administration: According to manufacturer's directions.

Note: To be used within 2 hours of reconstitution. Injection is strictly by the intradermal route, and any penetration into subcutaneous tissue should be avoided. The injection is given in the arm, in the deltoid region or on the external surface of the top of the thigh, and should cause a wheel with an "orange-peel" appearance of approximately 6-8mm in diameter. It is recommended not to protect the injection site.

POM **BCG vaccine** *(WMF 19.3.1.1)*
Injection (Powder for solution for injection), Live bacteria of a strain derived from the bacillus of Calmette and Guérin.

POM **BCG vaccine** *(EDL 20.2.1)*
Injection, dried powder for reconstitution in multidose amps of 1 ml, 5 ml.

POM **BCG Vaccine** *(Pasteur Merieux/May & Baker)*
Tuberculosis vaccine obtained from live bacteria of strain derived from the bacillus of Calmette and Guerin; lyophilised powder for intradermal use.
20 dose vial + 1 amp of 2 ml diluent.

17.1.1.2 Diphtheria, pertussis and tetanus vaccines

DIPHTHERIA

Diphtheria is a bacterial infection caused by *Corynebacterium diphtheriae*, transmitted from person to person through close physical and respiratory contact. Diphtheria vaccine is a formaldehyde-inactivated preparation of diphtheria toxin, adsorbed onto a mineral carrier to increase its antigenicity and reduce adverse reactions. Immunized individuals can be infected by toxin-producing strains of diphtheria but systemic manifestations of the disease do not occur.

When administered for primary

immunization in infants, diphtheria vaccine is almost always given together with pertussis and tetanus vaccines as part of a *three-component* preparation (DPT).

A *two-component* diphtheria vaccine with tetanus but without pertussis exists in two forms, DT and Td. Diphtheria-tetanus vaccine for children (DT) is used for primary immunization in infants who have contraindications to pertussis vaccine; it is also used in children under the age of 10 years for reinforcing immunization against diphtheria and tetanus in those countries which recommend it. Tetanus-diphtheria vaccine for adults, adolescents and children over 10 years of age (Td), which has a reduced amount of diphtheria toxoid to reduce the risk of hypersensitivity reactions, is used for primary immunization in persons over the age of 10 years; it is also used for reinforcing immunization in persons over the age of 10 years in those countries that recommend it.

PERTUSSIS

Pertussis (whooping cough) is a bacterial respiratory infection caused by *Bordetella pertussis*. Many of the symptoms are thought to be caused by toxins released by *B. pertussis*. Whole cell vaccine composed of whole pertussis bacteria killed by chemicals or heat is effective in preventing serious illness. It causes frequent local reactions and fever and rarely it may be associated with neurological reactions. Neurological complications after pertussis infection are considerably more common than after the vaccine. It is combined with diphtheria-tetanus vaccine for primary immunization unless immunization against pertussis is contraindicated. Single component pertussis vaccines are available in some countries for use when the pertussis component has been omitted from all or part of the primary immunization schedule. An acellular form of the vaccine is also available.

In some countries it is recommended that children with a personal or family history of febrile convulsions or a family history of idiopathic epilepsy should be immunized. It is also recommended that children with well-controlled epilepsy are immunized. Advice on prevention of fever should be given at the time of immunization. In children with evolving neurological problems, immunization with pertussis should be deferred until the condition is stable; in such children diphtheria and tetanus vaccine should be offered for primary immunization, and there may be an opportunity at a later date to complete immunization with a single-component pertussis vaccine. Where there is doubt advice should be sought from a paediatrician.

TETANUS

Tetanus is caused by the action of a neurotoxin of *Clostridium tetani* in necrosed tissues such as occur in dirty wounds. Tetanus vaccine is available as a single component vaccine for primary immunization in adults who have not received childhood immunization against tetanus and for reinforcing immunization. The vaccine is also used in the prevention of neonatal tetanus and in the management of clean wounds and tetanus-prone wounds. Some countries recommend a maximum of 5 doses of tetanus vaccine in a life-time; for the fully immunized patient reinforcing doses at the time of a tetanus-prone injury should only be required if more than 10 years have elapsed since the last dose.

Neonatal tetanus due to infection of the baby's umbilical stump during unclean delivery is the cause of many deaths of newborn infants. Control of neonatal tetanus may be achieved by ensuring adequate hygiene during delivery and by ensuring protective immunity of mothers in late pregnancy. Tetanus vaccine is highly effective and the efficacy of two doses during pregnancy in preventing neonatal tetanus ranges from 80–100%. Women of child-bearing age may be immunized by a course of 5 doses (3 primary and 2 reinforcing) of tetanus vaccine.

Wounds are considered to be tetanus-prone if they are sustained *either* more than 6 hours before surgical treatment of the wound *or* at any interval after injury and show one or more of the following: a puncture-type wound, a significant degree of devitalized tissue, clinical evidence of sepsis, contamination with soil/manure likely to contain tetanus organisms. All wounds should receive thorough surgical toilet. Antibacterial prophylaxis may also be required for tetanus-prone wounds.

- For *clean wounds*, fully immunized individuals (those who have received a total of 5 doses of tetanus vaccine at

appropriate intervals) and those whose primary immunization is complete (with boosters up to date) do not require tetanus vaccine; individuals whose primary immunization is incomplete or whose boosters are not up to date require a reinforcing dose of tetanus vaccine (followed by further doses as required to complete the schedule); non-immunized individuals (or whose immunization status is not known) should be given a dose of the vaccine immediately (followed by completion of the full course of the vaccine if records confirm the need).

- For *tetanus-prone wounds*, management is as for clean wounds with the addition of a dose of antitetanus immunoglobulin (section 17.2.2) given at a different site; in fully immunized individuals and those whose primary immunization is complete (see above) the immunoglobulin is needed only if the risk of infection is especially high (for example, contamination with manure). Antibacterial prophylaxis (with benzylpenicillin, or amoxicillin with clavulanic acid, or metronidazole) may also be required for tetanus-prone wounds.

Diphtheria, pertussis, and tetanus vaccine (DPT)

DPT VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 800, 1990.

Indications: Active immunization against diphtheria, tetanus and pertussis.

Contra-indications: See introductory notes and notes above.

Precautions: See introductory notes and notes above; in cases of severe reaction, the pertussis component should be omitted and the primary course of immunization completed with diphtheria and tetanus vaccine.

Adverse effects: See introductory notes; tetanus component rarely associated with peripheral neuropathy; pertussis component rarely associated with convulsions and encephalopathy.

Advice to patients: Notify physician of persistent pain on urination or blood in urine.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Primary immunization of children against diphtheria, Pertussis and tetanus, by intramuscular injection , INFANT 0.5 ml at 6, 10 and 14 weeks (see WHO schedule, section 17.1.1).

POM **DPT vaccine** *(WMF 19.3.1.2)*
Injection, Diphtheria and tetanus toxoids and pertussis vaccine adsorbed onto a mineral carrier.

POM **DPT vaccine** *(EDL 20.2.1)*
Injection, in 5 ml, 10 ml vials.

POM **DPT Vaccine** *(Aventis Pasteur /May & Baker)*
A mixture of diphtheria formol toxoid, tetanus formol toxoid, and pertussis vaccine adsorbed onto aluminium hydroxide.
1 dose x 1 amp. (0.5 ml)
10 doses x 1 vial (5 ml).

Dose: By s.c. or i.m. injection, primary vaccination, 3 injections of 0.5 ml at intervals of 1 month; Boosters, one injection of 0.5 ml a year after the last primary injection, then 1 injection 5 years later.

DIPHTHERIA AND TETANUS VACCINE (DT) (for children under 10 years)

DT VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 800, 1990.

Indications: Active immunization of children under 10 years against diphtheria and tetanus (see notes above).

Contra-indications: See introductory notes; adults and children over 10 years of age (see notes above).

Precautions: See introductory notes.

Adverse effects: See introductory notes; tetanus component rarely associated with peripheral neuropathy.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Primary immunization of children against diphtheria and tetanus when pertussis immunization is contraindicated, by intramuscular injection, CHILD under 10 years 3 doses each of 0.5 ml with an interval of not less than 4 weeks between each dose (see also WHO schedule, section 17.1.1).

Reinforcing immunization of children against diphtheria and tetanus, by intramuscular injection, CHILD under 10 years of age, 0.5 ml at least 3 years after completion of primary course of DPT or DT immunization.

POM **DT vaccine** *(WMF 19.3.1.2)*
Injection, Diphtheria and tetanus toxoids

adsorbed onto a mineral carrier.

Tetanus and diphtheria vaccine (Td) (for adults, adolescents and children over 10 years)

TD VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 800, 1990.

Indications: Active immunization of adults and children over 10 years of age against tetanus and diphtheria (see notes above).

Contra-indications: See introductory notes; children under 10 years (see notes above).

Precautions: See introductory notes.

Adverse effects: See introductory notes; tetanus component rarely associated with peripheral neuropathy.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Primary immunization of unimmunized adults and children over 10 years of age against tetanus and diphtheria, by intramuscular injection, ADULT and CHILD over 10 years of age, 3 doses each of 0.5 ml with an interval of not less than 4 weeks between each dose.

Reinforcing immunization of adults and children over 10 years of age against tetanus and diphtheria, by intramuscular injection, ADULT and CHILD over 10 years of age, 0.5 ml 10 years after completing primary course.

POM **Td vaccine** *(WMF 19.3.1.2)*

Injection, Diphtheria (low dose) and tetanus toxoid adsorbed onto a mineral carrier.

TETANUS VACCINE

Synonym: Tetanus Toxoid

TETANUS VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 800, 1990.

Indications: Active immunization against tetanus and neonatal tetanus; wound management (tetanus-prone wounds and clean wounds).

Contra-indications: See introductory notes and notes above.

Precautions: See introductory notes and notes above.

ANTITETANUS IMMUNOGLOBULIN: IF SCHEDULE REQUIRES TETANUS VACCINE AND ANTITETANUS IMMUNOGLOBULIN TO BE ADMINISTERED AT THE SAME TIME, THEY SHOULD BE ADMINISTERED USING SEPARATE SYRINGES AND SEPARATE SITES.

Adverse effects: see introductory notes; tetanus component rarely associated with peripheral neuropathy.

Nursing considerations: •Obtain history of allergies and reactions to immunization; inject IM in the vastus lateralis (midthigh laterally) or deltiod; not for IV use.

•Avoid use of hot or cold compresses; may increase severity of local reaction.

•May cause mild fever or soreness, swelling, and redness at the site of injection; these local reactions last 1-2 days.

•Used for prevention and not treatment of tetanus infections.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY; SOME COUNTRIES RECOMMEND A MAXIMUM OF 5 DOSES OF TETANUS VACCINE IN A LIFE-TIME.

Primary immunization of unimmunized adults against tetanus, by intramuscular injection, ADULT 3 doses each of 0.5 ml with an interval of 4 weeks between each dose.

Reinforcing immunization of adults against tetanus, by intramuscular injection, ADULT 2 doses each of 0.5 ml, the first 10 years after completion of primary course, and the second dose 10 years later.

Immunization of women of child-bearing age against tetanus, by intramuscular injection, woman of child-bearing age, 3 primary doses each of 0.5 ml with an interval of not less than 4 weeks between the first and second doses and 6 months between the second and third doses; 2 reinforcing doses each of 0.5 ml, the first 1 year after completion of the primary course and the second dose 1 year later; unimmunized pregnant woman 2 doses of 0.5 ml with an interval of 4 weeks between each dose (second dose at least 2 weeks before delivery) and 1 dose during each of subsequent 3 pregnancies (maximum 5 doses)

Management of tetanus-prone wounds and clean wounds, by intramuscular or deep subcutaneous injection, ADULT 0.5 ml, the dose schedule being dependent upon the immune status of the patient and the level of contamination of the wound (see also notes above and under Antitetanus Immunoglobulin, section

17.2.2).

POM **Tetanus vaccine** *(WMF 19.3.1.2)*
Injection, Tetanus toxoid adsorbed onto a mineral carrier.

POM **Tetanus Vaccine** *(EDL 20.2.1)*
Injection, Formol toxoid in 0.5 ml amp, 5 ml vial.

POM **TETAVAX®** *(Aventis Pasteur/May & Baker)*
Adsorbed tetanus vaccine prepared from tetanus formol toxoid.
1 dose x 0.5 ml syringe
1 dose x 0.5 ml amp. x 20 amps.
10 doses x 5 ml vial. x 10 vials.
20 doses x 10 ml vial x 10 vials.
Dose: By S.C. or I.M. injection, primary vaccination, 2-3 injections of 0.5 ml at intervals of 1-6 months.
Booster vaccination: 1 injection a year after the primary injection and then, every 10 years.
Note: The absorbed vaccine must not be frozen.

17.1.1.3 Hepatitis B vaccine

Hepatitis B is caused by hepatitis B virus. It is transmitted in blood and blood products, by sexual contact and by contact with infectious body fluids. Persons at increased risk of infection because of their life-style, occupation or other factors include parenteral drug abusers, individuals who change sexual partners frequently, health care workers who are at risk of injury from blood-stained sharp instruments and haemophiliacs. Also at risk are babies born to mothers who are HbsAg-positive (hepatitis B virus surface antigen positive) and individuals who might acquire the infection as the result of medical or dental procedures in countries of high prevalence. The main public health consequences are chronic liver disease and liver cancer rather than acute infection. Routine immunization is recommended and has been implemented in some countries. Plasma-derived hepatitis B vaccine is highly efficacious. Over 90% of susceptible children develop a protective antibody response. A recombinant DNA vaccine is also available.

HEPATITIS B VACCINE

HEPATITIS B VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 858, 1995.
Indications: Active immunization against hepatitis B.
Contra-indications: See introductory notes.
Precautions: See introductory notes.
Adverse effects: See introductory notes; abdominal pain and gastrointestinal disturbances; muscle and joint pain, dizziness and sleep disturbance; occasionally cardiovascular effects.
Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization of children against hepatitis B, by intramuscular injection, INFANT 0.5 ml either Scheme A at birth and at 6 and 14 weeks of age, or Scheme B at 6, 10 and 14 weeks of age (see WHO schedule, section 17.1.1).
Immunization of unimmunized high risk persons against hepatitis B, by intramuscular injection, ADULT and CHILD over 15 years of age, 3 doses of 1 ml, with an interval of 1 month between the first and second dose and 5 months between the second and third doses; CHILD under 15 years, 0.5 ml.

NOTE: DIFFERENT PRODUCTS MAY CONTAIN DIFFERENT CONCENTRATIONS OF ANTIGEN. CONSULT MANUFACTURER'S LITERATURE.
ADMINISTRATION: THE VACCINE SHOULD BE GIVEN IN THE DELTOID REGION IN ADULTS AND OLDER CHILDREN; ANTEROLATERAL THIGH IS THE PREFERRED SITE IN INFANTS AND YOUNG CHILDREN; IT SHOULD NOT BE INJECTED INTO THE BUTTOCK (VACCINE EFFICACY REDUCED); SUBCUTANEOUS ROUTE USED FOR PATIENTS WITH THROMBOCYTOPENIA OR BLEEDING DISORDERS.

POM **Hepatitis B vaccine** *(WMF 19.3.1.3)*
Injection, Inactivated hepatitis B surface antigen adsorbed onto a mineral carrier.

POM **Hepatitis B vaccine** *(EDL 20.2.2)*
Injection, 0.2 mg per ml in 0.5 ml, 1 ml vials.

POM **ENGERIX-B®** *(GSK)*
Second generation Hepatitis B vaccine containing Hepatitis-B surface antigen (HBsAg) 20 mcg per ml adsorbed on 0.5 mg aluminium hydroxide; Suspension in vial. Substrate: Yeast cells.
Pack - 1 ml vial.
Dose: By i.m. injection, Adult and child over 10 years, 1 ml (20 mcg); repeated 1 month and 6 months later (0,1,6

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schedule). For more rapid immunization (e.g. for travellers), 1 ml (as above); repeated 1 month and 2 months later (0,1,2 schedule), with a booster at 12 month.

Booster: using 0,1,6 schedule, 1 ml every 5 years and for 0,1,2 schedule, 1 ml every 8 years.

Neonate and child under 10 years, 0.5 ml given as above.

Note: The adsorbed vaccine should never be frozen. As with all vaccinations, a solution of 1:1000 adrenaline should be available for injection should an anaphylactic reaction occur. Prior to vaccination, the vaccine should be well shaken and be visually inspected for any colour variations or particulate matter. Once shaken, the vaccine is slightly opaque.

POM **EUVAX B®** *(Aventis Pasteur /May & Baker)*

Genetically derived 2nd generation Hepatitis B Vaccine containing Hepatitis B surface antigen (HBsAg) 20 mcg per ml adsorbed onto Aluminium hydroxide; susp. in 1 ml vial.

Dose: See under ENGERIX B

POM **GENHEVAC-B®** *(Aventis Pasteur /May & Baker)*

Genetically derived 3rd generation Hepatitis B Vaccine containing Hepatitis-B surface (HBs) antigen 20 mcg per ml of suspension adsorbed onto aluminium hydroxide; susp. in single dose syringe. Substrate: Mammalian CHO cells (Chinese Hamister Ovary cells).

Pack - 0.5 ml single dose syringe.

Dose: By i.m. injection in the deltoid (adult) or antero-lateral thigh (infant), 0.5 ml (same dose for all ages) as follows:

AGE/USE	PRIMARY VACCINATION	BOOSTER	SCHEDULE
For rapid immunization			
All ages/high risk groups and travellers	3 doses at one month interval	At 12th month then every 5 years	0,1,2...12
Reduced Schedule			
Subject over 10 years of age	2 doses at one month interval, and 3rd dose six months after the first	Every 5 years	0,1,6.
Subject from Birth to 10 years	2 doses at one month interval, and 3rd dose six months after the first	Every 5-10 years	0,1,6.

With Hepatitis A Vaccine

POM **TWINRIX®** *(GSK)*

Hepatitis A and B.

With DTP Vaccine

POM **TRITANRIX®** *(GSK)*

Hepatitis B and DTP; for 6 weeks primo-vaccination only.

17.1.1.4 Measles vaccines

Measles is an acute viral infection transmitted by close respiratory contact. In some countries routine immunization of children against measles is given as one dose of a single component vaccine; in other areas, a two-dose schedule has been found to be more applicable. In developing countries, clinical efficacy is usually greater than 85%. Convulsions and encephalitis are rare complications. Measles vaccine is administered in many countries as part of a combined preparation with mumps vaccine and rubella vaccine (MMR vaccine); a single-dose primary immunization is followed by a reinforcing dose 2–5 years later.

Single-component vaccines or MMR may be used in the control of outbreaks of measles and should be offered to susceptible children within 3 days of exposure. It is important to note that MMR vaccine is **not** suitable for prophylaxis following exposure to mumps or rubella since the antibody response to the mumps and rubella components is too slow for effective prophylaxis.

MEASLES VACCINE

MEASLES VACCINES SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORTS OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 840, 1994, AND NOTE, WHO TECHNICAL REPORT SERIES, NO. 848, 1994

Indications: Active immunization against measles.

Contra-indications: See introductory notes; hypersensitivity to any antibiotic present in vaccine—consult manufacturer's literature; hypersensitivity to egg or gelatin.

Precautions: See introductory notes; pregnancy (Appendix 2); **interactions**: Appendix 1.

Adverse effects: See introductory notes; rashes sometimes accompanied by convulsions; rarely, encephalitis and thrombocytopenia.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization of children against measles, by intramuscular or deep subcutaneous injection, INFANT at 9

months of age, 0.5 ml (see WHO schedule, section 17.1.1).
Prophylaxis in susceptible children after exposure to measles, by intramuscular or deep subcutaneous injection within 72 hours of contact, CHILD over 9 months of age 0.5 ml.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Measles vaccine** *(WMF 19.3.1.4)*
Injection (Powder for solution for injection), Live, attenuated measles virus.

POM **Measles Vaccine** *(EDL 20.2.1)*
Injection, in 0.5 ml amp.

POM **RIMEVAX®** *(GSK)*
Measles vaccine, Live, Schwartz strain, containing not less than 1000 TCID 50 and not more than 25 mcg neomycin per 0.5ml dose; pellet in single dose vial.
10 dose x 1 vial

POM **ROUVAX®** *(Aventis Pasteur/May & Baker)*
Measles vaccine from hyperattenuated virus of Schwarz strain; freeze-dried powder with Isotonic sodium chloride solution.
1 vial x 1 dose + Syringe of diluent.
1 vial x 10 doses.

MEASLES, MUMPS, and RUBELLA (MMR) VACCINE

MMR VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORTS OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 840, 1994 AND NOTE, WHO TECHNICAL REPORT SERIES, NO. 848, 1994.

Indications: Active immunization against measles, mumps and rubella.

Contra-indications: See introductory notes; pregnancy (Appendix 2); hypersensitivity to any antibiotic present in vaccine—consult manufacturer's literature; hypersensitivity to egg.

Precautions: See introductory notes; history of convulsions—advice on controlling fever (see below); **interactions**: Appendix 1.

POST-IMMUNIZATION FEVER: MALAISE, FEVER OR RASH MAY OCCUR FOLLOWING THE FIRST DOSE OF MMR VACCINE, MOST COMMONLY ABOUT 1 WEEK AFTER IMMUNIZATION AND LASTING 2–3 DAYS. CARERS SHOULD BE ADVISED THAT THE CHILD CAN BE GIVEN PARACETAMOL TO REDUCE THE FEVER FOLLOWED IF NECESSARY BY A SECOND DOSE 4–6 HOURS LATER. IF FEVER PERSISTS AFTER THE SECOND DOSE OF PARACETAMOL, MEDICAL ADVICE SHOULD BE SOUGHT.

AFTER A SECOND DOSE OF MMR VACCINE, ADVERSE REACTIONS ARE CONSIDERABLY LESS COMMON THAN AFTER THE FIRST DOSE.

Adverse effects: See introductory notes; malaise, fever, rash most common after first dose (see above); occasionally parotid swelling; rarely meningoencephalitis, idiopathic thrombocytopenic purpura.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Primary immunization of children against measles, mumps and rubella, by intramuscular or deep subcutaneous injection, CHILD 12–15 months, 0.5 ml.
Reinforcing immunization of children against measles, mumps and rubella, by intramuscular or deep subcutaneous injection, CHILD 0.5 ml 2–5 years after primary dose.
Prophylaxis in susceptible children after exposure to measles (see notes above), by intramuscular or deep subcutaneous injection within 72 hours of contact, CHILD 12 months of age and older, 0.5 ml.

POM **MMR vaccine** *(WMF 19.3.1.4)*
Injection, Live, attenuated measles virus, mumps virus and rubella virus.

POM **TRIMOVAX®** *(Aventis Pasteur /May & Baker)*
Injection, Live measles virus (Schwarz strain) 1000 TCID, live mumps virus (Urabe AM-9 strain) 5000 TCID, live rubella virus (Wistar RA 27/3M strain) 1000 TCID; in a powder with 0.5 ml water for injection as diluent. After reconstitution, the vaccine is clear, with a colour varying from yellow to violet-red.
1 single-dose vial + 1 syringe of 0.5 ml diluent.

Dose: By s.c. or i.m. injection, a single injection of 0.5 ml of reconstituted vaccine. Infants below 12 months, 2 injections at interval of 6 months.

Note: Any reconstituted vaccine must be used immediately. However, reconstituted vaccine can be stored at +2°C to 8°C protected from light, for the period not exceeding 8 hours.

17.1.1.5 Poliomyelitis vaccines

Poliomyelitis is an acute viral infection spread by the faecal-oral route which can cause paralysis of varying degree. There are two types of vaccine against poliomyelitis: oral and injectable. Oral

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poliomyelitis vaccine (OPV) is composed of three types of live attenuated poliomyelitis viruses. The efficacy of OPV in preventing paralytic polio in developing countries ranges from 72% to 98% and is the vaccine of choice in eradication of the disease. Oral poliomyelitis vaccine may need to be repeated in patients with diarrhoea or vomiting. Those infected wth HIV should receive poliomyelitis vaccine according to the standard schedule but the vaccine is **contraindicated** in those with primary immune deficiency or those who are immunosuppressed. The need for strict personal hygiene must be stressed as the vaccine virus is excreted in the faeces. The contacts of a recently vaccinated baby should be advised particularly of the need to wash their hands after changing the baby's nappies. After primary immunization reinforcing doses may be given. Inactivated polio vaccine (IPV) is injectable and composed of inactivated strains of three types of poliomyelitis virus. It should be used for individuals who are immunosuppressed or for their household contacts.

POLIOMYELITIS VACCINE (OPV) (live attenuated)

OPV SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 800, 1990.

Indications: Active immunization against poliomyelitis.

Contra-indications: See introductory notes; primary immunodeficiency or immunosuppression; not to be taken with food which contains a preservative; hypersensitivity to any antibiotic present in vaccine—consult manufacturer's literature.

Precautions: See introductory notes; pregnancy (Appendix 2); **interactions**: Appendix 1.

Adverse effects: Rarely, vaccine-associated poliomyelitis in recipients of vaccine and contacts of recipients.

Nursing considerations: •Administer only orally; not for parenteral use.

•Do not give within one month of other live virus vaccines.

•Evaluate for history of allergies and reactions to vaccination.

•Monitor patient for anaphylaxis which include inability to breathe and bronchospasm.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Primary immunization of children against poliomyelitis, by mouth, CHILD 3 drops at birth and at 6, 10 and at 14 weeks of age (see WHO schedule, section 17.1.1).

Reinforcing immunization of children against poliomyelitis, by mouth, CHILD 3 drops at least 3 years after completion of primary course and a further 3 drops at 15–19 years of age.

Primary immunization of unimmunized adult against poliomyelitis, by mouth, ADULT 3 doses each of 3 drops with an interval of at least 4 weeks between each dose.

Reinforcing immunization of adults against poliomyelitis, by mouth, ADULT 3 drops 10 years after completion of primary course.

NOTE: SOME COUNTRIES CONSIDER REINFORCING IMMUNIZATION UNNECESSARY IN ADULTS UNLESS TRAVELLING TO ENDEMIC AREAS.

POM **Poliomyelitis vaccine (OPV)** *(19.3.1.5)*
Oral suspension, Live, attenuated poliomyelitis virus, types 1, 2, and 3.

POM **Poliomyelitis Vaccine** *(EDL 20.2.1)*
Oral suspension, live attenuated.

POM **Oral Polio Vaccine B.P.** *(GSK)*
Suspension of 3 highly attenuated live sabin's type poliomyelitis viruses; in vials of 20 doses.

POM **SABIN ORAL POLIO** *(Aventis Pasteur/ May & Baker)*
Live oral trivalent poliomyelitis vaccine prepared on primary monkey kidney cells.
1 dose x 1 vial
10 doses x 1 vial.
20 doses x 1 vial

Dose: By mouth, *primary vaccination*, entire content of a monodose vial or 2 drops from a multidose vial 4-6 weekly; a total of 4 oral doses.

Booster vaccination: 1 oral dose a year after the 3rd dose and then, every 5 years.

POLIOMYELITIS VACCINE (IPV) (inactivated)

IPV SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORTS OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 673, 1982 AND ADDENDUM 1985, WHO TECHNICAL REPORT SERIES, NO. 745, 1987.

Indications: Active immunization against poliomyelitis in patients for whom live vaccine is contraindicated (see notes above) or in persons in countries not wishing to use live vaccine.
Contra-indications: See introductory notes.
Precautions: See introductory notes.
Adverse effects: See introductory notes.
Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Primary immunization of children against poliomyelitis, by subcutaneous injection, child 0.5 ml at 6, 10 and 14 weeks of age
Reinforcing immunization of children against poliomyelitis, by subcutaneous (or intramuscular) injection, child 0.5 ml at least 3 years after completion of the primary course and a further 0.5 ml at 15–19 years of age.
Primary immunization of unimmunized adults against poliomyelitis, by subcutaneous injection , ADULT 3 doses each of 0.5 ml with intervals of at least 4 weeks between each dose.
Reinforcing immunization of adults against poliomyelitis, by subcutaneous injection, ADULT 0.5 ml 10 years after completion of primary course.

NOTE: SOME COUNTRIES CONSIDER REINFORCING IMMUNIZATION UNNECESSARY IN ADULTS UNLESS TRAVELLING TO ENDEMIC AREAS.

POM **Poliomyelitis vaccine (IPV)** *(WMF 19.3.1.5)*
Injection, Inactivated poliomyelitis virus, types 1, 2, and 3.

17.1.2 Vaccines for specific groups of individuals

17.1.2.1 Influenza vaccine
17.1.2.2 Meningococcal polysaccharide vaccine
17.1.2.3 Mumps vaccine
17.1.2.4 Rabies vaccine (inactivated)
17.1.2.5 Rubella vaccine
17.1.2.6 Typhoid vaccine
17.1.2.7 Yellow fever vaccine

There are several other vaccines available which are used in different countries but are not yet recommended for routine use throughout the world.

Allergic patients require specific immunotherapy.

17.1.2.1 Influenza vaccine

While most viruses are antigenically stable, the influenza viruses A and B (especially A) are constantly changing their antigenic structure as indicated by changes in the haemagglutinins (H) and neuraminidases (N) on the surface of the viruses. It is essential that **influenza vaccines** in use contain the H and N components of the prevalent strain or strains. The changes are monitored and recommendations are made each year regarding the strains to be included in influenza vaccines for the following season. The recommended vaccine strains are grown on chick embryos and the vaccine is therefore contraindicated in individuals hypersensitive to egg. There are three forms of influenza vaccine; whole virion vaccine (not recommended for use in children because of the increased risk of severe febrile reactions), split-virion vaccine and surface-antigen vaccine.

The vaccines will not control epidemics and they are recommended only for those at high risk. Annual immunization is recommended in the elderly and those of any age with diabetes mellitus, chronic heart disease, chronic renal failure, chronic respiratory disease including asthma, or immunosuppression due to disease or drug treatment.

HAEMOPHILUS INFLUENZAE TYPE B VACCINE

Indications: Prevention of *Haemophilus influenzae* type b (Hib) invasive infections in infants from 6 weeks of age, as children under the age of 13 months are at high risk of Hib infections. This risk falls after the age of 5 years. However, it may be given to those over the age of 5 years who are at increased risk of invasive Hib infections like sicklers or asplenic children or adults.
Contra-indications: Hypersensitivity to any of the vaccine ingredients, particularly the tetanus protein. Fever or acute infection.
Precautions: If administered concurrently with measles, mumps and rubella (MMR) vaccine, the two vaccinations should be made at two separate sites. Shelf life is 36 months and reconstituted vaccine must be used immediately. Recommended storage

temperature is +2 to +8 °C; not to be frozen.

Dose: Child (6 weeks to 6 months), 3 injections at intervals of one month; followed by a booster injection at 18 months; 6 to 12 months, 2 injections 1 month apart; followed by a booster injection at 18 months of age; 1 to 5 years, one single injection.

The immunization dose is 0.5 ml.

Method of Administration: Reconstitute the freeze-dried vaccine using the diluent provided. Shake until the dissolution is complete. The preferred route of administration is I.M., although it may also be given by deep subcutaneous injection. Make sure the needle does not penetrate a blood vessel. Do not inject intravascularly. Infants up to 2 years of age: in the anterolateral surface of the thigh (middle third). Children from 2 years of age: in the deltoid region.

POM **ACT-HIB®** *(Aventis Pasteur/May & Baker)*

Haemophilus influenzae type b polysaccharide conjugated to tetanus protein 10 mcg; freeze-dried with 0.4% sodium chloride solution as diluent (0.5 ml).

Single dose vial + syringe of diluent

Single dose vial + ampoule of diluent

Multidose vial + vial of diluent.

Note: Can be combined routinely in the same syringe with "Pasteur" DTP.

With D.T.P. Vaccine

POM **TETRAct-HIB®** *(Aventis Pasteur/May & Baker)*

Haemophilus influenzae type b polysaccharide conjugated to tetanus protein 10mcg, injectable suspension of adsorbed D.T.P.; freeze-dried with 0.9% sodium chloride solution as diluent. Vial of one dose or 10 doses of freeze-dried Haemophilus type b conjugate vaccine and one prefilled syringe of D.T.P.

Indications: Combined prevention, from 2 months of age of invasive infections caused by *Haemophilus influenzae* type b, diphtheria, tetanus and pertussis.

Dose: Preferably by I.M. injection, Child (from 2 months), *Primary immunization*, 3 injections of 0.5 ml at 1-2 months interval.

Booster: 1 injection one year after the primary immunization.

Method of Administration: Reconstitute the freeze-dried vaccine with the D.T.P. suspension. Shake before use to obtain a homogenous suspension; the suspension is usually cloudy, whitish in appearance. Give by I.M. or S.C. in the antero-lateral region of the thigh (middle third). To minimise the potential adverse reactions, the I.M. route is preferred since the D.T.P. vaccine is adsorbed.

With DPT Vaccine and Poliomyelitis Vaccine

POM **PENTAct-HIB®** *(Aventis Pasteur /May & Baker)*

Haemophilus influenzae type b polysaccharide conjugated to tetanus protein 10 mcg, injectable suspension of adsorbed D.T.P. and inactivated poliomyelitis vaccine; freeze-dried with water for injection as diluent.

Single-dose vial of Haemophilus type b conjugate vaccine and a pre-filled by-pass syringe containing adsorbed D.T.P. and inactivated poliomyelitis vaccine.

Indications: Combined prevention of invasive disease caused by *Haemophilus influenzae* type b, diphtheria, tetanus, pertussis and poliomyelitis.

Dose: Preferably by I.M. injection, child (from 2 months), *Primary immunization*, 3 injections of 0.5 ml at 1-2 months interval.

Booster: 1 injection one year after the primary immunization.

Method of Administration: Reconstitute the freeze-dried product of Haemophilus type b conjugate vaccine with the adsorbed D.T.P. and inactivated poliomyelitis vaccine. Shake to obtain a homogenous suspension; the suspension is usually whitish in appearance. Give by I.M. or S.C. injection, but the I.M. route is usually preferred since the D.T.P. and inactivated poliomyelitis vaccine are adsorbed.

INFLUENZA VACCINE

INFLUENZA VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 814, 1991.

Indications: Active immunization against influenza in individuals at risk.

Contra-indications: See introductory notes; whole virion vaccine not recommended in children; hypersensitivity to any antibiotic present in vaccine—consult manufacturer's literature; hypersensitivity to egg

Precautions: See introductory notes; **interactions**: Appendix 1.

Adverse effects: See introductory notes; occasionally, severe febrile reactions—particularly after whole virion vaccine in children.

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Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization against influenza (annually for high-risk persons), by intramuscular or deep subcutaneous injection, ADULT and CHILD over 13 years, 0.5 ml as a single dose; CHILD 6–35 months, 0.25 ml repeated after at least 4 weeks if child not previously infected or vaccinated; CHILD 3–12 years of age, 0.5 ml, with a second dose after at least 4 weeks if child not previously infected or vaccinated.

POM **Influenza vaccine** *(WMF 19.3.2.1)*
Injection, Inactivated influenza virus, types A and B.

17.1.2.2 Meningococcal polysaccharide vaccine

Meningococcal polysaccharide vaccine is effective against serogroups A and C of *Neisseria meningitidis* but infants respond less well than adults. Immunity to some meningococcal vaccines may be insufficient to confer adequate protection against infection in infants under about 2 years of age and the minimum age recommended by manufacturers varies from 2 months to 2 years. It is indicated for persons at risk of serogroups A and C meningococcal disease in epidemics (where it must be administered early in the course of the epidemic) or endemic areas and as an adjunct to chemoprophylaxis in close contacts of persons with the disease. It is indicated for visits of longer than 1 month to areas of the world where risk of infection is high.

MENINGOCOCCAL A & C VACCINE

MENINGOCOCCAL POLYSACCHARIDE VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORTS OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 594, 1976 AND ADDENDUM 1980 INCORPORATING ADDENDUM 1976 AND 1977, WHO TECHNICAL REPORT SERIES, NO. 658, 1981.

Indications: Active immunization against meningitis and septicaemia caused by *N. meningitidis* group A and C serotypes.

Contra-indications: See introductory notes.

Precautions: See introductory notes.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization against infection by N. meningitidis groups A and C, by deep subcutaneous or by intramuscular injection, ADULT and CHILD (see notes above and manufacturer's literature), 0.5 ml as a single dose.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

Adverse effects: See introductory notes.

POM **Meningococcal A & C vaccine** *(WMF 19.3.2.2)*
Injection (Powder for solution for injection), Inactivated polysaccharide antigens of *Neisseria meningitidis* (meningococcus) groups A and C.

POM **Meningococcal vaccine** *(EDL 20.2.2)*
Injection, 0.5 mg, 2.5 mg; powder for reconstitution in multidose vials.

POM **MENCEVAX AC®** *(GSK)*
Meningitis A and C vaccine containing 50 mcg of Group A and 500 mcg of Group C polysaccharide antigens of Neisseria meningitidis; powder in 50 dose vial plus diluent (25 ml).
1 x 0.5 ml vial.

POM **MENGIVAC (A+C)®** *(Aventis Pasteur /May & Baker)*
Meningococcal polysaccharide Vaccine containing purified and lyophylised *Neisseria meningitidis* (meningococcus) groups A and C; pale powder which on reconstitution forms clear or slightly opalescent solution
1 vial x 1 dose (plus 1 syringe of 0.5 ml diluent)
25 vials x 50 dose (plus 25 vials of 25 ml diluent).

17.1.2.3 Mumps vaccine

Mumps vaccine is used for active immunization against mumps. In some countries the single antigen vaccine is no longer available and a combined measles, mumps and rubella vaccine (MMR vaccine; section 17.1.1.4) is used for primary immunization.

MUMPS VACCINE

MUMPS VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORTS OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 840, 1994 AND NO. 848, 1994.

Indications: Active immunization against mumps.

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Contra-indications: See introductory notes; pregnancy (Appendix 2); hypersensitivity to any antibacterial present in the vaccine—consult manufacturer's literature; hypersensitivity to egg.

Precautions: See introductory notes; avoid in children under 1 year.

Adverse effects: Parotid swelling; rarely, unilateral nerve deafness, meningitis, encephalitis.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization of children against mumps, by subcutaneous injection, child over 1 year 0.5 ml.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Mumps vaccine** *(WMF 19.3.2.3)*
Injection (Powder for solution for injection), Live attenuated strain of mumps virus.

17.1.2.4 Rabies vaccine (inactivated)

Rabies vaccine is used as part of the *post-exposure treatment* to prevent rabies in patients who have been bitten by rabid animals or animals suspected of being rabid. Treatment is dependent upon the individual's immune status and upon the level of risk of rabies in the country concerned (consult national immunization schedule); in certain circumstances such as patients with incomplete prophylaxis or unimmunized individuals *passive immunization* with rabies immunoglobulin may be indicated (see Rabies Immunoglobulin, section 17.2.4). Treatment should also include thorough wound cleansing.

The vaccine is also used for *pre-exposure prophylaxis* against rabies in those at high risk such as laboratory workers, veterinary surgeons, animal handlers and health workers who are likely to come into close contact with infected animals or patients with rabies. Pre-exposure prophylaxis is also recommended for those living or travelling in enzootic areas who may be exposed to unusual risk.

RABIES VACCINE (inactivated) (prepared in cell culture)

RABIES VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS ON RABIES VACCINE (INACTIVATED) FOR HUMAN USE PRODUCED IN CONTINUOUS CELL LINES, PUBLISHED IN THE REPORTS OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 760, 1987 AND AMENDMENT 1992, WHO TECHNICAL REPORT SERIES, NO. 840, 1994.

Indications: Active immunization against rabies; pre-exposure prophylaxis, post-exposure treatment (see notes above).

Contra-indications: See introductory notes.

Precautions: See introductory notes.

RABIES IMMUNOGLOBULIN: IF SCHEDULE REQUIRES RABIES VACCINE AND RABIES IMMUNOGLOBULIN TO BE ADMINISTERED AT THE SAME TIME, THEY SHOULD BE ADMINISTERED USING SEPARATE SYRINGES AND SEPARATE SITES.

Adverse effects: See introductory notes; pain, erythema and induration at injection site; nausea, myalgia; hypersensitivity—less likely with vaccines from human sources.

Nursing considerations: •Withhold corticosteroid therapy during immunization.
•May be given during pregnancy for post exposure immunization.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization against rabies: pre-exposure prophylaxis, by deep subcutaneous or by intramuscular injection, ADULT and CHILD 1 ml on days 0, 7 and 28, with reinforcing doses every 2–3 years for those at continued risk.

Immunization against rabies: post-exposure treatment (in unimmunized individuals), by deep subcutaneous or by intramuscular injection, ADULT and CHILD 5 doses of 1 ml on days 0, 3, 7, 14 and 28 (plus rabies immunoglobulin given on day 0, section 17.2.4; see notes above).

Immunization against rabies: post-exposure treatment (in fully immunized individuals), by deep subcutaneous or by intramuscular injection, adult and child 2 doses of 1 ml separated by 3–7 days (see notes above).

POM **Rabies vaccine** *(WMF 19.3.2.4)*
Injection, Inactivated rabies virus prepared in cell culture.

POM **Rabies Vaccine (HDCV)** *(EDL 20.2.2)*
Injection, in 1 ml vial.

POM **IMOVAX RABIES VERO®** *(Aventis Pasteur/May & Baker)*
Freeze-dried antirabies vaccine prepared on specialised monkey cells called Vero cells and

containing inactivated rabies virus Wister Strain PM/WI 38-1503-3M with protective activity equal to or greater than 2.5 i.u.
Pack: 1 single dose vial 1 + syringe diluent (0.5 ml).

POM **VERORAB®** *(Aventis Pasteur/May & Baker)*
Freeze-dried antirabies vaccine prepared on specialised monkey cells called Vero cells and containing inactivated rabies virus Wister Strain PM/WI 38-1503-3M with protective activity equal to or greater than 2.5 i.u.
Pack: 1 single dose vial 1 + syringe diluent (0.5 ml).

17.1.2.5 Rubella vaccine

Rubella vaccine should be given to women of child-bearing age if they are seronegative to protect them from the risks of rubella in pregnancy. It should not be given in pregnancy and patients should be advised not to become pregnant within one month of vaccination. However, congenital rubella syndrome has not been reported following inadvertent immunization shortly before or during pregnancy. There is no evidence that the vaccine is teratogenic and routine termination of pregnancy following inadvertent immunization should **not** be recommended. There is no risk to a pregnant woman from contact with recently vaccinated persons as the vaccine virus is not transmitted.

The vaccine may contain traces of antibiotics and if so should not be used in individuals with hypersensitivity to them.

In some countries the policy of protecting women of childbearing age has been replaced by a policy of eliminating rubella in children. Rubella vaccine is a component of the MMR vaccine (see section 17.1.1.4). Countries seeking to eliminate rubella should ensure that women of child-bearing age are immune and that over 80% of children are immunized.

RUBELLA VACCINE

RUBELLA VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 840, 1994 AND NOTE, WHO TECHNICAL REPORT SERIES, NO. 848, 1994.

Indications: Active immunization against rubella in women of child-bearing age.

Contra-indications: See introductory notes; pregnancy (see notes above); hypersensitivity to any antibiotic present in vaccine—consult manufacturer's literature; hypersensitivity to egg.

Precautions: See introductory notes; **interactions**: Appendix 1.

Adverse effects: See introductory notes; rash, lymphadenopathy; arthralgia and arthritis; rarely, thrombocytopenia, neurological symptoms.

Nursing considerations: •Obtain history of allergies and reactions to immunization; for S.C. inj only; inject into the outer aspect of upper arm.
•Reconstituted vaccine should be used within 8 hours.
•Advise patient not to become pregnant within 3 months of immunization due to possible risk of rubella-associated malformation; suggest use of contraceptives.
•Store in a refrigerator and protect from light; ensure solution is clear before use.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization of women of child-bearing age against rubella, by deep subcutaneous or by intramuscular injection, adult, 0.5 ml as a single dose.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO THE MANUFACTURER'S DIRECTIONS.

POM **Rubella vaccine** *(WMF 19.3.2.5)*
Injection (Powder for solution for injection), Live attenuated rubella virus.

POM **Rubella Vaccine** *(EDL 20.2.2)*
Injection, live attenuated, 1000 units in 0.5 ml.

POM **RUDIVAX®** *(Aventis Pasteur/May & Baker)*
Injection, live attenuated, 1000 units in 0.5 ml.

17.1.2.6 Typhoid vaccine

Typhoid vaccine is used for active immunization against typhoid fever and immunization is advised for those travelling to endemic areas. The efficacy of the vaccine is not complete and the importance of maintaining scrupulous attention to food and water hygiene as well as personal hygiene must also be emphasized.

Typhoid vaccine is available as a capsular polysaccharide injection.

In children under 2 years the injection may show sub-optimal response. Immunization is also recommended for laboratory workers handling specimens from suspected cases.

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A live oral typhoid vaccine containing an attenuated strain of *Salmonella typhi* (Ty21a) may also be available.

Typhoid vaccine

TYPHOID VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORT OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 840, 1994.

Indications: Active immunization against typhoid.

Contra-indications: See introductory notes.

Precautions: See introductory notes and notes above.

Nursing considerations: •Obtain history of allergies and reactions to immunization; give by S. or IM injection; not for intradermal use. Shake well before withdrawing from vial.

•Antipyretic may be given for fever.

•Withhold corticosteroid therapy during immunization.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization against typhoid fever, by mouth, ADULT and CHILD over 6 years, one dose given on days 0, 2, and 4 (total of 3 doses), with reinforcing doses every year for travellers to disease-endemic countries and every 3 years for those living in disease-endemic areas.

Immunization against typhoid fever, by deep subcutaneous or by intramuscular injection, ADULT and CHILD (see notes above) 0.5 ml, with reinforcing doses every 3 years for those at continued risk.

ADMINISTRATION: ACCORDING TO THE MANUFACTURER'S DIRECTIONS.

Adverse effects: See introductory notes.

POM **Typhoid vaccine** *(WMF 19.3.2.6)*

Capsule, Live attenuated strain of *Salmonella typhi* (Ty21a).

Injection, Vi capsular polysaccharide typhoid 25 microgram/0.5 ml.

POM **TYPHIM Vi**® *(Aventis Pasteur/May & Baker)*

Inactivated suspension of 0.025 mg *Salmonella typhi* per 0.5 ml in isotonic buffer solution.

Pack: 0.5 ml in a Pre-filled ready to use single dose disposable syringe; 10 ml in multidose (20 doses) vial.

ORAL TYPHOID VACCINE

Synonym: Typhoid Vaccine Live Oral Ty21a.

Therapeutic category: Vaccine, Inactivated Bacteria.

Indications: Live vaccine for oral active immunization against typhoid fever.

Contra-indications: Hypersensitivity to the vaccine or buffer components; congenital or acquired immune deficiency; co-administration with immunosuppressives or antimitotic drugs. Live vaccines should be avoided in HIV patients.

Precautions: Avoid administration during acute feverish illnesses and acute GI infections as well as during and up to 3 days after treatment with antibiotics or sulphonamides due to possible inhibition of the growth of vaccine organisms. The interval between the last dose of oral typhoid vaccine and beginning of the malaria prophylaxis should generally be 3 days.

Interactions: •Avoid co-administration with sulphonamides or antibiotics due to possible weakening of the immune response.

•Antimalarials.

Adverse effects: Nausea, vomiting, abdominal cramps, diarrhoea, urticarial exanthema; rarely anaphylactic reactions.

Advice to patients: See labels 23 and 25 in Appendix 6. Oral capsule should be taken 1 hour before a meal with cold or lukewarm drink, do not chew, swallow whole; systemic adverse effect may persist for 1-2 days. Take all 3 doses exactly as directed on alternate days to obtain a maximal response. Store in a refrigerator.

Dose: By mouth, Adult and Child above 6 years, *Primary immunization*, 1 capsule on alternate days (days 1, 3, and 5); *Booster immunization*: Repeat full course of primary immunization annually.

Note: The protection becomes effective on about the 10th day after administration and persists for at least one full year, in people under conditions of repeated or continued exposure to salmonella for at least 3 years. In case of travel from non-endemic to endemic areas a booster dose of vaccine is recommended annually.

POM **VIVOTIF BERNA**® *(Urashi)*

Capsule, Live attenuated *Salmonella typhi* strain Ty21a Colony-forming units not less than 2×10^9 in a lyophilised form; white/red e-c cap. Pack - 3.

17.1.2.7 Yellow fever vaccine

Yellow fever is a viral haemorrhagic fever endemic in some countries of South America and Africa. The disease is transmitted by *Haemagogus* and *Aedes* mosquito bites. The vaccine is highly immunogenic and offers about 10 years protection. Over 92% of children develop protective antibodies. It is recommended that all countries in which yellow fever is endemic should incorporate this vaccine into their immunization schedule. It is also used for travellers to endemic areas.

Yellow fever vaccine

YELLOW FEVER VACCINE SHOULD COMPLY WITH THE RECOMMENDATIONS PUBLISHED IN THE REPORTS OF THE WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION, WHO TECHNICAL REPORT SERIES, NO. 872, 1998.

Indications: Active immunization against yellow fever.

Contra-indications: See introductory notes; not recommended for infants under 6 months of age; hypersensitivity to any antibiotic present in vaccine—consult manufacturer's literature; hypersensitivity to egg.

Precautions: See introductory notes; pregnancy (Appendix 2); **interactions**: Appendix 1.

Adverse effects: See introductory notes; rarely encephalitis, generally in infants under 9 months.

Nursing considerations: •Obtain history of allergies, especially to eggs, and reactions to immunization.
•Avoid vigorous shaking; carefully swirl mixture until suspension is uniform. Use within 1 hour after reconstitution, and discard the remainder.
•Do not give within one month of other live virus vaccines.
•Must be kept frozen.

Dose: NOTE: NATIONAL IMMUNIZATION SCHEDULES MAY VARY.

Immunization of children against yellow fever, by subcutaneous injection, INFANT at 9 months of age, 0.5 ml (see WHO schedule, section 17.1.1).

Immunization of travellers and others at risk against yellow fever, by subcutaneous injection, ADULT and CHILD over 9 months of age 0.5 ml; INFANT 6–9 months of age 0.5 ml, only if risk of yellow fever is unavoidable (see Adverse Effects).

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Yellow fever vaccine** *(WMF 19.3.2.7)*
Injection (Powder for solution for injection), Live, attenuated yellow fever virus.

POM **Yellow Fever Vaccine** *(EDL 20.2.2)*
Injection, powder for reconstitution in 1, 5 and 10 dose vials.

POM **STAMARIL PASTEUR®** *(Aventis Pasteur/May & Baker)*
Heat stable freeze dried suspension of live attenuated yellow fever virus 17D strain in a special diluent.
Pack: 10 doses x 1 vial.
Dose: By s.c. or i.m. injection, *primary immunization*, 0.5 ml as a single dose.
Boosters: 0.5 ml every 10 years.
Note: Reconstituted vaccine should be properly shaken before use. It should be kept out of direct sunlight and used within one hour of reconstitution. Injection is in deltoid (adults) and anterio-lateral thigh (children).

17.1.3 Other vaccines

CHICKENPOX VACCINE

Synonym: Varicella vaccine
Indications: For the prevention of varicella infection commonly referred to as Chickenpox.
Contra-indications: As for Live vaccines; HIV, pregnancy.
Dose: Adult and child over 2 years of age, by I.M. injection, immunising dose of 0.5 ml of the reconstituted vaccine.

POM **OKAVAX®** *(Aventis Pasteur /May & Baker)*
Single dose vial + 1 syringe of diluent.

CHOLERA VACCINE

Indications: Prevention of cholera
Contra-indications: Acute infectious diseases; currently evolving diseases.
Adverse effects: Erythema, oedema, fever, stiffness, lasting for 24-48 hours.
Dose: By s.c. or i.m. injection as follows:

	Primary Vaccination	Boosters
Subjects over 10 years of age	2 doses of 0.5ml at 1 week to 1 month interval	1 dose of 0.5ml every 6 months
Subjects of 6 months to 10 years	2 doses of 0.25ml at 1 week to 1 month interval	1 dose of 0.25ml every 6 months

Below the age of 6 months , vaccination is not a requirement.
Note: The 2 doses of primary vaccination are for countries requiring complete primary

vaccination. In other countries, according to international health regulations, one dose of primary vaccination is sufficient.

POM **Cholera Vaccine** *(EDL 20.2.2.)*
Injection, in 1.5 ml, 5 ml, 10 ml, 50 ml amps or vials.

HEPATITIS-A VACCINE

Indications: Active immunization against hepatitis-A virus (HAV) infection.
Contra-indications: Hypersensitivity to any component of the vaccine or after signs of hypersensitivity due to previous administration of the vaccine; severe febrile conditions.
Precautions: Anaphylaxis or anaphylactoid reactions, as with all biologicals, adrenaline or any other suitable anti-anaphylactic drug should be readily available; thrombocytopenia (use with caution); pregnancy (use only when clearly needed).
Interactions:
•Avoid mixing with other vaccines (use different syringes and different injection sites when concomitant administration of other vaccine is necessary).
Adverse effects: Mild transient; less commonly, fever, malaise, fatigue, headache, nausea and loss of appetite.
Dose: By i.m. injection, Adult (16 years and over), 2 doses of 1ml (720 ELISA units) at interval of 2-4 weeks.
Child and adolescent (1-15 years): 2 doses of 0.5 ml (360 ELISA units) at interval of 2-4 weeks.
This regimen provides anti-HAV antibodies for at least 1 year. To extend the immunity for up to 10 years, a booster dose should be taken between 6-12 months after the first dose.
Note: **Administration** - To be injected i.m. in the deltoid region. Before use, shake the vial to obtain a slightly opaque white solution. Discard if the contents of the vial appear otherwise. *The vaccine should never be administered intravenously*.

POM **AVAXIM®** *(Aventis Pasteur /May & Baker)*
A suspension of formaldehyde-inactivated Hepatitis A virus (GBM grown in human diploid cells) 320 antigen units per ml adsorbed onto aluminium hydroxide
1 x 0.5 ml prefilled syringe
Shelf-Life: 24 months
Dose: By I.M. injection (see note below), 0.5 ml as single dose; booster dose 0.5 ml 6 months following the initial dose; further booster doses, 0.5 ml every 10 years.
Child (under 16 years): not recommended.
Note: The deltoid region is the preferred site of injection. The subcutaneous route may be used for patients with haemophilia.

POM **HAVRIX®** *(GSK)*
Hepatitis-A virus (HAV) is a sterile suspension containing in each 1 ml dose not less than 720 ELISA units of viral antigens adsorbed in 0.5 mg of aluminium hydroxide.

PNEUMOCOCCAL VACCINE

Pharmacology: A polyvalent vaccine prepared from purified pneumococcal antigens. The immunity provided is only effective against pneumococcal serotypes contained in the vaccine. This immunity is acquired from 10 to 15 days after the injection and lasts for about 5 years.
Indications: Prevention of pneumococcal infections, particularly of the respiratory tract, in high-risk subjects, in principle from the age of 2 years, including patients with sickle-cell disease(SS), asplenia, a history of splenectomy, or scheduled splenectomy, and in the elderly.
Contra-indications: Children under 2 years, pregnancy, current infection; marked reaction after a previous injection; revaccination within 5 years of previous injection (for pneumococcal infection).
Precautions: Because severe reactions may occur, revaccination requires strict compliance with contraindications. Benefits of such revaccination should also be evaluated bearing in mind that the efficacy of pneumococcal immunization has been established only in specific high-risk groups.
Shelf-life is 24 months. Recommended storage temperature is +2 to +8°C; do not freeze.
Interactions: •Immunosuppressive treatment is likely to reduce or abolish the immune response to the vaccine.
Adverse effects: Hypersensitivity reactions; occasionally redness, mild pain and induration at the injection site; low-grade fever of 24 hours duration; rarely functional impairment, minor general reactions such as fever, asthenia, chills, usually of less than 24 hours duration.
Dose: *Primary immunization*: one injection of 0.5 ml.
Booster: one injection of 0.5 ml which must not be given within 5 years except in very high-risk subjects or patients under immunosuppressive treatment.

Method of Administration: The preferred route of administration is intramuscular although it may also be given subcutaenously. Shake before use. Don't inject I.V.

POM **PNEUMO 23®** *(Aventis Pasteur/May & Baker)*
23-Purified polysaccharides of *Streptococcus pneumoniae* 25 mcg in a buffer solution; suspension for injection.
Single dose syringe x 0.5 ml.

17.2 Sera and immunoglobulins (Passive immunity)

17.2.1 Anti-D immunoglobulin (human)
17.2.2 Antitetanus immunoglobulin (human)
17.2.3 Diphtheria antitoxin
17.2.4 Rabies immunoglobulin (human)
17.2.5 Antivenom sera
17.2.6 Others

Antibodies of human origin are usually termed **immunoglobulins**. Material prepared from animals is called **antiserum**. Because of serum sickness and other allergic-type reactions that may follow injections of antisera, this therapy has been replaced wherever possible by the use of immunoglobulins.

All immunoglobulins and antisera should comply with WHO requirements for blood and plasma products.

CONTRAINDICATIONS AND PRECAUTIONS
Anaphylaxis, although rare, can occur and epinephrine (adrenaline) must always be immediately available during immunization.

Immunoglobulins may interfere with the immune response to live virus vaccines which should normally be given *either at least 3 weeks before or at least 3 months after* the administration of the immunoglobulin.

ADVERSE REACTIONS
Intramuscular injection. Local reactions including pain and tenderness may occur at the injection site. Hypersensitivity reactions may occur including, rarely, anaphylaxis.

Intravenous injection. Systemic reactions including fever, chills, facial flushing, headache and nausea may occur, particularly following high rates of infusion. Hypersensitivity reactions may occur including, rarely, anaphylaxis.

17.2.1 Anti-D immunoglobulin (human)

Anti-D immunoglobulin is prepared from plasma with a high titre of anti-D antibody. It is available to prevent a rhesus-negative mother from forming antibodies to fetal rhesus-positive cells which may pass into the maternal circulation. The aim is to protect any subsequent child from the hazard of haemolytic disease of the newborn. It should be administered following any potentially sensitizing episode (for example abortion, miscarriage, still-birth) immediately or within 72 hours of the episode but even if a longer period has elapsed it may still give protection and should be used. The dose of anti-D immunoglobulin given depends on the level of exposure to rhesus-positive blood. The injection of anti-D immunoglobulin is not effective once the mother has formed anti-D antibodies. It is also given following Rh_0 (D) incompatible blood.

Anti-D immunoglobulin (human)

PLASMA FRACTIONS SHOULD COMPLY WITH THE REQUIREMENTS FOR THE COLLECTION, PROCESSING AND QUALITY CONTROL OF BLOOD, BLOOD COMPONENTS AND PLASMA DERIVATIVES (REVISED 1992). WHO TECHNICAL REPORT SERIES NO 840, 1994, ANNEX 2

Indications: Prevention of formation of antibodies to rhesus-positive blood cells in rhesus-negative patients (see notes above).

Contra-indications: See introductory notes; known hypersensitivity.

Precautions: See introductory notes; caution in rhesus-positive patients for treatment of blood disorders; caution in rhesus-negative patients with anti-D antibodies in their serum; **interactions**: Appendix 1.

RUBELLA VACCINE: RUBELLA VACCINE MAY BE ADMINISTERED IN THE POSTPARTUM PERIOD AT THE SAME TIME AS ANTI-D IMMUNOGLOBULIN INJECTION, BUT ONLY USING SEPARATE SYRINGES AND SEPARATE CONTRALATERAL SITES. IF BLOOD IS TRANSFUSED, THE ANTIBODY RESPONSE TO THE VACCINE MAY BE INHIBITED AND A TEST FOR ANTIBODIES SHOULD BE PERFORMED AFTER 8 WEEKS AND THE SUBJECT REVACCINATED IF NECESSARY.

Adverse effects: See introductory notes.

Nursing considerations: •The product should not be shaken when reconstituting or transporting; reconstitute the product shortly before use with NS, according to manufacturer's guidelines; do not administer with other products.
•Pretreatment with paracetamol or increasing the time

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of infusion can prevent fever/chill reaction.
•Administer after sending the baby's cord blood to the laboratory for cross-matching, rhesus typing, Hgb.

Dose: NOTE: NATIONAL RECOMMENDATIONS MAY VARY.

Following birth of a rhesus-positive infant in rhesus-negative mother, by intramuscular injection, ADULT 250 micrograms immediately or within 72 hours (see also notes above).

Following any potentially sensitizing episode (for example amniocentesis, still-birth), by intramuscular injection, ADULT up to 20 weeks' gestation, 250 micrograms per episode (after 20 weeks, 500 micrograms) immediately or within 72 hours (see notes above)

Following Rh_0 (D) incompatible blood transfusion, by intramuscular injection, ADULT 10–20 micrograms per ml transfused rhesus-positive blood.

POM **Anti-D immunoglobulin** *(WMF 19.2.1)*
Injection, Anti-D immunoglobulin 250-microgram vial.

POM **Anti-D Immunoglobulin** *(EDL 20.1)*
Injection, Anti-D immunoglobulin 0.25 mg per ml.

POM **RhoGAM®** *(Biofem)*
Injection, Anti-D immunoglobulin 300 µg (1500 IU) per ml; sterile solution in prefilled single-dose syringe.
Pack: 5's; 25's.

Dose: For IM injection only. A single dose of RhoGAM contains sufficient anti-D (approximately 300 µg) to suppress the immune response to 15 mL (or less) of Rh-positive red blood cells. Additional doses of RhoGAM are indicated when the patient has been exposed to > 15 mL of Rh-positive red blood cells. Rhogam should be administered within 72 hours of delivery or exposure to Rh-positive red blood cells.

Postpartum (if the newborn is Rh-positive), 300 µg;
Antepartum: Prophylaxis at 26 to 28 weeks' gestation, 300 µg;
Antepartum: Amniocentesis, chorionic villus sampling (CVS) and percutaneous umbilical blood sampling (PUBS), 300 µg;
Antepartum: Abdominal trauma or obstetrical manipulation, 300 µg;
Antepartum: Ectopic pregnancy, 300 µg;
Antepartum: Abortion or threatened abortion at any stage of gestation with continuation of pregnancy, 300 µg;
Transfusion of Rh-incompatible blood or blood products, 300 µg.

Note: For intramuscular use only. Do not inject RhoGAM intravenously. In the case of postpartum use, the product is intended for maternal administration. Do not inject the newborn infant.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

NORMAL IMMUNOGLOBULIN, I.V.

Pharmacology: Human normal immunoglobulin (HNIG) is prepared from a pool of plasma and contains broad spectrum of antibodies to measles, mumps, varicella, hepatitis A, and other viruses that are currently prevalent in the general population. Each unit of plasma used is tested for the absence of hepatitis-B surface antigen and antibodies against HIV-1.

Indications: Special formulations of immunoglobulins for intravenous administration are available for *replacement therapy* for patients with congenital agammaglobulinaemia and hypogammaglobulinaemia, for the treatment of idiopathic thrombocytopenic purpura and Kawasaki syndrome, and for the prophylaxis of infection following bone-marrow transplantation and in children with symptomatic HIV infection who have recurrent bacterial infections.

Contra-indications: Hypersensitivity to I.M. or I.V. human immunoglobulin; IgA-deficient patients with circulating antibodies against IgA.

Precautions: Monitor signs of anaphylactic reactions during infusion; pregnancy; shaking causes foaming and denaturation of protein, only a clear solution may be infused.

Interactions: •Live virus vaccines: Normal immunoglobulin may *interfere with the immune response to live virus vaccines* which should therefore only be given *at least 3 weeks before or 3 months after* an injection of normal immunoglobulin (this does not apply to yellow fever vaccine since normal immunoglobulin does not contain antibody to this virus).
•Not to be mixed with any other medication.

Adverse effects: Malaise, flushing, chills, fever, dizziness, nausea, vomiting, diarrhoea, abdominal pain, back pain, CV and respiratory

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disturbances; rarely anaphylaxis.

Nursing considerations: •Do not mix with other medications.

•Skin testing should be performed as local irritation can occur and be misinterpreted as a positive reaction.

Dose: See lit.

POM **Human Immunoglobulin** *(EDL 20.1)*

Injection, Immunoglobulin 30 mg per ml; for I.V. injection.

17.2.2 Antitetanus immunoglobulin (human)

Antitetanus immunoglobulin of human origin is a preparation containing immunoglobulins derived from the plasma of adults immunized with tetanus toxoid. It is used for the management of tetanus-prone wounds in addition to wound toilet and if appropriate antibacterial prophylaxis and adsorbed tetanus vaccine (see section 17.1.1.2).

Antitetanus immunoglobulin (human)

PLASMA FRACTIONS SHOULD COMPLY WITH THE WHO REQUIREMENTS FOR THE COLLECTION, PROCESSING AND QUALITY CONTROL OF BLOOD, BLOOD COMPONENTS AND PLASMA DERIVATIVES (REVISED 1992). WHO TECHNICAL REPORT SERIES NO 840, 1994, ANNEX 2.

Indications: Passive immunization against tetanus as part of the management of tetanus-prone wounds.

Contra-indications: See introductory notes.

Precautions: See introductory notes.

TETANUS VACCINE: IF SCHEDULE REQUIRES TETANUS VACCINE AND ANTITETANUS IMMUNOGLOBULIN TO BE ADMINISTERED AT THE SAME TIME, THEY SHOULD BE ADMINISTERED USING SEPARATE SYRINGES AND SEPARATE SITES.

Adverse effects: See introductory notes.

Nursing considerations: •Obtain history of injury, tetanus immunizations, last tetanus toxoid injection, allergies, and reaction to immunizations.

•Thoroughly cleanse and remove all foreign matter from wound.

•Administer by IM injection only; use deltoid muscle for adult and children above 3 years and anterolateral aspect of the thigh in children below 3 years.

•Do not administer IV.

•Do not confuse tetanus immunoglobulin with tetanus toxoid, which is usually given at the same time to produce active immunization.

•Never administer tetanus immunoglobulin and tetanus toxoid in the same syringe (toxoid will be neutralized); toxoid may be given at a separate site.

•Refrigerate at 2°C to 8°C.

Dose: NOTE: NATIONAL RECOMMENDATIONS MAY VARY.

Management of tetanus-prone wounds, by intramuscular injection, ADULT and CHILD 250 units, increased to 500 units if wound older than 12 hours or there is risk of heavy contamination or if patient weighs more than 90 kg; second dose of 250 units given after 3–4 weeks if patient immunosuppressed or if active immunization with tetanus vaccine contraindicated (see also section 17.1.1.2).

POM **Antitetanus immunoglobulin** *(WMF 19.2.2)*

Injection, Antitetanus immunoglobulin 500 units/vial.

17.2.3 Diphtheria antitoxin

Diphtheria antitoxin is prepared from the plasma or serum of healthy horses immunized against diphtheria toxin or diphtheria toxoid. It is used for passive immunization in suspected cases of diphtheria without waiting for bacterial confirmation of the infection. A test dose should be given initially to exclude hypersensitivity. Diphtheria antitoxin is not used for prophylaxis of diphtheria because of the risk of hypersensitivity.

Diphtheria antitoxin

Indications: Passive immunization in suspected cases of diphtheria.

Precautions: Initial test dose to exclude hypersensitivity; observation required after full dose (epinephrine (adrenaline) and resuscitation facilities should be available).

Adverse effects: Anaphylaxis with urticaria, hypotension, dyspnoea and shock; serum sickness up to 12 days after injection.

Dose: NOTE: NATIONAL RECOMMENDATIONS MAY VARY.

Passive immunization in suspected diphtheria (see Precautions), by intramuscular injection, ADULT and CHILD 10 000–30 000 units in mild to moderate cases; 40 000–100 000 units in severe cases (for doses of more than 40 000 units, a portion should be given by intramuscular injection followed by the bulk of the dose intravenously after an interval of 0.5–2 hours).

POM **Diphtheria antitoxin** *(WMF 19.2.3)*

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Injection, Diphtheria antitoxin 10 000 units, 20 000 units/ vial.

17.2.4 Rabies immunoglobulin (human)

Rabies immunoglobulin is a preparation containing immunoglobulins derived from the plasma of adults immunized with rabies vaccine. It is used as part of the management of potential rabies following exposure of an unimmunized individual to an animal in or from a high-risk country. It should be administered as soon as possible after exposure without waiting for confirmation that the animal is rabid. The site of the bite should be washed with soapy water and the rabies immunoglobulin should be infiltrated round the site of the bite and also given intramuscularly. In addition rabies vaccine (see section 17.1.2.4) should be administered at a different site.

Rabies immunoglobulin (human)

PLASMA FRACTIONS SHOULD COMPLY WITH THE WHO REQUIREMENTS FOR THE COLLECTION, PROCESSING AND QUALITY CONTROL OF BLOOD, BLOOD COMPONENTS AND PLASMA DERIVATIVES (REVISED 1992). WHO TECHNICAL REPORT SERIES NO 840, 1994, ANNEXE 2

Indications: Passive immunization either post-exposure or in suspected exposure to rabies in high-risk countries in unimmunized individuals (in conjunction with rabies vaccine).

Contra-indications: See introductory notes; avoid repeat doses after vaccine treatment initiated; intravenous administration.

Precautions: See introductory notes.

RABIES VACCINE: IF SCHEDULE REQUIRES RABIES VACCINE AND RABIES IMMUNOGLOBULIN TO BE ADMINISTERED AT THE SAME TIME, THEY SHOULD BE ADMINISTERED USING SEPERATE SYRINGES AND SEPERATE SITES.

Adverse effects: See introductory notes.

Nursing considerations: •Obtain history of animal bites, allergies, and reaction to immunizations.

•Administered by infiltration at the site of the bite; may also be given IM.

•IM doses greater than 5 ml should be divided and given at different sites; avoid giving more than 5 ml at one injection site.

•Do not confuse rabies immunoglobulin with rabies vaccine. Rabies vaccine is a suspension of attenuated or killed microorganisms used to confer active immunity. Specific rabies immunoglobulin of human origin provides passive immunity.

•Do not give rabies vaccine and rabies immunoglobulin in the same syringe or at the same site.

Dose: NOTE: NATIONAL RECOMMENDATIONS MAY VARY.

Immunization against rabies: post-exposure (or suspected exposure) treatment, by intramuscular injection and wound infiltration, ADULT and CHILD 20 units/kg (half by intramuscular injection and half by wound infiltration).

POM **Rabies immunoglobulin** *(WMF19.2.4)*
Injection, Rabies immunoglobulin 150 units/ml, 2-ml vial, 10-ml vial.

POM **Rabies Immunoglobulin** (*Aventis Pasteur/May & Baker)*
(Antirabies Immunoglobulin Injection)
Dose: 20 units/kg, half by i.m. injection and half by infiltration around wound.

17.2.5 Antivenom sera

Acute envenoming from snakes or spiders is common in many parts of the world. The bite may cause local and systemic effects.

Local effects include pain, swelling, bruising and tender enlargement of regional lymph nodes. Wounds should be cleaned and pain may be relieved by analgesics.

If significant amounts of toxin are absorbed after a snake bite, this may result in early anaphylactoid symptoms such as transient hypotension, angioedema, abdominal colic, diarrhoea and vomiting, followed by persistent or recurrent hypotension and ECG abnormalities. Spontaneous systemic bleeding, coagulopathy, adult respiratory distress syndrome and acute renal failure may occur. Early anaphylactoid symptoms may be treated with epinephrine (adrenaline). **Snake antivenom sera** are the only specific treatment available but they can produce severe adverse reactions. They are generally only used if there is a clear indication of systemic involvement or severe local involvement or, if supplies are not limited, in patients at high risk of systemic or severe local involvement.

Spider bites may cause either necrotic or neurotoxic syndromes depending on the species involved. Supportive and symptomatic treatment is required and in the case of necrotic syndrome, surgical repair may be necessary. **Spider antivenom sera**, suitable for the species

involved, may prevent symptoms if administered as soon as possible after envenomation.

Antivenom sera

Indications: Treatment of snake bites and spider bites.
Precautions: Resuscitation facilities should be immediately available.
Adverse effects: Serum sickness; anaphylaxis with hypotension, dyspnoea, urticaria and shock.
Dose: Depends on the specific antivenom used; consult manufacturer's literature.
See below under the proprietary preparations.

Note: To avoid possible anaphylactic shock, BESREDKA method of administration should be used: inject 0.1 ml of serum subcutaneously and wait for 15 minutes; inject 0.25 ml of serum subcutaneously and wait for another 15 minutes. In the absence of adverse reactions, administer the rest of the dose by the chosen route of injection.

POM **Antivenom sera** *(WMF 19.2.5)*
Injection, Snake antivenom serum and spider antivenom serum.
NOTE: THERE ARE MANY ANTIVENOM SERA EACH CONTAINING SPECIFIC VENOM-NEUTRALIZING GLOBULINS. IT IS IMPORTANT THAT THE SPECIFIC ANTIVENOM SERUM SUITABLE FOR THE SPECIES CAUSING THE ENVENOMATION IS ADMINISTERED.

POM **Anti-Snake Bite Serum** *(EDL 20.1)*
Injection, Polyvalent, in 10 ml, 20 ml amps.

POM **FAV AFRICA®** *(Aventis Pasteur/May & Baker)*
Injection, Antisnake venom containing 9 valencies of sera of equine origin (Highly purified venom).
Pack - 1 amp. x 10 ml.
Note: Can be administered by direct i.v. or i.m. injection.

POM **IPSER AFRICA®** *(Aventis Pasteur/May & Baker)*
Anti-snake venom containing 9 valencies of immunoglobulin from equine immune serum.
Pack - 1 amp. x 10 ml.
Dose: Adult and child, the contents of 1-2 amps of the ASV are given by I.V. infusion over 30 minutes after diluting in Normal saline.
The dose can be repeated in 1-2 hours if symptoms of systemic envenoming persist.

17.2.6 Others

ANTI-GAS GANGRENE

Indications: Treatment of gas gangrene.
Adverse effects: Allergic and anaphylactic reactions, serum sickness.
Dose: See lit.

POM **Anti-Gas Gangrene** *(EDL 20.1)*
Injection, 10,000 units, 30,000 units in vials.

POM **Anti-Gas Gangrene** (*Aventis Pasteur / May & Baker)*
Injection, 10,000 units, 30,000 units; in vials.

ANTI-RABIES HYPERIMMUNE SERUM

Indications: Post-exposure prophylaxis of rabies.
Adverse effects: Serum sickness within 6 to 12 days of immunization; symptoms include skin eruptions, arthralgia, pruritus, lymphadenopathy, fever, headache, malaise, abdominal pain, anaphylaxis. Pain at injection site.
Nursing considerations: •Antirabies hyperimmune serum should be used only when rabies immunoglobulin is not available.
•*See under Rabies immunoglobulin.*
Dose: 40 to 55 units per kg at the same time of first dose of rabies vaccine.
Give half of dose by local infiltration at the site of the bite, and the remainder by I.M. injection.

POM **Anti-rabies Hyperimmune Serum** *(EDL 20.1)*
Injection, 1000 units in 5 ml amp.

POM **Antirabies Hyperimmune Serum** (*Aventis Pasteur/May & Baker)*
Injection, 1000 units in 5 ml amp.

ANTI-SCORPION SERUM

Indications: Post-exposure prophylaxis of scorpion sting.
Adverse effects: Serum sickness
Dose: See lit.

POM **Anti-scorpion Serum** *(EDL 20.1)*
Injection, 1 ml in amp.

POM **Antiscorpion Serum** (*Aventis Pasteur/ May & Baker)*
Injection, 1 ml in amp.

TETANUS ANTITOXIN (A.T.S.)

Synonym: TAT

Indications: For temporary (not exceeding 21 days) passive immunity against tetanus; prophylaxis of tetanus in non-vaccinated or inadequately vaccinated traumatology patients where the last booster was administered more than 10 days ago or where firm evidence of vaccination is not available or in vaccinated subjects with massive and highly contaminated wounds or suffering major blood loss; treatment of tetanus.

Contra-indications: Hypersensitivity to equine serum (risk of anaphylactic shock); pregnancy (anti-tetanus immunoglobulin of human origin (Tetaglobulin] should be used).

Precautions: Anaphylactic shock (BESREDKA method of admninistration is recommended - see under Anti-snake Bite Serum); subjects sensitized with equine serum.

Dose: Prophylaxis, by s.c. injection, 1,500-3,000i.u.

Treatment, by i.m. injection, 20,000-100,000 i.u; *neonatal tetanus*, 5,000-10,000 i.u.

By slow i.v. infusion, dilute in 500 ml physiological saline.

By intrathecal injection, 2,500 I.U. by direct lumbar injection along with corticosteroids parenterally.

By local injection: periumbilical for neonatal tetanus and pericervical for puerperal tetanus.

POM **Tetanus Antitoxin** *(EDL 20.1)*
Injection, 1500 units in amp; 10,000 units, 50,000 units in vials.

POM **A.T.S.** *(Aventis Pasteur /May & Baker)*
Injection, Tetanus antitoxin 1500 i.u., 10,000 i.u.
1500 i.u. in amp x 1 x 10
10,000 i.u in vial x 10 x 2 ml amp.

17.3 Diagnostic agents

The **tuberculin test** has limited diagnostic value. A positive tuberculin test indicates previous exposure to mycobacterial antigens through infection with one of the tubercle bacilli, or BCG vaccination. The tuberculin test does not distinguish between tuberculosis and other mycobacterial infection, between active and quiescent disease, or between acquired infection and seroconversion induced by BCG vaccination.

Tuberculin purified protein derivative (tuberculin PPD)

All tuberculins should comply with the WHO Requirements for Tuberculins (Revised 1985). WHO Expert Committee on Biological Standardization Thirty-sixth report. WHO Technical Report Series, No.745, 1987, Annex 1.

Indications: Test for hypersensitivity to tuberculoprotein.

Contra-indications: Should not be used within 3 weeks of receiving a live viral vaccine.

Precautions: Elderly; malnutrition; viral or bacterial infections (including HIV and severe tuberculosis), malignant disease, corticosteroid or immunosuppressant therapy—diminished sensitivity to tuberculin; avoid contact with open cuts, abraded or diseased skin, eyes or mouth.

Adverse effects: Occasionally nausea, headache, malaise, rash; immediate local reactions (more common in atopic patients); rarely, vesicular or ulcerating local reactions, regional adenopathy and fever.

Dose: NOTE: NATIONAL RECOMMENDATIONS MAY VARY.

Test for hypersensitivity to tuberculoprotein, by intradermal injection, ADULT and CHILD 5 or 10 units (1 unit may be used in hypersensitive patients or if tuberculosis is suspected). ADMINISTRATION: According to manufacturer's directions.

POM **Tuberculin PPD** *(WMF 19.1)*
Injection, Tuberculin purified protein derivative 100 units/ml, 10 units/ml.

POM **Tuberculin PPD** *(EDL 15.5)*
Injection, Tuberculin PPD 10 units, 100 units, 100,000 units per ml; in ml amp.

See Tuberculin PPD also under section 20.2.5

18. Dental formulary

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18.3 Vitamin preparations
18.4 Anti-infective drugs
18.4.1 Antibacterials
18.4.2 Antifungals
18.4.3 Antivirals
18.5 Corticosteroids
18.6 Mouthwashes
18.7 Drugs used in treating the pulp
18.8 Drugs used in treating orofacial pathologies
18.9 Others

18.1 Local anaesthetics

18.1.1 Injectable local anaesthetics
18.1.2 Agents for surface application

These agents provide safe, effective and dependable anaesthesia for virtually all forms of dental procedures with suitable duration.

18.1.1 Injectable local anaesthetics

Injectable local anaesthetic agents may be broadly classified as amides or esters according to the type of linkage within the hydrophilic groups. Local anaesthetic agents are metabolized by the liver and excreted by the kidney. Ester anaesthetics are metabolized by esterase in the blood. Local anaesthetic solutions for dental use are made from the hydrochloride salt of the local anaesthetic base. The solutions which are usually packaged in dental cartridges usually contain 1 mg/ml methylparaben as preservatives, individuals sensitive to one paraben generally show cross sensitivity to this preservative in the local anaesthetic. Some local anaesthetic solutions also contain vasoconstrictors while some do not. The concentration varies from one product to the other. Local anaesthetics are often not effective when injected into an infected area, because inflammed tissues liberate acidic substances creating a pH of between 4-6 as compared to the normal value of 7.4. The reduced pH lowers the anaesthetic base content and thus impedes penetration of neural membrane.

Because of their action of blocking nerve conduction when administered systemically they can alter the function of the heart in transmission of impulses. Most agents currently used for local anaesthesia are not vasoconstrictors, thus epinephrine or others are included in the solution. By localising the solution to the site, they prolong the anaesthetic effect and decrease the amount which gets into the systemic circulation.

Localized reaction: These are well tolerated, but repeated injections into the same site over a period should be avoided. The vasoconstrictor effect may lead to tissue anoxia, delayed wound healing and necrosis.

There may be systemic toxic reactions in small children and elderly patients. Symptoms of such toxicity are mainly convulsions which are

transient and not lethal. Administration of oxygen is the most effective treatment. Cardiac arrhythmia or arrest is the most common cause of death from lidocaine overdosage in animals.

LIDOCAINE

Synonym: Lignocaine.
Indications: Local anaesthesia in dental surgery.
Contra-indications, Precautions, etc: see Lidocaine in Section 3.4.

POM **Lidocaine** *(EDL)*
Injection, Lidocaine 2%, adrenaline 1 in 80,000; in dental cartridges.
Cream and spray, see lidocaine section 15.1.2

MEPIVACAINE

Indications: Infiltration and block anaesthesia
Contra-indications, Precautions, etc: See under Lidocaine.

POM **Mepivacaine**
Injection, Mepivacaine HCl 2%, levonordefrin 1 in 20,000: in dental cartridges of 1.8 ml or 2.2 ml.

PRILOCAINE

Indications: Infiltration and block anaesthesia in dental surgery.
Contra-indications: Anaemia, congenital or acquired methaemoglobinaemia, hypersensitivity to prilocaine.
Precautions: Epilepsy, conduction disturbances; respiratory, hepatic or renal impairment.
Adverse effects: Methaemoglobinaemia and cyanosis particularly in doses exceeding 600 mg; allergic reactions.
Dose: With **Felypressin**, max 600 mg.
See lit.

POM **Prilocaine** *(EDL 13.1)*
Injection, Prilocaine 3% with felypressin 0.03 units per ml; in dental cartridge of 1.8 ml or 2.2 ml.

18.1.2 Agents for surface application

These agents differ from the injectables in that they are selected because of their ability to penetrate the oral mucosa. The concentration is in the range of 2-5% which is higher than that of injectable preparations to facilitate diffusion through the mucous membrane. About 2-5 minutes are required for their maximum effectiveness and the duration of anaesthesia is shorter than the injectables. Majority of the drugs used in topical anaesthetics are insoluble in water but soluble in alcohol, propylene glycol, polyethylene glycol, such agents are lidocaine, chlorobutanol and lidocaine base.
These agents are applied topically to the oral mucosa for such conditions as relieve of ulcer pains and oral wounds, taking impressions in patients with excessive gag reflex and also when intra-oral radiographs are to be taken.
Toxic Reactions: The reactions, clinical manifestations and treatment of reactions are similar to those of the injectables.
Precautions: The area of application could be limited, and caution should be taken when applying topical anaesthetic agents to severely traumatised mucosa as well as septic areas.
Topical anaesthetic agents may also come in pressurized containers. They are more effective than when solutions are applied with cotton swabs but it is equally difficult to control the amount of material expelled as well as limiting the area to be covered.
A common adverse effect is that of hypersensitivity caused by repeated contacts especially in individuals who are allergic to the ester-type anaesthetics.

BENZOCAINE

Indications: Temporary relief of ulcer pains, wounds and injured areas of oral mucosa. Use prior to injection, during the taking of dental impressions and intraoral radiographs in patients with excessive gag reflex.
Contra-indications, Precautions, etc: See under Lidocaine.
Dose: See lit.

POM **Benzocaine** *(EDL 13.1)*
Lozenge, Benzocaine 10 mg.

LIDOCAINE

Indications: Surface anaesthetic for use in the mouth, throat, upper GIT.
Contra-indications, Precautions, etc: See Lidocaine in Section 3.4

POM **Lidocaine** *(EDL 13.1)*
Cream, lidocaine 5%
Spray, lidocaine 0.2%

POM **LIDOCADREN®** *(Dizpharm)*
Cream, lidocaine 5%
Spray, lidocaine 0.2%

CHLOROBUTANOL plus BENZOCAINE

Indications: Topical local anaesthetic in pain associated with pulpitis, dressing for exposed

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pulp; dressing for post extraction socket.

POM **SEDATIVE DRESSING**® *(Crutcher Dental)*
Solution, Chlorobutanol 4%, benzocaine 4%, eugenol 46%, peruvian balsam 46%.

CHOLINE SALICYLATE

Indications: Recurrent aphthous ulcer; oral and perioral lesions, erythema multiforme.

POM **BONJELA**®
Oral gel, Choline salicylate 8.7%, cetalkonium chloride 0.01%; in a flavoured gel base.
Pack - 10 g in tube.

18.2 Analgesics

18.2.1 Non-narcotic analgesics
18.2.2 Narcotic analgesics
18.2.3 Non-steroidal anti-inflammatory drugs (NSAIDs)

18.2.1 Non-opioid analgesics and antipyretics

See under section 1.8.1

18.2.2 Opioid analgesics

DIHYDROCODEINE

Indications: Severe pain following maxillo-facial trauma; post surgical operation.
Contra-indications, Precautions, etc: See Dihydrocodeine in Section 1.8.2.

See section 1.8.2 for the preparations of Dihydrocodeine

PENTAZOCINE
Indications: Severe dental pain, jaw fractures.
Contra-indications, Interactions, etc: See Pentazocine in Section 1.8.2.
Dose: By mouth, 50-100 mg every 4 hours.

See section 1.8.2 for the other preparations of Pentazocine

18.2.3 Non-steroidal anti-inflammatory drugs (NSAIDs)

DIFLUNISAL

Indications: Mild to moderate pain following dental extraction, third molar surgery; temporo-mandibular joint (TMJ) pain dysfunction syndrome; dry socket, localised oteitis.
Contra-indications, Precautions, etc: See Diflunisal in Section 2.1.1.
Dose: By mouth, initially 1000 mg as a single dose; then 500 mg 12 hourly.
Not recommended for children under 12 years.

See section 2.1.1 for the preparations of Diflunisal

IBUPROFEN

Indications: Mild to moderate pain following dental extraction; TMJ pains.
Contra-indications, Precautions, etc: See Ibuprofen in Section 2.1.1.
Dose: By mouth, 400 mg every 4-6 hours as necessary not exceeding 2400 mg daily.
Child: 20-40 mg/kg daily in divided doses. Not recommended for children under 6 years.

See section 2.1.1 for the preparations of Ibuprofen

MEFENAMIC ACID

Indications: Mild to moderate pain following dental extraction, third molar extraction; TMJ pain.
Contra-indications, Precautions, etc: See Mefenamic acid in Section 2.1.1.
Dose: By mouth, Adult, 500 mg 3 times daily.

See section 2.1.1 for the preparations of Mefenamic acid.

NIMESULIDE

Indications: Treatment of painful inflammatory conditions associated with dental surgery.
Contra-indications, Precautions, etc: See Nimesulide in Section 2.1.1.
Dose: By mouth, Adult, 100 mg twice daily; may be increased if necessary to 200 mg twice daily.

See Section 2.1.1 for the preparations of Nimesulide

18.3 Vitamin preparations

VITAMIN B COMPLEX

Indications: Adjunct to treatment with broad spectrum antibiotics, angular cheilitis, glossitis.
Dose: 3-6 tabs daily in divided doses.
Infants and young children: 2.5 ml daily.
Older children (school age): 2.5-5 ml daily.

See Section 6.7 for the preparation of

Vitamin B Complex

VITAMIN C

Indications: Spongy and bleeding gums in advanced scurvy, loosening of teeth; adjunct in the treatment of oral wounds and fractures of jaw bones.
Dose: By mouth, *in scurvy*, 0.5-1 g 2-3 times daily.

See Section 6.7 for the preparations of Vitamin C

18.4 Anti-infective drugs

18.4.1 Antibacterials
18.4.2 Antifungals
18.4.3 Antivirals

18.4.1 Antibacterials

PENICILLINS

Indications: Dento-alveolar abscess, cellulitis, Ludwigs angina, osteomyelitis, periodontal abscess; prior to carrying out dental procedures on patients with cardiac defect due to rheumatic fever; in patients receiving corticosteroids, antineoplastic or immunosuppressive drugs; prophylactic use prior to dental treatment of patients with prosthetic joint replacement; acute ulcerative gingivitis; streptococcal sore throat.

See section 9.1.1.1 for details on the various Penicillins and their Preparations

CLINDAMYCIN

Indications: Osteomyelitis
Contra-indications, Precautions, etc: See Clindamycin in Section 9.1.2.10
Dose: By mouth, 150-300 mg 6 hourly.

See section 9.1.2.10 for the preparations of Clindamycin

ERYTHROMYCIN

Indications: A substitute in penicillin hypersensitive patients.
Contra-indications, Precautions, etc: See Erythromycin in Section 9.1.2.4.
Dose: By mouth, Adult, 1-2 g daily in 4 divided doses.

See section 9.1.2.4 for the preparations of Erythromycin

METRONIDAZOLE

Indications: Anaerobic infections, acute ulcerative gingivitis, cancrum oris, dental abscesses, chronic periodontitis.
Contra-indications, Precautions, etc: See Metronidazole in Section 9.1.2.6
Dose: *Acute ulcerative gingivitis*, by mouth, 200 mg 3 times daily for 3 days; child (1-3 years), 50 mg 3 times daily; 3-7 years, 100 mg twice daily; 7-10 years, 100 mg 3 times daily.

See section 9.1.2.6 for details and the preparations of Metronidazole

TETRACYCLINE

Indications: Mouth-wash in the treatment of painful ulceration, recurrent minor and major aphthous ulcers, primary herpetic gingivostomatitis; erosive lichen planus.
Contra-indications, Precautions, etc: See Tetracycline in section 9.1.2.3.
Administration: To be used as Tetracycline mixture containing 250 mg tetracycline per 10 ml; but where not available, the contents of a 250 mg capsule can be stirred in a small amount of water (about 10 ml) and used as follows:
10 ml to be held in the mouth for 2-3 minutes 3 times daily for not longer than 3 days followed by a break of at least 3 days before treatment is recommenced (to avoid oral thrush). The mixture should preferably not be swallowed.
Note: Tetracycline stains the teeth; avoid in children under 12 years of age.

See section 9.1.2.3 for the preparations of Tetracycline

18.4.2 Antifungals

AMPHOTERICIN B

Indications: Candidiasis, chronic irritation of oral mucosa; post radiation; histoplasmosis.
Adverse effects: Allergic dermatitis
Dose: See under the preparations below.

POM **Amphotericin B**
Lozenges, Amphotericin 10 mg.
Dose: Dissolve 1 lozenge slowly in the mouth 4 times daily after food; increased up to 8 daily in severe infections.
Duration of treatment, 10-15 days.
Suspension, Amphotericin 100 mg per ml
Dose: Place 1 ml in the mouth after food and retain near lesions 4 times daily for 14 days.

MICONAZOLE

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Therapeutic category: Broad-spectrum antimycortic.
Pharmacology: Miconazole nitrate is a broad spectrum antimycotic with a bactericidal action against gram positive bacteria. It is effective against dermatophytes, yeasts, candida and other species of fungi.
Indications: Oral thrush; perleche; buccal mycosis; elimination of the GI load of Candida spp. in recurrent *Candida vaginitis*, diarrhoea caused by Candida spp., prophylaxis in immuno compromised patients.
Precautions: Pregnancy.
Adverse effects: Nausea; diarrhoea on long-term treatment.
Dose: By mouth, (Tablets), 500 mg 3 times daily; allow to slowly melt in the mouth before swallowing.
Oral gel (25 mg per ml): Adult, 5-10 ml in the mouth after food and retain near the lesions before swallowing, 4 times daily; child (under 2 years), 2.5 ml twice daily; 2-6 years, 5 ml twice daily; over 6 years, 5 ml 4 times daily.
Duration of treatment usually 3-10 days.

POM **DAKTARIN®** *(Janssen-Cilag)*
Oral gel, Miconazole 2%.
Pack - 40 g (in tube).

POM **MYCOHEAL®** *(Supreme)*
Oral gel, Miconazole 2%.
Pack - 40 g (in tube).

See section 9.2 for the other preparations of Miconazole

NYSTATIN

Indications: Candidiasis, denture stomatitis, angular stomatitis, thrush in infants.
Dose: By mouth, Adult and Children, 1 ml of suspension(100,000 units) 4 times daily; to be held in contact with the lesions for as long as possible. Treatment to be continued for 2 days after the lesions have resolved.

See Section 9.2 for the preparations of Nystatin

18.4.3 Antivirals

ACICLOVIR

Indications: Herpes simplex, Herpes zoster, hairy leucoplakia.
Precautions, Interactions, etc: See Aciclovir in Section 9.5.1.

See Section 9.5.1 for the preparations of Aciclovir

18.5 Corticosteroids

CORTICOSTEROIDS

Indications: Aphthous ulceration, desquamative gingivitis, stomatitis, denture stomatitis, traumatic ulceration, angular stomatitis, osteoarthritis of temporomandibular joint (TMJ), erosive lichen planus.
Contra-indications: Untreated oral infections.

See section 10.3 for other corticosteroids and their preparations

18.6 Mouthwashes

A mouth wash is generally a liquid with pleasant taste and odour which is used to rinse the mouth. They also serve as vehicles for therapeutic or prophylactic agents. Mouth washes containing 0.2% aqueous solution of chlorhexidine gluconate has been reported to reduce supragingival plaque and gingivitis when used regularly. Unpleasant side effects such as staining of tooth structure, tongue and anterior restorations may occur with use; there may also be a reduction in taste sensation. Some surface active agents are also included in mouthwashes which enhances its penetration into surgical wounds, periodental pockets and other oral lesions.
Indications: Generally useful for oral hygiene, cleaning debris from oral wounds, oral hygiene for patients wearing fixed orthodontic appliances, cleaning removable dentures, supra gingival plaque reduction, gingivitis, oral hygiene post immobilisation of the jaws, inflammed mucous membrane and halitosis.

CHLORHEXIDINE

Indications: As above; inhibition of plaque formation.
Dose: Rinse the mouth with 10 ml for about 1 minute 2-3 times daily.

OTC **Chlorhexidine** *(EDL 13.2)*
Mouth-Wash, Chlorhexidine 0.2% solution

OTC **CORSODYL®** *(Reals)*
Mouth-wash, Chlorhexidine gluconate 0.2%; clear or slightly opalescent pink solution with aniseed and peppermint odour.
Pack - 300 ml.

GLYCEROL

Indications: As above

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OTC **Glycerol** *(EDL 13.2)*
Compound Glycerol Mouth-Wash

OTC **Moko Glycerine Borax** *(New Healthway)*
Mouth wash, Glycerine 88%, Borax decahydrate 12%.
Pack - 50 ml.

HEXETIDINE

Indications: As above
Dose: Gargle with 15ml undiluted for about 30 seconds 2-3 times daily.

OTC **Hexetidine** *(EDL 13.2)*
Mouth-wash, Hexetidine 0.1%

OTC **HEXEDENE®** *(Pharma-Deko)*
Mouth-wash, Hexetidine 0.1%; red clear solution.

HYDROGEN PEROXIDE

Indications: As above; cleansing of oral lesions.
Dose: Gargle with 15 ml in half a tumblerful of water for 2-3 minutes 2-3 times daily.

OTC **Hydrogen Peroxide** *(EDL 13.2)*
Mouth-wash, Hydrogen peroxide 6% (20 volumes); aqueous solution.

NYSTATIN

Indications: Oral candidiasis, dentine stomatitis.
Dose: 1 ml in the mouth after food and retain near lesions 4 times daily.

POM **Nystatin** *(EDL 13.2)*
Solution, Nystatin 100,000 units per ml

PHENOL

Indications: As above; acute gingivitis. Use diluted with equal volume of warm water.

OTC **Phenol** *(EDL 13.2)*
Compound Phenol Mouth-Wash.

SODIUM FLUORIDE

Sodium fluoride is a representative fluoride. Various fluorides can serve as alternatives.
Indications: Prevention of dental caries.
Contra-indications: Not for areas where drinking water is fluoridated or where fluorine content is naturally high.
Adverse effects: In recommended doses toxicity unlikely; occasional white flecks on teeth at recommended doses; rarely yellowish-brown discoloration if recommended doses are exceeded.
Nursing considerations: •Tablets may be dissolved in the mouth or sucked and taken preferably in the evening.
•When using mouthwashes, rinse mouth for 1 minute and spit out (most effective when used immediately after brushing teeth). Avoid eating, drinking, or rinsing mouth for 15 minutes after use.
•Avoid giving with milk or dairy products.
Dose: *Prevention of dental caries*, as oral rinse, CHILD over 6 years, 10 ml 0.05% solution daily or 10 ml 0.2% solution weekly.
NOTE: FLUORIDATED TOOTHPASTES ARE ALSO A CONVENIENT SOURCE OF FLUORIDE FOR PROPHYLAXIS OF DENTAL CARIES.

OTC **Sodium flouride** *(WMF 27.2)*
Mouth wash, Sodium fluoride 0.05%, 0.2%.

OTC **Sodium fluoride** *(EDL 13.2)*
Mouth-wash, Sodium fluoride 2%.

OTC **ORALMINT®** *(Pharma-Deko)*
Mouth-wash, sodium fluoride 2%.
Rinse the mouth with 20 ml undiluted solution for 30 seconds.

THYMOL

Indications: Breath problems caused by tobacco, strong smelling foods, drinks and germs; it kills bacteria that cause dental plaque and is effective against gingivitis.
Contra-indications: Hypersensitivity to any of the components.
Precautions: Not to be swallowed.
Adverse effects: Irritant to the gastric mucosa when swallowed.
Dose: Gargle with 20 ml undiluted solution for 15-30 seconds.

OTC **Thymol** *(EDL 13.2)*
Compound Thymol Mouthwash.

OTC **RINSTERINE®** *(Pharma-Deko)*
Mouth-wash, Thymol 0.063%, menthol 0.042%, methyl salicylate 0.055%, ethanol 28.4%, benzoic acid 0.125%, caramel acid proof 0.008%, eucalyptol 0.091%.
Pack - 200 ml.

ZINC CHLORIDE plus ZINC SULPHATE

Indications: Astringent mouth wash.
To be diluted with 20 times its volume of warm water before use (15 ml to a tumblerful of warm

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water).

OTC **Zinc Chloride plus Zinc Sulphate** *(EDL 13.2)*
Mouth-wash, Zinc chloride 1%, zinc sulphate 2%.

18.7 Drugs used in treating the pulp

FORMOCRESOL

Indications: Vital pulpotomy for primary teeth and pulpotomy in necrotic permanent teeth. Intracanal; medicament during root canal therapy.

PARAFORMALDEHYDE

Indications: Devitalising deciduous pulp

POM **Paraformaldehyde**
Paste, Paraformaldehyde 1 g, lignocaine 0.06 g, carmine 0.5 g, propylene glycol 0.75 ml, carbowax 1.5 g.

CRESOL

Indications: Used locally in dilute solutions for its antiseptic and anaesthetic action. When applied to the cavity of a carious tooth it will relieve toothache temporarily. It is also used in agents for sterilization of the root canals during root canal therapy.

POM **BEECHWOOD CREOSOTE**
Indications: Non-vital pulpotomy

POM **SPAD®**
Indications: Acute, subacute and chronic pulpitis, pulpectonies, pulp modification..

POM **IVANOFF®**
Formula G:
Quick setting: Lead orthoplumbate 600 mg, zinc oxide 56.5 g, calcined aluminium 600 g, aluminium hydroxide 12.5 g, colophony 19 g.
Slow setting: Lead orthoplumbate 400 g, zinc oxide 56.5 g, aluminium hydroxide 18.5 g, colophony 19 g.
Indications: Filling of root canals.

POM **ALVEOSPAD®**
Acriflavine HCl 0.45 g, cetocal 1.36 g, ethyl P–aminobenzoate 2.72 g, menthol 1.81 g, clove oil 1.81 g, absorbable gauze 9.5 g, excipient to 100 g.
Indications: Alveolitis.
Dose: Introduce a quantity of Alveospad into the socket after extraction.

POM **PULPISEDOL®**
Tetracaine Chloride 4 g, benzalkonium bromide 0.5 g, essence of clove 2 g, excipient to 100 g.
Indications: Acute pulpitis
Dose: Insert a cotton wool impregnated with pulpisedol into the exposed cavity and cover with temporary cement.

18.8 Drugs used in treating orofacial pathologies

CARBAMAZEPINE

Indications: Trigeminal neuralgia, glosso-pharyngeal neuralgia, post-herpetic neuralgia.
Contra-indications, Precautions, etc: See Carbamazepine in Section 1.7.1.
Dose: By mouth, 200 g in the morning and 100 g at night; may be increased up to a max. 800-1000 mg daily depending on the severity and patients response.

See section 1.7.1 for the preparations of Carbamazepine

PREDNISOLONE

Indications: Bell palsy, erythema multiforme, pemphigus.
Contra-indications, Precautions, etc: See Prednisolone in Section 10.3.
Dose: By mouth, 60 mg daily for 5 days which should be tailed down on a sliding scale for 5 days.

See section 10.3 for the preparations of Prednisolone

BETAMETHASONE

Indications: Oral pemphigoid, epidermolysis bullosa.
Contra-indications, Precautions, etc: See Betamethasone in Section 10.3

See section 10.3 for the preparations of Betamethasone

18.9 Others

Calcium hydroxide is used clinically as a pulp capping agent and in pulpotomy on vitally exposed pulps. It allows the recovery of the cells of the pulpal tissue to permit a reparative response following the initial acute inflammatory reactions. It is also applied in all large vital exposures of teeth which are not fully developed in order to promote completion of apex formation. Calcium hydroxide also protects underlying pulp from irritation by the

acidity of some dental cements, acid used to etch enamel surface prior to restoration by an acid resin etch bonding technique and the irritating component of composite filling materials.

Zinc Oxide-eugenol is widely used as temporary filling materials, crown cements, root canal sealers and as components of periodental dressing materials. It has both analgesic and topical local anaesthetic effects on both the hard and soft tissues in the mouth. In addition, the Zinc oxide preparations have antiseptic properties as well as providing a good thermal insulation for metallic filling materials. These agents should not be used under resin restorations since one of the components, eugenol, acts as an inhibitor of the polymerization reaction of the unfilled and filled resin.

CALCIUM HYDROXIDE PREPARATIONS

Indications: Indirect pulp capping, direct pulp capping, vital pulpotomy, antiseptic root canal dressing.

POM **DYCAL®**
Base: Calcium tungstate 17.6%, calcium phosphate 31.4%, zinc oxide 8.7% in glycol salicylate base.
Catalyst: Calcium hydroxide 51%, zinc oxide 9.23%, zinc stearate 0.29% in ethylene toluene sulphonamide.

ZINC OXIDE-EUGENOL PREPARATIONS

Indications: Therapeutic bases, temporary fillings, crown cements, periodental surgical dressings and root canal sealers.

POM **COE-PAK®**
Two pastes of 50g each
Paste 1: Zinc oxide 45%, magnesium oxide 32%, mineral oil 6%, peanut oil 11% resin oil 6%.
Paste 2: Polymerised resin 53%, ethyl cellulose and lanolin 4%, 3% each of peruvian balsam and chlorothymol.

FLUORIDE PREPARATIONS

Indications: Prevention of dental caries

POM **FLUORITAB®**
Tablets, Sodium fluoride 2.21 mg (equiv. to 1 mg fluoride ion).
Dose: One tab each day to be chewed before swallowing.

POM **FLURA–LOZ®**
Lozenge, Sodium fluoride 2.21 mg (equiv to 1 mg fluoride ion).
Dose: One lozenge daily.

POM **FLUORIDENT®**
Gel, Sodium fluoride 2%, hydrogen fluoride 0.34% phosphoric acid 0.98%.

DESENSITIZING AGENTS

Indications: Exposed dentine, erosion, severe attrition.

POM **LORVIC® Desensitizer**
Aqueous gel, strontium chloride 3.96%, sodium fluoride 0.42%; in 10 g bottle.
Dose: To be applied to the exposed dentine weekly

ARTIFICIAL SALIVA

Indications: Temporary or permanent salivary gland dysfunction (xerostomia). Post radiation of jaw lesions.

POM **MOI-STIR®**
Aqueous solution of carboxymethyl cellulose, sorbitol, potassium chloride, calcium, chloride, sodium chloride, magnesium chloride; with methyl and propyl parabens as preservatives. Packed as a pump spray.

POM **SALIVART®**
Aqueous solution of carboxymethyl cellulose, sorbitol, potassium chloride, calcium chloride, magnesium chloride, potassium monohydrogen phosphate. Packed as sterile aerosol with CO_2 propellant.

POM **SALIVA-AID®**
Aqueous solution of carboxymethyl cellulose, sorbitol, potassium chloride, calcium chloride, sodium chloride with propyl paraben as preservative.
Packed as pump spray.

POM **XERO-LUBE®**
Aqueous solution of carboxymethyl cellulose, sorbitol, potassium chloride, calcium chloride, sodium chloride, magnesium chloride, sodium fluoride; with methyl paraben as preservative. Packed as pump spray.

19. Antidotes and other substances used in poisoning

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19.1 General care and non-specific treatment
19.2 Specific antidotes
19.2.1 Paracetamol overdosage
19.2.2 Opioid analgesic overdosage
19.2.3 Organophosphate and carbamate poisoning
19.2.4 Iron poisoning and iron and aluminium overload
19.2.5 Heavy metal poisoning
19.2.6 Methaemoglobinaemia
19.2.7 Cyanide poisoning
19.2.8 Heparin overdosage
19.2.9 Anticoagulant overdosage

These notes are only guidelines and it is strongly recommended that poisons information centres be consulted in cases where there is doubt about the degree of risk or about appropriate management.

19.1 General care and non-specific treatment

All patients who show features of poisoning should generally be admitted to hospital. Patients who have taken poisons with delayed actions should also be admitted, even if they appear well; delayed-action poisons include acetylsalicylic acid, iron, lithium, paracetamol, paraquat, tricyclic antidepressants and warfarin. The effects of modified-release or prolonged-release preparations are also delayed. However, it is often impossible to establish with certainty the identity of the poison and the size of the dose but information on the type and timing of poisoning may be useful for symptomatic management. Few patients require active removal of the poison.

Most patients must be treated symptomatically and monitored. Particular care must be given to maintenance of respiration and blood pressure. Assisted ventilation may be required. Cardiac conduction defects and arrhythmias often respond to correction of underlying hypoxia, acidosis, or other biochemical abnormalities. Hypothermia which may develop in patients who have been unconscious for some hours is best treated by wrapping the patient in blankets to conserve body heat. Convulsions which are prolonged or recurrent may be controlled by intravenous diazepam. In some situations removal of the poison from the stomach by gastric lavage may be appropriate (see below). Activated charcoal can bind many poisons in the stomach and therefore prevent absorption. Active elimination techniques such as repeated administration of activated charcoal can enhance the elimination of some drugs after they have been absorbed (see below). Other techniques to enhance elimination of poisons after their absorption are only practical in hospital and are only suitable for a small number of patients and only to a limited number of poisons. Methods include haemodialysis and haemoperfusion. Alkalinization of urine can be used to increase the elimination of salicylates. Forced alkaline diuresis is no longer recommended.

Gastric lavage

The dangers of attempting to empty the stomach have to be balanced against the toxicity of the ingested poison, as assessed by the quantity ingested, the inherent toxicity of the poison, and the time since ingestion. Gastric emptying is clearly unnecessary if the risk of toxicity is small or if the patient presents too late. Emptying the stomach may be of value if undertaken within 1–2 hours after ingestion. The main risk is with inhalation of stomach contents and gastric lavage should **not** be undertaken in drowsy or comatose patients without assistance of an anaesthetist so that the airway can be protected by a cuffed endotracheal tube. Gastric lavage must not be attempted after corrosive poisoning or for hydrocarbon products which could be dangerous if aspirated.

Emesis

Induction of emesis for the treatment of poisoning is **not recommended**. There is no evidence that it prevents absorption of the poison and it may increase the likelihood of aspiration. Furthermore, the effects of the emetic substance may complicate diagnosis.

Prevention of absorption

Given by mouth **activated charcoal** can bind many poisons in the gastrointestinal system, thereby reducing their absorption. The sooner it is given, the more effective it is, but it may be effective for up to 1 hour after ingestion of the poison. It may be effective several hours after poisoning with modified-release preparations or drugs with anticholinergic (antimuscarinic) properties. It is relatively safe and particularly useful for prevention of absorption of poisons which are toxic in small amounts, for example, antidepressants. Furthermore, repeated doses of activated charcoal enhance the faecal elimination of some drugs (that undergo enterohepatic or enteroenteric recycling) several hours after ingestion and after they have been absorbed, for example phenobarbital, theophylline.

ACTIVATED CHARCOAL

Indications: Treatment of acute poisoning.

Contra-indications: Poisoning by hydrocarbons with high potential for harm if aspirated; poisoning by corrosive substances—may prevent visualization of lesions caused by poison.

Precautions: Drowsy or unconscious patients—risk of aspiration (intubate before administration via nasogastric or gastric tube); not effective for poisoning with alcohols, clofenotane (dicophane, DDT), cyanides, malathion, and metal salts including iron and lithium.

Adverse effects: Black stools; vomiting, constipation or diarrhoea; pneumonitis—due to aspiration.

Dose: *Poisoning (prevention of absorption)*, by mouth, ADULT 50–100 g as a single dose, as soon as possible after ingestion of poison; INFANT 1 g/kg as a single dose; CHILD 1–12 years, 25 g as a single dose (50 g in severe poisoning). *Poisoning (active elimination)*, by mouth, ADULT and CHILD over 1 year, 25–50 g initially, then 25–50 g every 4–6 hours; INFANTS 1 g/kg every 4–6 hours.

OTC **Activated charcoal** *(WMF4.1)*
Powder (Powder for oral suspension), Activated charcoal.

19.2 Specific antidotes

19.2.1 Paracetamol overdosage
19.2.2 Opioid analgesic overdosage
19.2.3 Organophosphate and carbamate poisoning
19.2.4 Iron poisoning and iron and aluminium overload
19.2.5 Heavy metal poisoning
19.2.6 Methaemoglobinaemia
19.2.7 Cyanide poisoning
19.2.8 Heparin overdosage
19.2.9 Anticoagulant overdosage

19.2.1 Paracetamol overdosage

As little as 10–15 g or 150 mg/kg of paracetamol taken within 24 hours may cause severe hepatocellular necrosis and less frequently renal tubular necrosis. The only early features of poisoning, nausea and vomiting, usually settle within 24 hours. Persistence beyond this time, often with the onset of right subcostal pain and tenderness, usually indicates the development of liver damage which is maximal 3–4 days after ingestion. In spite of a lack of significant early symptoms, patients who have taken an overdose of paracetamol should be transferred to hospital urgently.

Administration of activated charcoal should be considered if paracetamol in excess of 150 mg/kg or 12 g, whichever is smaller, is thought to have been ingested within the previous hour.

Acetylcysteine or **methionine** protect the liver if given within 10–12 hours of ingesting paracetamol. Acetylcysteine, given intravenously is most effective within 8 hours of overdosage, but is effective for up to and possibly beyond 24 hours. Alternatively, methionine may be given by mouth provided the overdose was ingested within 10–12 hours and the patient is not vomiting. However, acetylcysteine is the preferred treatment. Concurrent use of activated charcoal and specific oral antidotes should be avoided.

In remote areas methionine should be

given, since administration of acetylcysteine outside hospital is not generally practicable. Once the patient is in hospital the need to continue antidote treatment can be assessed from plasma-paracetamol concentrations.

Acetylcysteine

Indications: Paracetamol overdosage
Precautions: Asthma
Adverse effects: Hypersensitivity reactions including rashes, anaphylaxis.
Dose: *Paracetamol overdosage*, by intravenous infusion, ADULT and CHILD initially, 150 mg/kg in 200 ml glucose 5% over 15 minutes, followed by 50 mg/kg in 500 ml glucose 5% over 4 hours, then 100 mg/kg in 1000 ml glucose 5% over 16 hours.

NOTE: CHILDREN ARE GIVEN THE SAME DOSES OF ACETYLCYSTEINE AS ADULTS, BUT THE VOLUME OF INFUSION MAY NEED TO BE REDUCED TO AVOID FLUID OVERLOAD.

POM **Acetylcysteine** *(WMF 4.2.1)*
Injection (Concentrate for dilution for infusion), Acetylcysteine 200 mg/ml, 10-ml ampoule.

DL-METHIONINE

Indications: Paracetamol overdosage
Precautions: Severe liver disease—may precipitate hepatic encephalopathy; avoid concurrent use with activated charcoal.
Adverse effects: Nausea, vomiting, drowsiness, irritability.
Dose: *Paracetamol overdosage*, by mouth, ADULT and child over 6 years, 2.5 g initially, followed by 3 further doses of 2.5 g every 4 hours, child under 6 years 1 g initially, followed by 3 further doses of 1 g every 4 hours.

POM **DL-Methionine** *(WMF 4.2.1)*
Tablets, DL-Methionine 250 mg.

POM **Methionine** *(EDL 4.2)*
Tablet, Methionine 250 mg.

19.2.2 Opioid analgesic overdosage

Opioids cause varying degrees of coma, respiratory depression and pinpoint pupils. **Naloxone** is a specific antidote indicated if there is coma or bradypnoea. Naloxone has a shorter duration of action than many opioids so close monitoring and repeated injections are required depending on respiratory rate and depth of coma; naloxone may alternatively be given by intravenous infusion. The effects of some opioids such as buprenorphine are only partially reversed by naloxone.

Acute withdrawal syndromes may be precipitated by the use of naloxone in patients with a physical dependence on opioids or in overdosage with large doses; a withdrawal syndrome may occur in neonates of opioid-dependent mothers.

NALOXONE

Indications: Opioid overdosage; postoperative respiratory depression (section 3.5).
Precautions: Physical dependence on opioids or other situations where acute withdrawal syndrome may be precipitated (see above); pregnancy (Appendix 2); breastfeeding (Appendix 3); cardiovascular disease.
Adverse effects: Nausea, vomiting, sweating—may also be due to opioid withdrawal.
Nursing considerations: •Monitor respiratory rate, heart rate, B.P.; keep oxygen and other resuscitative measures available.
•Since duration of narcotic effect may exceed that of naloxone, patient may relapse into respiratory depression; repeated doses of naloxone may be ordered.
Dose: *Overdosage of opioids*, by intravenous injection, ADULT 0.8–2 mg repeated at intervals of 2–3 minutes to a maximum of 10 mg, if respiratory function does not improve, question diagnosis; CHILD 10 micrograms/kg; a subsequent dose of 100 micrograms/kg if no response

NOTE: NALOXONE HYDROCHLORIDE MAY BE ADMINISTERED IN THE SAME DOSES BY INTRAMUSCULAR OR SUBCUTANEOUS INJECTION, BUT ONLY IF THE INTRAVENOUS ROUTE IS NOT FEASIBLE (SLOWER ONSET OF ACTION).

Overdosage of opioids, by continuous intravenous infusion using an infusion pump, adult 10 mg diluted in 50 ml glucose 5% intravenous infusion at a rate adjusted according to response.

POM **Naloxone** *(WMF 4.2.2)*
Injection (Solution for injection), Naloxone HCl 400 micrograms/ml, 1-ml ampoule.

POM **Naloxone** *(EDL 4.2)*
Injection, Naloxone 0.4 mg; in 1 ml amp

19.2.3 Organophosphate and carbamate poisoning

Organophosphates are absorbed through the bronchi and intact skin as well as from the gastrointestinal tract. Initial treatment of organophosphate or carbamate poisoning includes prevention of further absorption by emptying the stomach by gastric lavage, moving patient to fresh air supply, removing contaminated clothing and washing contaminated skin. A clear airway must be maintained.

Organophosphates inhibit cholinesterases and thus prolong the effects of acetylcholine. Toxicity depends on the particular compound involved, and onset after skin exposure may be delayed. **Atropine** will reverse the muscarinic effects of acetylcholine and is used (in conjunction with oximes such as pralidoxime) with additional symptomatic treatment.

Additional treatment for carbamate poisoning is generally symptomatic and supportive. **Atropine** may be given but may not be required because of the rapidly reversible type of cholinesterase inhibition produced (oximes should not be given).

ATROPINE

Indications: Organophosphate and carbamate poisoning; premedication (section 3.2); antispasmodic (section 4.2); mydriasis and cycloplegia (section 13.3).
Precautions: Children, elderly, Down syndrome; angle-closure glaucoma; myasthenia gravis; gastrointestinal disorders; prostatic enlargement; cardiac disorders; pyrexia; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions**: Appendix 1.
Dose: *Organophosphate poisoning*, by intramuscular or intravenous injection (depending on severity of poisoning), ADULT 2 mg (child 20 micrograms/kg) every 5–10 minutes until the skin becomes flushed and dry and tachycardia develops.

POM **Atropine** *(WMF 4.2.3)*
Injection (Solution for injection), Atropine sulfate 1 mg/ml, 1-ml ampoule.

POM **Atropine** *(EDL 4.2)*
Injection, Atropine (as sulphate) 1 mg; in 1 ml amp.

19.2.4 Iron poisoning and iron and aluminium overload

Mortality from iron poisoning is reduced by specific therapy with deferoxamine which chelates iron. Before administration of **deferoxamine** the stomach should be emptied by gastric lavage (with a wide-bore tube) within 1 hour of ingesting a significant quantity of iron or if radiography reveals tablets in the stomach. Deferoxamine is also used to diagnose and treat chronic iron overload. It is used in the diagnosis of aluminium overload and to treat aluminium overload in patients with end-stage renal failure undergoing maintenance haemodialysis.

DEFEROXAMINE

Synonym: Desferrioxamine
Indications: Acute iron poisoning; chronic iron overload; aluminium overload
Precautions: Renal impairment (Appendix 4); eye and ear examinations before and at 3-month intervals during treatment; aluminium encephalopathy (may exacerbate neurological dysfunction); pregnancy (Appendix 2); breastfeeding (Appendix 3); children under 3 years (may retard growth).
Adverse effects: Anaphylaxis; flushing, urticaria, hypotension, shock (especially if given by too rapid intravenous infusion); gastrointestinal disturbances; fever, headache, arthralgia, myalgia; arrhythmias; renal impairment; blood disorders; neurological disturbances including neuropathy, paraesthesia, and dizziness; convulsions; Yersinia and mucormycosis infections; visual disturbances (including lens opacity and retinopathy) and hearing loss; rash; rarely, growth retardation (in young children); rarely, adult respiratory distress syndrome; pain on intramuscular or subcutaneous injection; local irritation on prolonged subcutaneous infusion; reddish-brown discoloration of urine.
Nursing considerations: •Administer by I.M. injection; give I.V. only if patient is in shock and change to I.M as soon as possible.
•May turn urine pink.
•Keep adrenaline ready in case of anaphylaxis.

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Dose: *Acute iron poisoning*, by slow intravenous infusion, ADULT and CHILD initially 15 mg/kg/hour, reduced after 4–6 hours so that total dose does not exceed 80 mg/kg in 24 hours.

Chronic iron overload, by subcutaneous or intravenous infusion, ADULT and CHILD lowest effective dose, usually within range of 20–60 mg/kg/day on 4–7 days a week.

Aluminium overload in end-stage renal failure, by intravenous infusion, ADULT and CHILD 5 mg/kg, once a week during last hour of dialysis.

Diagnosis of iron overload, by intramuscular injection, ADULT and CHILD 500 mg.

Diagnosis of aluminium overload, by intravenous infusion, ADULT and CHILD 5 mg/kg during last hour of dialysis.

RECONSTITUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS. FOR FULL DETAILS AND WARNINGS RELATING TO ADMINISTRATION FOR THERAPEUTIC OR DIAGNOSTIC PURPOSES, SEE MANUFACTURER'S LITERATURE.

POM **Deferoxamine** *(WMF 4.2.4)*
Injection (Powder for solution for injection or infusion), Deferoxamine mesilate 500-mg vial.

POM **Deferoxamine** *(EDL 4.2)*
Injection, Deferoxamine (as mesilate) 500 mg; in vial.

19.2.5 Heavy metal poisoning

Heavy metal poisoning may be treated with a range of antidotes including **dimercaprol**, **penicillamine**, **potassium ferric hexacyanoferrate** and **sodium calcium edetate**. Penicillamine is also used to promote excretion of copper in Wilson disease.

Dimercaprol

Synonym: BAL; British Anti-Lewisite.

Indications: Acute poisoning by antimony, arsenic, bismuth, gold, mercury, possibly thallium; adjunct (with sodium calcium edetate) in lead poisoning.

Contra-indications: Not indicated for iron, selenium or cadmium poisoning; severe hepatic impairment (unless due to arsenic poisoning).

Precautions: Hypertension; renal impairment (discontinue or use with extreme caution if renal failure occurs during treatment); any abnormal reaction such as hyperpyrexia should be assessed; elderly; pregnancy; breastfeeding.

Adverse effects: Hypertension, tachycardia; malaise, nausea, vomiting, abdominal pain, salivation, lacrimation, sweating, burning sensation in the mouth, throat and eyes; feeling of constriction in throat and chest; headache, muscle spasms, tingling of the extremities; fever in children; local pain and abscess at injection site.

Nursing considerations: •Administer by deep I.M. only; avoid I.V. route. May massage injection site after drug is given.
•Keep urine alkaline because chelate dissociates in acid media causing renal damage; oral sodium bicabonate may be prescribed.
•Drug has an unpleasant, garlic-like odour.
•Avoid contact with skin to prevent skin reaction.

Dose: *Poisoning by heavy metals*, by intramuscular injection, ADULT 400–800 mg in divided doses on first day, then 200–400 mg daily in divided doses on the second and third days, then 100–200 mg daily in divided doses on subsequent days (single doses generally should not exceed 3 mg/kg, but in severe poisoning initial single doses up to 5 mg/kg may be required); CHILD calculate on basis of body-weight using same unit dose/kg as for adult in similar clinical circumstances.

POM **Dimercaprol** *(WMF 4.2.5)*
Oily injection (Solution for injection), Dimercaprol 50 mg/ml in arachis (peanut) oil, 2-ml ampoule.

POM **Dimercaprol** *(EDL 4.2)*
Injection, Dimercaprol 50 mg per ml; in 2 ml amp.

Penicillamine

Indications: Poisoning by heavy metals, particularly lead and copper; Wilson disease; severe rheumatoid arthritis (section 2.1.2).

Contra-indications: Hypersensitivity; lupus erythematosus.

Precautions: Monitor throughout treatment including blood counts and urine tests; renal impairment (Appendix 4); pregnancy (Appendix 2); avoid concurrent

gold, chloroquine or immunosuppressive treatment; avoid oral iron within 2 hours of a dose; **interactions**: Appendix 1.

BLOOD COUNTS: IN WILSON DISEASE, CONSIDER WITHDRAWAL IF PLATELET COUNT FALLS BELOW 120 000/MM3 OR WHITE BLOOD CELLS BELOW 2500/MM3 OR IF 3 SUCCESSIVE FALLS WITHIN REFERENCE RANGE (CAN RESTART AT REDUCED DOSE WHEN COUNTS RETURN TO REFERENCE RANGE BUT PERMANENT WITHDRAWAL NECESSARY IF NEUTROPENIA OR THROMBOCYTOPENIA RECUR).

PATIENT ADVICE: IN WILSON DISEASE WARN PATIENT TO TELL DOCTOR IMMEDIATELY IF SORE THROAT, FEVER, INFECTION, NON-SPECIFIC ILLNESS, UNEXPLAINED BLEEDING AND BRUISING, PURPURA, MOUTH ULCERS OR RASH DEVELOP.

Adverse effects: Initially nausea (less of a problem if taken with food and on retiring), anorexia, fever; taste loss (mineral supplements not recommended); blood disorders including thrombocytopenia, neutropenia, agranulocytosis and aplastic anaemia; proteinuria, rarely haematuria (withdraw immediately); haemolytic anaemia, nephrotic syndrome, lupus erythematosus-like syndrome, myasthenia gravis-like syndrome, polymyositis (rarely with cardiac involvement), dermatomyositis, mouth ulcers, stomatitis, alopecia, bronchiolitis and pneumonitis, pemphigus, Goodpasture syndrome and Stevens-Johnson syndrome also reported; male and female breast enlargement reported; rash early in treatment (usually allergic—may need temporary withdrawal), late rashes (reduce dose or withdraw treatment).

Dose: *Heavy metal poisoning*, by mouth, ADULT 1–2 g daily in 4 divided doses before food (continue until urinary lead stabilised at less than 500 micrograms/day); CHILD 20–25 mg/kg daily in divided doses.
Wilson disease, by mouth, ADULT 1.5–2 g daily in divided doses before food; maximum 2 g daily for 1 year then maintenance 0.75–1 g daily; ELDERLY 20 mg/kg daily in divided doses adjusted according to response; CHILD up to 20 mg/kg daily in divided doses; minimum 500 mg daily.

POM **Penicillamine** *(WMF 4.2.5)*
Capsules, Penicillamine 125 mg [not included on WHO Model List], 250 mg.
Tablets, Penicillamine 125 mg [not included on WHO Model List], 250 mg.

POTASSIUM FERRIC HEXACYANOFERRATE

Synonym: Prussian Blue
Indications: Thallium poisoning
Contra-indications: Constipation; paralytic ileus.
Adverse effects: Constipation, dark stools.
Dose: *Treatment of thallium poisoning*, by duodenal tube, ADULT 125 mg/kg in 100 ml of mannitol 15% twice daily (until urinary thallium stabilized at 500 micrograms or less/day).

POM **Potassium ferric hexacyanoferrate** *(WMF 4.2.5)*
Powder for oral solution, Potassium ferric hexacyanoferrate.

SODIUM CALCIUM EDETATE

Synonym: Calcium EDTA; Edetate Calcium Disodium.
Indications: Lead poisoning.
Precautions: Renal impairment.
Adverse effects: Renal tubular necrosis; nausea, diarrhoea, abdominal cramps; thrombophlebitis (if given too rapidly or as too concentrated a solution), fever, malaise, headache, myalgia, thirst, chills, histamine-like responses (sneezing, nasal congestion, lacrimation) and transient hypotension.
Nursing considerations: •Administer preferably by IM injection. 1 ml of 1% Procaine HCl may be added to each ml of calcium EDTA to minimize pain at injection site.
•Avoid rapid IV infusions.
•Monitor BUN, Creatinine, Urinalysis, I&O, and ECG during therapy.
Dose: *Treatment of lead poisoning*, by intravenous infusion, ADULT and CHILD up to 40 mg/kg twice daily for up to 5 days; repeated if necessary after interval of 48 hours.
DILUTION AND ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Sodium calcium edetate** *(WMF 4.2.5)*
Infusion (Concentrate for solution for infusion), Sodium calcium edetate 200 mg/ml, 5-ml ampoule.

POM **Sodium Calcium Edetate** *(EDL 4.2)*
Injection, Sodium calcium edetate 200 mg per ml; 5 ml amp.

19.2.6 Methaemoglobinaemia

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Methylthioninium chloride can lower the levels of methaemoglobin in red blood cells and is used in the treatment of methaemoglobinaemia. In large doses, it may cause methaemoglobinaemia and therefore methaemoglobin levels should be monitored during treatment.

METHYLTHIONINIUM CHLORIDE

Synonym: Methylene Blue
Indications: Acute methaemoglobinaemia.
Contra-indications: Severe renal impairment; methaemoglobinaemia due to chlorate or induced by sodium nitrite in treatment of cyanide poisoning.
Precautions: G6PD deficiency—may cause haemolytic anaemia; monitor blood methaemoglobin throughout treatment; pregnancy; breastfeeding.
Adverse effects: Nausea, vomiting, abdominal pain, chest pain, headache, dizziness, confusion, profuse sweating; hypertension or hypotension reported; haemolytic anaemia—in G6PD deficiency; methaemoglobinaemia—with high dosage; bluish skin discoloration; blue saliva, urine and faeces.
Dose: *Acute methaemoglobinaemia*, by slow intravenous injection over several minutes ADULT and CHILD 1–2 mg/kg as a single dose; may be repeated after 1 hour if required.
ADMINISTRATION: ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Methylthioninium chloride** *(WMF 4.2.6)*
Injection (Solution for injection), Methylthioninium chloride 10 mg/ml, 10-ml ampoule.

19.2.7 Cyanide poisoning

Cyanide poisoning may be treated with **sodium nitrite** followed by **sodium thiosulfate**.

SODIUM NITRITE

Indications: Cyanide poisoning (together with sodium thiosulfate).
Precautions: Monitor plasma methaemoglobin levels; severe cardiovascular or cerebrovascular disease
Adverse effects: Vasodilatation resulting in syncope, hypotension, tachycardia, flushing, headache; methaemoglobinaemia; cyanosis, dyspnoea, tachypnoea, nausea, vomiting and abdominal pain.
Dose: *Cyanide poisoning*, by intravenous injection over 5–20 minutes, ADULT 300 mg (followed by sodium thiosulfate); further dose of 150 mg after 30 minutes if symptoms recur; child 4–10 mg/kg (initially lower dose).

POM **Sodium nitrite** *(WMF 4.2.7)*
Injection (Solution for injection), Sodium nitrite 30 mg/ml, 10-ml ampoule.

SODIUM THIOSULFATE

Indications: Cyanide poisoning (together with sodium nitrite); pityriasis versicolor (section 15.1.2).
Dose: *Cyanide poisoning, after sodium nitrite*, by slow intravenous injection over about 10 minutes, ADULT 12.5 g; further dose of 6.25 g after 30 minutes if symptoms recur; child 400 mg/kg.

POM **Sodium thiosulfate** *(WMF 4.2.7)*
Injection (Solution for injection), Sodium thiosulfate 250 mg/ml, 50-ml ampoule.

19.2.8 Heparin overdosage

PROTAMINE

See under section 6.2.2

19.2.9 Anticoagulant overdosage

PHYTOMENADIONE (Vitamin K_1)

See under section 6.2.2

20. Medical laboratory index

RETURN

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20.1 Clinical chemistry tests

20.1.1 Whole blood, serum or plasma tests
20.1.2 Urine clinical chemistry tests (Urinalysis)
20.1.3 Faecal clinical chemistry tests
20.1.4 Cerebrospinal fluid (CSF) chemistry tests

20.1.1 Whole blood, serum or plasma tests

A. RENAL FUNCTION TESTS

Renal functions may be assessed by measuring blood urea nitrogen (BUN) and serum creatinine. Renal function decreases with age, which must be taken into account when interpreting test values.

These tests primarily evaluate glomerular functions by assessing the glomerular filteration rate(GFR).

In many renal diseases, urea and creatinine accumulate in the blood because they are not excreted properly. These tests also aid in determining drug dosage for drugs excreted through the kidneys.

(a) CREATININE

Reference (Normal) Range:

Males: 0.7-1.4 mg%

Females: 0.4-1.2 mg%.

The reference values are slightly lower in children. Values depend on muscle mass.

Analyte: Creatinine is a nitrogenous waste product formed from the metabolism of creatinine in the skeletal muscle. Creatinine diffuses freely throughout the body water. It is filtered from the ECF by the kidney and excreted mainly in the urine.

Value of Test: Measurement of serum or plasma creatinine is an important test of kidney function. It is recommended in preference to the measurement of serum or plasma urea because it is a better indicator of overall renal function and progress in renal failure. Serum creatinine levels are less affected than urea levels by age, dehydration, and catabolic states, e.g. fever, sepsis, and internal bleeding; changes in diet such as low intake of protein.

Test Method: Jaffe-Slot modified alkaline

picrate colorimetric method.

Specimen: Fresh serum or plasma which must be free from haemolysis.

Interpretation of Results: *Increases* - Any disease or condition that causes a fall in GFR will increase plasma creatinine levels. Diseases that can cause renal failure with a reduced GFR include glomerulonephritis, pyelonephritis and renal tuberculosis; cancer of the bladder, haemorrhage, septicaemia are other causes of renal failure and increased plasma creatinine levels. Non-renal causes include strenuous exercise and the effects of drugs such as salicylates, ascorbic acid, cephalosporin antibiotic.

Uraemia is the presence of excessive amounts of creatinine, urea, and other nitrogenous waste products in the blood, as occurs in renal failure.

Decreases - Generally of little clinical significance. Diseases associated with muscle wasting reduce the level of creatinine in the blood.

(b) UREA OR BLOOD UREA NITROGEN (BUN)

Reference (Normal) Range: Adults: 20-46 mg%

Infants: 8-35 mg%.

The reference values increase with age. Values are slightly lower in females and also in children.

Analyte: Urea is the main waste product of protein breakdown in liver. It passes into the circulation and is excreted by the kidneys. Depending on a person's state of hydration, some of the urea is reabsorbed into the blood; the rate of reabsorption being inversely related to the rate of urine flow.

Value of test: As a test of renal function, the measurement of plasma is less useful than that of plasma creatinine; no advantage in measuring both.

Test Method: Diacetyl monoxime urea method.

Specimen: Serum or plasma.

Interpretation of Results: *Increases* - A marked and prolonged increase indicates damaged renal function. See under creatinine. Non-renal causes of increase include dehydration, diuretic therapy, GI blood loss; any condition associated with increased protein breakdown such as pneumonia, surgery, typhoid fever, malaria, major trauma, meningitis.

Decreases - Low urea levels may be found in pregnancy, malnutrition and AIDS, severe liver disease, water overload.

B. LIVER FUNCTION TESTS

(a) LIVER ENZYMES

See under the Serum Enzyme Tests below.

(b) BILIRUBIN

Reference (Normal) Range: Total Bilirubin-Adult: 0.2-1.3 mg%; Newborns: 0.5-4.0 mg%. Highest values in the first 3-5 days of life.

Analyte: Bilirubin is formed from the breakdown of erythrocytes and other haem (iron porphyrin) - containing proteins such as myoglobin and cytochromes. Bilirubin is either conjugated (direct) which is water-soluble unconjugated (indirect) which is not soluble in water. Conjugated bilirubin is deconjugated and reduced by bacteria in the intestine to form **urobilinogen**. In a healthy individual about 5% of total plasma bilirubin is conjugated and 95% or more, unconjugated.Urine contains a trace of urobilinogen and no bilirubin.

Value of Test: The measurement of serum or plasma bilirubin is usually performed to investigate the causes of liver disease and jaundice, and to monitor a person's progress, an infant with serious neonatal jaundice (high levels of unconjugated bilirubin).

Test Method: Jendrassik and Grof bilirubin method.

Specimens: Fresh serum or plasma from EDTA or heparin anticoagulated blood (not more than 24 hour hold).

Interpretation of Results: A rise in the level of bilirubin in the blood is called hyper-bilirubinaemia. Main causes include:

(i) Overproduction of bilirubin (unconjugated) caused by an excessive breakdown of red cells (haemolytic jaundice), e.g. haemolytic disease of the newborn, incompartible blood transfusion, drugs.

(ii) Liver cell damage with increase in both conjugated and unconjugated bilirubin (hepatocellular jaundice), e.g. hepatitis, typhoid, drugs.

(iii) Metabolic disturbances in the liver involving defective conjugation, transport and/or excretion of bilirubin, e.g. neonatal jaundice also known as "physiological jaundice".

(iv) Partial or complete stopping of the flow bile with a build up of conjugated bilirubin in the blood (obstructive jaundice or cholestasis).

(c) ALBUMIN

Reference (Normal) Range: 3.0-4.5 g% or g/100 ml.

Analyte: Albumin is produced entirely in the liver and constitutes about 60% of total serum protein. It regulates the flow of water between

the plasma and the tissue fluid thereby helping to check oedema. It also binds and inactivates substances including bilirubin and drugs such as penicillin, sulphonamides, salicylates, etc.

Value of Test: Serum albumin is mainly measured to investgate liver diseases, protein energy malnutrition, disorders of water balance, nephrotic syndrome, and protein-losing GI diseases.

Test Method: Bromocresol green (BCG) binding method.

Specimens: Non-lipaemic, non-icteric patient's serum; the blood must be collected with minmum of venous stasis and haemolysis should be avoided. Bilirubin, haemoglobin, lipids and salicylates can interfere in the test.

Interpretation of Results: *Increases* - Serum albumin levels are rarely raised except artefactually by prolonged venous stasis.

Decreases - Hypoalbuminaemia occurs whenever there is increased plasma volume (e.g. in pregnancy). Pathological causes include:

(i)Low protein intake as in protein energy malnutrition.

(ii)Malabsorption as in chronic pancreatitis, sprue.

(iii)Loss of albumin from the body in urine as in the nephrotic syndrome.

(iv)An increase in the body's need for protein, e.g. as a result of infection, or following surgery or serious tissue damage when protein is required for energy and repair.

NOTE: The measurement of total plasma proteins (albumin, globulin, fibrinogen) or total serum proteins (albumin and globulin) has only limited clinical value. Most of the causes of low total protein levels below (60 g/l) are due to reduced albumin concentrations or more rarely to severe immunoglobulin deficiency.

C. SERUM ENZYME TESTS

(a) ASPARTATE AMINOTRANSFERASE (AST)

Reference (Normal) Range: Up to 42 U/litre (tested at 37 °C).

Other AST methods give much lower reference values, particularly UV colorimetric methods in which incubation is carried out at 25 °C.

Analyte: The enzymes, aspartate amino-transferase (AST), previously known as glutamate oxaloacetate transaminase GOT), and alanine aminotransferase (GPT), are concerned with amino acid metabolism. Large amounts of AST are found in the liver, kidneys, cardiac muscle, and skeletal muscle while small amounts can be found in the brain, pancrease and lungs. ALT is found principally in the liver. When there is liver cell damage the serum or plasma levels of both enzymes are raised.

Value of Test: Measurement of AST activity is mainly performed to investigate liver disease and myocardial infarction.

The determination of serum or plasma AST is preferred to that of ALT because AST enzyme activity is also a useful indicator of myocardial damage; also the difference in the raised levels of the two enzymes in liver cell damage is small and does not justify measuring both AST and ALT.

Test Method: Reitman-Frankel AST method.

Specimens: Fresh serum or plasma free from haemolysis.

Interpretation of Results: Very high AST activities usually accompany liver disease especially when there is hepatocellular damage, e.g. in hepatitis. Elevated serum AST is found in myocardial infarction. Other causes of raised AST levels include other diseases involving cellular injury, e.g. severe bacterial infections, malaria, pneumonia, infectious mononucleosis, pulmonary infarcts, tumours; also muscle disorders and following surgery, injury, or blood transfusion.

(b) ALANINE AMINOTRANSFERASE (ALT)

Alanine aminotransferase (ALT) formerly known as serum glutamic-pyruvic transaminase (SGPT) is found in the liver with lesser amounts in the heart, skeletal muscles, and kidney. Although, ALT values are relative specific for cell damage, ALT is less sensitive than AST, and extensive or severe liver damage is necessary before abnormally increase levels are produced. ALT also increases less consistently and less markedly than AST after an acute myocardial infarction.

(c) *alpha*-AMYLASE

Reference (Normal) Range: 70-340 U/litre or 37.8-183.8 Caraway Somogyi units/100 ml.

Analyte: The enzyme *alpha*-amylase is present in large amounts in pancreatic juice and saliva. Pancreatic amylase hydrolyses starches not split by salivary amylase. Some of the pancreatic amylase is absorbed into the blood and is excreted in the urine. Acute inflammation of the pancrease (pancreatitis) causes the release of large amounts of amylase into the circulation.

Value of Test: Measurement of serum or plasma amylase activity is used to differentate acute pancreatitis from other acute abdominal disorders.

Test Method: Caraway Somogyi starch-iodine amylase method.

Specimens: Fresh unhaemolysed serum or heparinised plasma.
Plasma from oxalated, EDTA, or citrated anticoagulated blood must not be used.
Interpretation of Results: Marked increase (5 or more times normal) is virtually diagnostic of acute pancreatitis. Moderate increase may be due to renal failure, salivary gland obstruction or inflammation as with mumps, diabetic keto-acidosis, opiate drugs, alcoholism, hypothermia, ectopic pregnancy; almost any acute abdominal emergency, and also cholecystitis, perforated peptic ulcer, or peritonitis.

(d) CREATINE KINASE (CK)
Creatine kinase (ck), known formerly as creatine phosphokinase (CPK), is found primarily in heart muscle, skeletal muscle, and brain tissue. CK levels are used primarily to aid in the diagnosis of acute myocardial or skeletal muscle damage. However, vigorous exercise, a fall, or deep ontramuscular injections can cause significant increases in CK levels.

(e) LACTATE DEHYDROGENASE (LDH)
LDH catalyzes the interconversion of lactate and pyruvate and represents a group of enzymes present in almost all metabolizing cells. Measurement of LDH isoenzymes may aid in diagnosing myocardial infarction, hepatic disease, and lung disease.
(f) ALKALINE PHOSPHATASE (ALP)
ALP is produced primarily in the liver and in the bones. Increased serum ALP levels may result from biliary obstruction either extrahepatic (e.g., a store in the bile duct) or intrahepatic. Serum ALP levels also increase with increased osteoblastic activity, as occurs in paget's disease, hyperparathyroidism, osteomalacia, and others.

D. BLOOD OR PLASMA GLUCOSE

(a) GLUCOSE
Reference (Normal) Range:
Adult: Fasting (plasma) 64.8-115.2 mg%; Random (plasma) 59.4-133.2 mg%.
Children: Fasting (plasma) 43.2-95.4 mg%.
Newborn values are slightly lower, i.e. 19.8-79.2 mg%.
Reference values have little use today as plasma glucose results are now compared to definitive numerical criteria (see under interpretation of results). Venous plasma values are about 15% higher than whole blood values (except in anaemia).
Specimens: Blood glucose specimens are described as
(i) Fasting specimen - Blood collected after a period of no food intake usually 10 to 16 hours in adults, and about 6 hours in children unless longer time is indicated, e.g. in hypoglycaemia. Drinking of plain water is permitted.
(ii) Postprandial specimen - Blood collected after a meal usually taken as a 2 hour postprandial specimen.
(iii) Random specimen - Blood sample collected at any time, regardless of food intake.
Interpretation of Results: *Increases* (Hyperglycaemia) - In adult with symptoms, a random venous plasma glucose of 199.8mg% or more obtained on two separate occasions is diagnostic. Random values below 140.4mg% and fasting values below 115.2mg% exclude a diagnosis of diabetes mellitus.
Other causes of hyperglycaemia include pancreatic disease; endocrine disorders such as thyrotoxicosis and Cushing's syndrome; steroid therapy. Surgery, injury, shock, infections or severe burns can cause transient hyperglycaemia.
Decreases (Hypoglycaemia) - May be found in severe malnutrition, kwashiorkor, severe liver disease, alcoholic excess, insulin secreting tumours, Addison's disease, certain drug therapy (quinine, quinidine), over treatment of diabetes, severe malaria.

(b). GLUCOSE TOLERANCE TEST (GTT)
Glucose tolerance: A GTT measures the ability of the body to tolerate, or cope with, a standard dose of glucose. The degree of tolerance to the glucose, as shown by a change in the blood level, is mainly dependent on the rate of glucose absorption and on the insulin response. Tolerance is reduced when insulin is insufficient or absent.
Value of test: A GTT is usually requested to investigate glycosuria or when a random or fasting blood glucose is suggestive but not diagnostic of diabetes. Not necessary in children.
Specimens: Fasting and 2 hour post glucose blood samples.
Interpretation of Results: The following diagnostic criteria (WHO) are for venous plasma glucose results:

(1) *Healthy*	Fasting	<115.2 mg%
	2 hour specimen	<140.4 mg%
(2) *Diabetic*	Fasting	>or=140.4 mg%
	2 hour specimen	> or =199.8 mg%
(3) *Impaired glucose tolerance*	Fasting	<140.4 mg%
	2 hour specimen	142.2-198 mg%

Note: For asymptomatic patients, two abnormal

values greater than 199.8 mg% are needed to establish a diagnosis of diabetes mellitus.

E. ELECTROLYTES

(a) SODIUM AND POTASSIUM

Reference (Normal) Range:

Sodium: 134-146 mEq/l (134-146 mmol/l).

Potassium:

Adults: 3.6 - 5.0 mEq/l (3.6 - 5.0 mmol/l).

Newborns: 4.0-5.9 mEq/l (4.0-5.9 mmol/l).

Values are highest immediately after birth.

Analyte: *Sodium* is the main extracellular cation. The plasma sodium level is a major factor in the control of water homeostasis and extracellular fluid volume

Potassium is the principal intracellular cation, 98% of which is maintained within the cells by the ATP dependent mechanism known as the sodium pump. Here, any sodium which diffuses into cells is actively excreted in exchange for potassium. Insulin also accelerates the cellular uptake of potassium and elevated levels of plasma potassium encourage secretion of insulin. Dietary potassium intake isnormally in excess of requirement and the surplus is excreted via the kidneys.

Value of Test: The measurement of sodium, potassium, or both electrolytes is usually requested in the assessment of renal function, to assist in the management of a patient that is unconscious or confused or diabetic patient with ketoacidosis, to assess and monitor states of dehydration (particularly an infant losing fluid), to monitor diuretic therapy and to assist in fluid replacement therapy.

Test Method: Flame photometer.

Specimens: Unhaemolysed plasma or serum which must be separated from the cells 2.5 hours. Avoid anticoagulants containing sodium or potassium; lithium heparin can be used.

Interpretation of Results:

Sodium

Increases (Hypernatraemia) usually due to dehydration with the rise in sodium (also chloride and urea) being the result of a concentrating effect. May be caused by severe vomiting, prolonged diarrhoea, profuse sweating, fever, polyuria as in diabetes, hyperaldosteroidsm, Cushing's syndrome, inadequate water intake.

Decreases (Hyponatraemia) may accompany severe illness including viral and bacterial infections, malaria, heart attacks, heart failure, strokes, and tumours of the brain and lungs. Others include surgery or severe accident, diuretic therapy, side effect of some drugs, hypoadrenalism (Addison's disease), svere renal impairment and salt-losing nephritis.

Potassium

Increases (Hyperkalaemia) may be due to excessive I.V. infusion or increased ingestion of potassium; reduced renal excretion, renal failure with oliguria, anuria, acidosis; Addison's disease; hypoaldosteronaemia; leakage of cellular potassium following acute starvation, gross haemolysis, diabetic ketoacidosis, dehydration, severe tissue injury.

Decreases (Hypokalaemia) may be caused by inadequate intake of potassium in the diet and long term starvation; increased loss of potassium due to prolonged vomiting or diarrhoea, renal tubular failure, diuretics, hyperaldosteroidism; redistribution from plasma into cells, insulin therapy, metabolic or respiratory alkalosis.

20.1.2 Urine clinical chemistry tests (Urinalysis)

Urinalysis provides basic information regarding renal function, urinary tract disease, and the presence of certain systemic disease such as diabetes mellitus.

VOLUME

Reference (Normal) Range: 1-2 litres per 24 hours.

The volume of urine excreted daily depends on fluid intake, diet, climate, and other physiological factors.

Specimen: 24 hour urine.

Interpretation of Results: **Polyuria** (more than 2 litres per day) may be due to diabetes mellitus (increase in the osmolality of the filtrate preventing the normal reabsorption of water, i.e. osmotic diuresis); diabetes insipidus (the secretion of antidiuretic hormone is reduced). Other causes of polyuria include diuretic therapy, intravenous glucose and/or saline, chronic renal failure, Addison's disease. **Oliguria** (decrease in the volume of urine excreted) occurs when the renal blood flow and/or GFR are reduced and may be caused by hypotension (due to severe dehydration or cardiac failure), acute glomerulonephritis, acute tubular necrosis. **Anuria** is complete cessation of urine flow and is usually due to severe damage to the renal tubules (acute tubular necrosis). **Nocturia** is excretion of more than 500 ml of urine by an adult at night.

APPEARANCE

Reference (Normal) Range: Freshly passed urine is clear and pale to dark yellow in colour. A dilute urine appears pale in colour and a concentrated one has a dark yellow appearance. The yellow colour is due to the pigments

urochrome, urobilin, and porphyrins. A normal urine when alooed to stand for sometime may form a white phosphate deposit if the urine is alkaline (dissolved by a drop of acetic acid) or a pink uric acid deposit if the urine is highly acidic or concentrated (disappears on warming). A "mucus" cloud may also form if normal urine is left to stand.

Interpretation of Results: **Colourless** urine may be due to dilution, diabetes mellitus or insipidus. **Cloudy** urine due to presence of pus cells and bacteria may be caused by urinary tract infections. **Red and cloudy** urine due to presence of blood (haematuria) may be caused by blackwater fever and other conditions causing intravascular haemolysis; may also be caused by Phenolthalein (a laxative). **Yellowish-brown or green-brown** urine due to presence of bile pigments or increased amounts of urobilin (oxidized urobilinogen) may be caused by bancortian filariasis.

pH

Reference (Normal) Range: Freshly passed urine is slighly acidic, around pH 6.0 (ranges from 4.5 to 9).

Specimen: Fresh midstream urine.

Test as soon as possible after collection.

Interpretation of Results: Alkaline pH may indicate such conditions as alkalosis, a proteus infection, or acetazolamide use. It may also reflect changes caused by leaving the urine sample at room temperature.

RELATIVE MASS DENSITY (SPECIFIC GRAVITY)

Reference (Normal) Range: 1.010-1.030.

The value depends on the state of hydration of the person and the time of day. It is highest at the begining of the day.

Value of Test: To investigate the concentrating and diluting ability of the kidneys. Normal mass density is mainly proportional to the urea and sodium concentrations in the urine. High values occur when urine contains glucose, protein or other heavy particles.

Specimen: Midstream, first morning urine. The patient should not take any fluid for 10 hours before the sampling. Testing random urine specimens has little clinical value.

Interpretation of Results:

Low values: May indicate poor tubular reabsorption or excessive fluid intake. Generally, the greater the volume of urine excreted the lower is its density and the its colour. It may occur with diabetes insipidus, which decreases urine concentration.

High values: May be due to heavy perspiration, dehydration, or to the presence of substances not usually found in urine such as glucose or protein (if not corrected for in the test method). Increased specific gravity may occur with such conditions as diabetes mellitus (excess glucose in the urine) or nephrosis (excess protein in the urine).

Specific gravity, *fixed at 1.010* (the same as plasma), occurs when the kidneys lose their power to concentrate or dilute.

PROTEIN

Reference (Normal) Range: 50-80 mg/24 hr.

Proteinuria: Most plasma proteins are too small to pass through the glomeruli of the kidneys and small amount that filters through is reabsorbed into the blood by the tubules. Normal urine contains only trace amounts of protein (less than 50 mg per 24 hours). Proteinuria is when more than trace amounts of protein are found in the urine.

Value of Test: To diagnose and monitor proteinuria, e.g. in pregnancy and nephrotic syndrome.

Test Methods:

(a) Protein reagent strip test.

(b) Sulphosalicylic acid test.

Specimen: Fresh urine. 24 hour urine for quantitative test.

Interpretation of Results: **Proteinuria** may be caused by acute glomerulonephritis due to increased permeability of the glomerular basement membrane; pyogenic or tuberculous pyelonephritis; severe lower urinary tract infection; nephrotic syndrome characterised by heavy proteinuria and oedema; eclampsia when there is moderate to marked proteinuria; urinary schistosomiasis usually accompanied by both proteinuria and haematuria; severe febrile illnesses including malaria; diabetic nephropathy sometimes causes a nephrotic syndrome; hypertension; accompanying haematuria.

NOTE: Whenever proteinuria is found, the urine should be examined for bacteria, pus cells, red cells, and casts.

GLUCOSE

Glycosuria: Glucose which passes from the blood into the glomerular filtrate is normally reabsorbed back into the circulation by the kidney tubules. Usually less than 15 mg% is excreted in the urine. Glycosuria (or more correctly **glucosuria**) is the presence of more than the usual amount of glucose in the urine. The highest level that the blood glucose level reaches before glycosuria occurs is known as **renal threshold for glucose** and is normally 160-180 mg %.

Value of Test: To screen for and monitor

diabetes.

Test Methods:

(a) Glucose reagent strip test.

(b) Benedict's test.

Specimen: Midstream urine. If not tested immediately, store at 2-8 °C to prevent glycolysis.

Interpretation of Results: Glycosuria may be caused by

(a) A rise in the concentation of blood glucose with the kidney tubules being unable to reabsorb the increased amount of glucose in the glomerular filtrate, e.g. in untreated diabetes mellitus.

(b) A reduced rate of reabsorption of glucose by the kidney tubules as occurs in serious tubular damage or an inherited defect of tubular absorption causing a lowering of the glucose renal threshold (known as renal glycosuria).

(c) An increase in the rate of glomerular filtration as may sometimes occur during pregnancy.

NOTE: The blood glucose level should be measured whenever glucose is found in urine and the patient is not a known diabetic receiving glucose intravenously.

KETONES

Ketonuria: Acetoacetate, *beta*-hydroxybutyrate and acetone are collectively referred to as ketone bodies or simply as ketones. The excretion of more than a trace of these substances in the urine is called ketonuria. Ketones are strong acids and may overcome the buffering systems in the blood and so cause ketoacidosis.

Value of Test: To detect and monitor ketonuria, e.g. in diabetes.

Test Method:

(a) Ketone reagent strip test.

(b) Ketone reagent tablet test.

(c) Nitroprussside tube or tile test.

Specimen: Midstream urine. The urine must be soon after it is passed before the acetoacetate is carboxylated to acetone.

Interpretation of Results: Ketonuria may be caused by untreated diabetes; conditions of starvation when fat metabolism is increased; eating a diet that is very low in carbohydrates; severe dehydration following prolonged vomiting or diarrhoea; glycogen storage disease.

BILIRUBIN

Reference (Normal) Range: Nil.

Bilirubinuria: Bilirubin is not normally detected in the urine. When it is found, the condition is referred to as bilirubinuria. Urine containing 0.5 mg% or more of bilirubin has a characteristic yellow-brown colour (hepatocellular jaundice) or a yellow-green appearance (obstructive jaundice).

Value of Test: To assist in the diagnosis of hepatocellular and obstructive jaundice.

Test Methods:

(a) Bilirubin strip test.

(b) *Ictotest* tablet test.

(c) Fouchet's test.

Specimen: Freshly passed urine. Protect the specimen from daylight and flourescent light because bilirubin is rapidly oxidized by ultraviolet light to bilverdin which is not detected by the reagents used in the tests.

Interpretation of Results: Bilirubinuria occurs whenever there is an increase of conjugated bilirubin in the blood, e.g. in obstructive jaundice and also in hepatocellular jaundice when the blood usually contains both conjugated and unconjugated bilirubin.

Bilirubin is not found in the urine in haemolytic jaundice or in other conditions in which the excess bilirubin in the blood is of the unconjugated type.

In early stages of viral hepatitis, bilirubinuria together with raised aminotransferase levels can be found before a patient becomes clinically jaundiced.

UROBILINOGEN

Reference (Normal) Range: Trace amount.

Urobilinogen in urine: It is normal to find small amounts of urobilinogen in the urine derived from that which is reabsorbed from the intestine. The concentration of urobilinogen in the urine is therefore dependent on the amount of bilirubin being produced and entering the intestine and the on ability of the liver to excrete the urobilinogen coming to it from the intestine.

Value of Test: Urine is often tested for increases in urobilinogen when investigating haemolysis (haemolytic jaundice) or liver disorders in which liver function is impaired.

Test Methods:

(a) Ehrlich's test.

(b) Urobilinogen strip tests.

Specimen: Freshly passed urine is required because urobilinogen which is colourless is rapidly oxidized to the orange pigment urobilin which is not detected by the tests.

Interpretation of Results: *Increases*: Haemolytic disease; paralytic ileus or enterocolitis; hepatocellular damage or hepatic congestion; cirrhosis of the liver.

Decrease or absence of urine urobilinogen: obstruction of bile ducts; hepatocellular damage; absence or reduction of the normal

intestinal flora (necessary to convert conjugated bilirubin to urobilinogen) which may occur in neonates or following intensive antimicrobial therapy.

HAEMOGLOBIN

Haemoglobinuria: The presence of free haemoglobin in the urine is called haemoglobinuria. It occurs with severe intavascular haemolysis when the amount of haemoglobin being released into the plasma is more than can be taken up by haptoglobin (the plasma protein that binds free haemoglobin to prevent it being lost from the body). The renal threshold for free haemoglobin is 1.0-1.4 g/l.

Value of Test: To investigate intravascular haemolysis.

Test Methods:

(a) Reagent strip tests

(b) Guaiac test.

Specimen: Urine containing haemoglobin appears brown or brown-grey in colour and is usually cloudy. It should be tested as soon as possible after it has been passed.

Interpretation of Results: Haemoglobinuria occurs with severe intravascular haemolysis. It is associated with severe falciparum malaria; typhoid fever; G6PD deficiency following the ingestion of certain drugs; *E. coli* septicaemia; incompatible blood transfusion; snake bites that cause acute haemolysis; sickle cell disease crisis with severe haemolysis; severe viral haemorrhagic fever accompanied by intravascular haemolysis.

NITRITE

Reference (Normal) Range: Nil.

Nitrite in Urine: Urine from a healthy person does not contain nitrite. The detection of nitrite in urine is a useful test in the investigation of urinary tract infections caused by nitrate-reducing bacteria. Most pathogenic bacteria reduce the nitrate normally found in urine to nitrite.

Value of Test: To assist in the diagnosis of urinary tract infection.

Test Methods:

(a) Reagent strip tests

(b) Modified Griess test.

Specimen: The most suitable specimen for testing is urine that has remained in the bladder for 4-8 hours such as the first passed urine of the morning.

Interpretation of Results: Bacteria that produce the enzyme nitrate reductase are able to reduce nitrate to nitrite namely *E. coli, Salmonella species, Proteus species, Klebsiella species.* A negative test can not rule out urinary tract infection because the causative organism may be one that does not reduce nitrate to nitrite, e.g. *Enterococcus faecalis, Staphylococcus albus, Pseudomonas* species, *Candida species.*

20.1.3 Faecal clinical chemistry tests

OCCULT BLOOD

Reference (Normal) range: Nil.

Analyte: Bleeding into the GIT may be rapid with the vomiting of blood (haematemesis) or the passage of blood through the rectum (melaena). When the bleeding is chronic with only small amounts of blood being passed in the faeces, the blood (or its breakdown products) is not recognised in the faeces and is referred to as occult (hidden) blood.

Value of Test: To investigate the cause of iron deficiency anaemia or to assit in the diagnosis of bleeding lesions of the GIT, e.g. peptic ulcer, carcinoma, or diverticulosis.

Specimen: Collect a small sample each day for 3 days. Patient should not eat meat or vegetables containing peroxidases for 2 days before the test. Test as soon as possible after collection or preserve by storing at 2-8 ^{o}C if delay is inevitable.

Interpretation of Results: The commonest causes of positive occult blood tests are hookworm infection, peptic ulcer, and bleeding from oesophageal varices due to cirrhosis of the liver. Other causes include carcinoma in the GIT, erosive gastritis due to alcohol or drugs, swallowed blood from recurrent nose-bleeds.

LACTASE DEFICIENCY

Analyte: Lactase is an enzyme which converts lactose to glucose and galactose. If lactase is deficient, lactose is not digested or absorbed but ferments to lactic acid with the production of gas. This causes abdominal pain and diarrhoea which may be persistent and severe especially in young children. When there is lactase deficiency faecal specimens usually contain lactose and have low pH due to the presence of lactic acid.

Value of Test: To investigate deficiency.

Test Method: Benedict's reagent or *Clinitest.*

Specimen: Freshly passed fluid faecal specimen.

Interpretation of Results: Lactase deficiency is indicated if a faecal specimen contains sugar (lactose) and has a pH of 6.0 or below.

EXCESS FAT

Steatorrhoea: Most dietary fat is absorbed in the small intestine with very little being excreted in the faeces. Disorders of fat

absorption cause excessive amounts of fat to be excreted in the faeces (steatorrhoea).

Value of Test: To investigate disorders of fat absorption.

Interpretation of Results: Steatorrhoea can occur with sprue, giardiasis, strongyloidiasis, capillariasis, chronic pancreatitis, and less commonly pancreatic or biliary obstruction.

20.1.4 Cerebrospinal fluid (csf) chemical tests

Value of Tests: The biochemical testing of cerebrospinal fluid (c.s.f.) is performed to assist in the diagnosis of meningitis and other disorders of the central nervous system.

C.S.F. PROTEIN

Reference (Normal) Range: 15-40 mg%.

The range for ventricular fluid is slightly lower. Values up to 100 mg% are normal for newborn infants.

Interpretation of Results: *Increases* may occur in all forms of meningitis, cerebral malaria, brain tumours, cerebral injury, spinal cord compression, poliomyelitis, polyneuritis; also in diseases which cause changes in plasma proteins such as multiple myeloma.

C.S.F. GLUCOSE

Reference (Normal) Range: 45-72 mg%.

The c.s.f. (lumbar) glucose is usually 60-80 % of blood glucose.

Interpretation of Results: *Decreases:* Low c.s.f. glucose levels are fond in most forms of meningitis, particularly pyogenic meningitis when glucose may even be absent. In viral meningitis however, the c.s.f. glucose is often normal.

Increases: A raised c.s.f. glucose is found when there is a raised blood glucose and sometimes with encephalitis or following damage to cerebral capillaries.

20.2 Haematological tests

Blood contains three types of formed elements: RBCs, WBCs, and platelets. A complete blood count (CBC) includes Hb, haematocrit (Hct), total WBCs, total RBCs, mean cell volume (MCV) and platelet count.

A. ERYTHROCYTES (RBCs)

(a) ERYTHROCYTE COUNT OR RBC COUNT

The RBC count is the number of RBC found in a cubic millimetre (mm^3) of whole blood; it provide an indirect estimate of the blood's Hb content.

Reference (Normal) Range:

MALE: 4.3-5.9 x $10^6/mm^3$

FEMALE: 3.5-5.0 x $10^6/mm^3$.

Specimen: 4 ml whole blood collected into, sequestrene, heparin or ammonium potassium oxalate bottle. Sequestrene is the anticoagulant of choice (1 mg to 1 ml of blood).

Interpretation of Results: Erythrocytosis is a condition associated with an elevation of red cell count, haemoglobin concentration and packed cell volume significantlu above normal. Primary increase in red cell count is found in polycythaemia vera (leukaemia) while secondary increase exists in chronic obstructive lung disease and in cyanotic congenital heart diseases with hypoxaemia.

(b) HAEMATOCRIT (Hct) OR PACKED CELL VOLUME (PCV)

Hct measures the percentage by volume of packed RBCs in a whole blood sample after centrifugation. The Hct value and is usually three times the Hb value and is given as a percent or fraction of 1.

References (Normal) Range:

MALE: 39-40%.

FEMALE: 33-43%.

Interpretation of Results: Low Hct values may be associated with anaemia, overhydration or blood loss while high Hct values may be caused by polycythaemic vera or dehydration.

(c) HAEMOGLOBIN (Hb)

Hb test measures the amount of Hb in grams in 1 dl of whole blood and provides an estimate of the oxygen carrying capacity of the RBCs. The Hb value depends on the number of RBCs and the amount of the Hb in each RBC.

Reference (Normal) Range:

MALE: 14-18 g/dl

FEMALE: 12-16 g/dl.

Interpretation of Results: Low Hb values are usually found in anaemia.

(d) RBC INDICES

RBC indices are used to determine the RBC size, Hb concentration, and Hb weight and are used mainly to categorize anaemias.

(i) Mean cell Volume (MCV) is the ratio of the Hct to the RBC count. It essentially assesses average RBC size and reflects any variation in RBC size (i.e, arisocytosis).

MCV is defined as:

$$\frac{\text{Hct (\%)} \times 100}{\text{RBC count (in millions)}} = \text{MCV}.$$

References (Normal) Range: 90 ± 10.

Interpretation of Results: Low MCV indicates microcytic (undersized) RBCs, as occurs in iron deficiency. High MCV indicates macrocytic (oversized) RBCs, asa occurs in a

vitamin B^{12} or folic acid deficiency.

(ii) Mean Cell Hb (MCH) assesses the amount of Hb in an average RBC. MCH is defines as:

Hb x 10
RBC count (in millions) = MCH

Reference (Normal) Range: 30 ± 4.

(iii) Mean Cell Hb Concentration (MCHC) represents the average concentration of Hb in an average RBC and is defined as:

Hb x 100
Hct = MCHC.

References (Normal) Range: 34 ± 3.

Interpretation of Results: Low MCHC indicates hypochromia (pale RBCs resulting from decreased Hb concentration) as occurs in iron deficiency.

(iv) Erythrocyte Sedimentation Rate (ESR) measures the rate of RBC settling of whole, uncoagulated blood over time, and it primarily reflects plasma composition.

Reference (Normal) Range:
MALE: 0-20 mm/hr
FEMALE: 0-30 mm/hr

Interpretation of Results: ESR values increases with acute or chronic infection, tissue necrosis or infarction, well-established malignancy, and rheumatoid collagen diseases.

B. LEUCOCYTES (WBCs)

(a) LEUCOCYTE OR WBC COUNT

The WBC count is the number of WBCs in a cubic millimetre of whole blood.

Reference (Normal) Range: 4,000-11,000 / mm^3

Specimen: As for RBC.

Interpretation of Results: Leucocytes or increased WBC count is usually associated with bacterial infection. It may also result from leukaemia or tissue necrosis. Leucopemia or decreased WBC count indicates bone marrow depression, which may result from metastatic carcinoma, lymphoma, or toxic reactions to substances such as antineoplastic agents.

(b) WBC DIFFERENTIAL

The WBC differential evaluates the distribution and morphology of the five major types of WBCs - the granulocytes (i.e., neutrophils, basophils, eosinophils) and the nongranulocytes (i.e., lymphocytes, monocytes). A certain percentage of each type comprises the total WBC count.

(i) NEUTROPHILS

Reference (Normal) Range: 2,500-7,500 / cu.mm

Neutrophils constitute 40-75 % of WBC.

Specimen: Fresh films. Satisfactory films can also be made from sequestrene blood up to 1 hour after collection. Films from blood left longer or from heparinised blood are less satisfactory.

Interpretation of Results: **Neutrophilia or Neuttrophilic leucocytosis** is a total neutrophil count of more than 7500 cells/cu.mm, and it occurs in infetions (bacteria, viral or fungal); metabolic disorders such as gout; neoplasms and other malignancies; drugs such as corticosteroids; acute phases of rheumatoid arthritis; trauma and haemorrhage, etc. **Neutropenia** is reduction in the number of circulating neutrophils below 2500 cells/cu.mm and it can be drug-induced such as antihistamines. **Chronic idiopathic neutropenia (agranulocytosis)** is a neutrophil count of 500-2000 cells/cu.mm and it occurs in acute viral infections such as hepatitis; bacterial infections, e.g. typhoid; aplastic anaemia; hypersplenism; anaphylaxis.

(ii) EOSINOPHILS

Reference (Normal) Range: 40-440 /cu.mm

Eosinophils constitute 1-6 % of WBC.

Specimen: As for Neutrophils.

Interpretation of Results: **Eosinophilia (Eosinophil leucocytosis)** is a total eosinophil count of more than 440 cells/cu.mm and it occurs in allergic disorders; parasitic diseases such as worm infestation and malaria; skin disorders such as scabies; drugs such as penicillin, streptomycin, chlorpromazine; neoplasms such as eosinophilic leukaemia; pernicious anaemia. **Eosinopenia** can be due to drug or hormone therapy such as adrenocortical steroids, adrenaline; endocrine diseases; response to stress such as acute infections, surgery, burns, severe exercise, etc; aplastic anaemia.

(iii) BASOPHILS (MAST CELLS)

Reference (Normal) Range: 0-100 /cu.mm

Basophils constitute less than 1 % of WBC.

Specimen: As for Neutrophils.

Interpretation of Results: **Basophilia (Basophilic leucocytosis)** is a total basophil count in excess of 100 cells/cu.mm and can be found in chronic myelogenous leukaemia (CML) , hypersensitivity states, iron deficiency anaemia, etc. **Basophilopenia** or decrease in basophils may not be noticeable due to the small number of these cells in the blood.

(iv) LYMPHOCYTES

Lymphocytes play a dominant role in immunological activity and appear to produce antibodies.

Reference (Normal) Range: 1500 - 3300 / cu.mm

Lymphocytes constitute 20-45 % of WBC.

Specimen: As for Neutrophils.

Interpretation of Results: **Lymphocytosis** or increased number of lymphocytes usually accompanies a normal or decreased total WBC count is most commomly caused by viral infection. It occurs in acute infections such as pertusis, measles; chronic infections such as tuberculosis, secondary syphilis; endocrine disorders such as thyrotoxicosis; neoplasms such as chronic lymphocytic leukaemia and non-Hodgkin's lymphomas; infants and young children. **Lymphopenia** or decreased number of lymphocytes may be caused by severe debilitating illness immunodeficiency or AIDS (acquired immune deficiency syndrome) which attacks T_4 cells of the T lymphocytes.

(v) MONOCYTES

Monocytes are phagocytic cells. They constitute 0-7% of WBC.

Interpretation of Results: Monocytosis or increased number of monocytes may be caused by tuberculosis (TB), subacute bacterial endocarditis, or during the recovery phase of some acute infections.

C. PLATELETS

These are the smallest formed elements in the blood, anf they are involved in blood clotting and vital to the formation of a haemostatic plug after vascular injury.

Reference (Normal) Range: 150,000 - 300,000/mm^3 (1.5 -3.0 x 10"/L)

Specimen: Sequestrene or heparin specimen (as for neutrophils). Test can be done up to 8 hours after collection.

Interpretation of Results: **Thrombocytopenia** or decreased platelets count can occur with a variety of conditions such as idiopathic thrombocytopenic purpura or, occasionally, from such drugs as quinidine and sulphonamides. **Thrombocythaemia** (too many platelets) is found in polycythaemia, essential thrombocytosis. **Thrombasthemia** is defective platelet function.

D. TOTAL BLOOD VOLUME

Reference (Normal) Range: 6-8 %/b.wt.
MALE: 4-7 litres (60-95 ml/kg).
FEMALE: 3-4.9 litres (44-85 ml/kg).
Specimen: Whole blood.

E. BLEEDING TIME

Reference (Normal) Range:
0-5 minutes (Duke's method).
7-11 minutes (Ivy's method).
Specimen: 5 ml whole blood in sodium citrate bottle.

F. PROTHROMBIN TIME

Reference (Normal) Range: 10-14 seconds (Quick one stage method).
Specimen: As for bleeding time. Note that prothrombin time is useless in patient on heparin therapy.

G. COAGULATION TIME

Reference (Normal) Range:
11 minutes (Lee & White).
3 minutes (Dale & Laidlaw).
Specimen: As for bleeding time.

20.3 Diagnostic Agents

20.3.1 Gastric Function
20.3.2 Myasthenia Gravis
20.3.3 Ophthalmology
20.3.4 Radio-contrast Media
20.3.5 Tuberculosis
20.3.6 Endocrine Disorders
20.3.7 HIV Test Kits

20.3.1 Gastric Function

HISTAMINE

Pharmacology: It acts on various tissues of the body via two receptors namely H_1 and H_2 receptors. Its stimulant action on gastric acid secretion is mediated via H_2-receptors.

Indications: To test the secretory action of the stomach in pernicious anaemia, atrophic gastritis, gastric cancer, duodenal ulcer, Zollinger-Ellison syndrome; after vagotomy or gastric resection.

Precautions: History of asthma or allergy; elderly patients.

Adverse effects: Headache, tachycardia, nervousness, flushing, bronchospasm.

Dose: By s.c. injection, 0.3-0.5 mg base (1 mg base is equivalent to 2.75 mg phosphate); to be administered after the administration of a large dose of an antihistamine.

POM **Histamin Phosphate** *(EDL 15.1)*
Injection, Histamine phosphate 2.75 mg per ml; in 1ml amp.

PENTAGASTRIN

Pharmacology: A synthetic analogue of the natural polypeptide hormone, gastrin. It has similar effects as the natural hormone particularly, in stimulating the secretion of gastric acid.

Indications: To test the secretory action of the stomach; see under histamine.

Contra-indications: Hypersensitivity to the drug; acute peptic ulcer.

Precautions: Pancreatic, hepatic or biliary tract disease; high doses can inhibit gastric acid secretion.
Adverse effects: Abdominal cramps, nausea, vomiting, palpitation (usually less severe than those of histamine).
Dose: By s.c. injection, 0.006 mg/kg b. wt.

POM **Pentagastrin** *(EDL 15.1)*
Injection, Pentagastrin 0.25 mg per ml; in 2 ml amp.

20.3.2 Myasthenia gravis

EDROPHONIUM

Pharmacology: A synthetic, short-acting, reversible anticholinesterases. After i.v. injection, action starts within 30-60 seconds and lasts about 5 minutes.
Indications: Diagnosis of myasthenia gravis; to distinguish between myasthenic crisis and cholinergic crisis.
Contra-indications: Intestinal or urinary tract obstruction, bradycardia, hypotension.
Precautions: Bronchial asthma, recent MI, peptic ulcer, cardiac disease, epilepsy, hyperthyroidism.
Interactions:
•Procainamide, quinidine (may antagonise the cholinergic effect).
•Effect of suxamethonium may be enhanced.
Adverse effects: Nausea, vomiting, diarrhoea, abdominal cramps, excessive salivation; other cholinergic reactions include excessive lacrimation, hypotension, bradycardia, seizures, weakness, dysphagia, paralysis, sweating, urinary retension, bronchospasm, mucle cramps.
Nursing considerations: •Use a tuberculin syringe with an IV needle for easier administration.
•IM route may be used in adults and children without suitable veins; reactions are the same but may be delayed slightly.
•Monitor vital signs frequently, particularly respirations. Atropine should always be kept available to reverse toxic reactions; provide respiratory support if needed.
•Observe closely for adverse effects; may indicate toxicity.
Dose: By I.V. injection (over 1 minute), *diagnosis of myasthenia gravis*, Adult, 2 mg followed after 30 seconds (if well tolerated) by 8 mg.
By I.M. injection (if no suitable vein is found) 10 mg.
Child, by I.V. injection, 20 mcg/kg followed after 30 seconds (if well torelated) by 80 mcg/kg.
By I.M. injection (if no suitable vein is found) 100 mcg/kg.
Note: Atropine sulphate should always be available to treat overdose or severe cholinergic reactions.

POM **Edrophonium** *(EDL 15.2)*
Injection, Edrophonium chloride 10 mg per ml; in 1 ml amp.

20.3.3 Ophthalmology

For general information on the use of eye drops, see chapter 13.
Fluorescein sodium is used in ocular diagnostic procedures and for locating damaged areas of the cornea due to injury or disease.
Tropicamide is a short-acting relatively weak mydriatic that dilates the pupil and paralyses the ciliary muscle. It facilitates the examination of the fundus of the eye.

FLUORESCEIN

Indications: Detection of lesions and foreign bodies in the eye.
Contra-indications: Avoid use with soft contact lenses.
Precautions: SKILLED TASKS: TRANSIENT BLURRING OF VISION—ADVISE PATIENT NOT TO OPERATE MACHINERY OR DRIVE UNTIL VISION IS CLEAR.
Administration: *Detection of lesions and foreign bodies in eye*, by ocular instillation, ADULT and CHILD instil sufficient solution dropwise to stain damaged area.

POM **Fluorescein** *(WMF 14.1)*
Eye drops, solution, Fluorescein sodium 1%.

POM **Fluorescein Sodium** *(EDL 15.3)*
Eye-drops, Fluorescein sodium 2%
Injection, Fluorescein sodium 10%
Paper strips, Impregnated with the dye.

TROPICAMIDE

Tropicamide is a representative mydriatic. Various drugs can serve as alternatives.
Indications: Dilatation of the pupil to examine the fundus.
Precautions: Patients aged over 60 years and hypermetropic (long-sighted)—may precipitate acute angle-closure glaucoma; darkly pigmented iris, more resistant to pupillary dilatation—exercise caution to avoid overdosage.
SKILLED TASKS: AVOID OPERATING MACHINERY OR DRIVING FOR 1–2 HOURS AFTER MYDRIASIS.

Adverse effects: Transient stinging and raised intraocular pressure; on prolonged administration—local irritation, hyperaemia, oedema and conjunctivitis.

Administration: *Dilatation of pupil to examine the fundus*, by ocular instillation, ADULT and CHILD 1 drop, 15–20 minutes before examination of eye.

POM **Tropicamide** *(WMF 14.1)*
Eye drops, solution, Tropicamide 0.5%.

20.3.4 Radio-constrast media

Radiographic contrast media are needed for delineating soft tissue structures such as blood vessels, stomach, bowel loops and body cavities not otherwise visualized by standard X-ray examination. The contrast media in this group containing heavy atoms (metal or iodine) absorb a significantly different amount of X-rays than the surrounding soft tissue, thereby making the examined structures visible on radiographs.

Barium sulfate is a metal salt which is used to delineate the gastrointestinal tract. It is not absorbed by the body and does not interfere with stomach or bowel secretion or produce misleading radiographic artefacts. Barium sulfate may be used in either single- or double-contrast techniques or computer-assisted axial tomography. For double contrast examination gas can be introduced into the gastrointestinal tract by using suspensions of barium sulfate containing carbon dioxide or by using separate gas-producing preparations based on sodium bicarbonate. Air administered through a gastrointestinal tube can be used as an alternative to carbon dioxide to achieve a double-contrast effect.

Amidotrizoates (meglumine amidotrizoate and sodium amidotrizoate) are iodinated ionic monomeric organic compounds. Both salts have been used alone in diagnostic radiography including computer-assisted axial tomography but a mixture of both is often preferred to minimize adverse effects and to improve the quality of the examination. Amidotrizoates are used in a wide range of procedures including urography and examination of the gallbladder, biliary ducts and spleen. Owing to their high osmolality and the resulting hypertonic solutions, they are associated with a high incidence of adverse effects. Radiodensity depends on iodine concentration, and osmolality depends on number of particles in a given weight of solvent. The osmolality for a given radiodensity can be reduced by using an ionic dimeric medium such as **meglumine iotroxate** which contains twice the number of iodine atoms in a molecule or by using a non-ionic medium such as **iohexol**. Low osmolality media such as iohexol are associated with a reduction in some adverse effects (see below), but they are generally more expensive. Iohexol is used for a wide range of diagnostic procedures including urography, angiography and arthrography and also in computer-assisted axial tomography. **Iopanoic acid** is an oral iodinated ionic monomeric organic compound. It is absorbed from the gastrointestinal tract, excreted into the bile and concentrated in the gallbladder thus making it ideal for cholecystography. **Propyliodone** is an iodinated organic compound which is used for the examination of the bronchial tract. **Meglumine iotroxate** is excreted into the bile after intravenous administration and used for cholecystography and cholangiography.

HYPERSENSITIVITY
Anaphylactoid reactions to iodinated radiocontrast media are more common with ionic, high osmolality compounds. Patients with a history of asthma or allergy, drug hypersensitivity, adrenal suppression, heart disease, previous reaction to contrast media, and those receiving beta-adrenoceptor antagonists (beta-blockers) are at increased risk. Non-ionic media are preferred for these patients and beta-blockers should be discontinued if possible.

AMIDOTRIZOATES

Amidotrizoates are representative iodinated ionic monomeric contrast media. Various media can serve as alternatives.

Indications: Urography, venography, operative cholangiography, splenoportography, arthrography, diskography; computer-assisted axial tomography.

Contra-indications: Hypersensitivity to iodine-containing compounds.

Precautions: History of allergy, atopy or

asthma; severe hepatic impairment; renal impairment (Appendix 4); dehydration—correct fluid and electrolyte balance before administration; multiple myeloma (risk if dehydrated, may precipitate fatal renal failure); cardiac disease, hypertension, phaeochromocytoma, sickle-cell disease, hyperthyroidism, elderly, debilitated or children—increased risk of adverse effects; pregnancy; breastfeeding; may interfere with thyroid-function tests; biguanides (withdraw 48 hours before administration; restart when renal function stabilized); **important**: because of risk of hypersensitivity reactions, adequate resuscitation facilities must be immediately available when radiographic procedures are carried out.

Adverse effects: Nausea, vomiting, diarrhoea, metallic taste, flushing, sensations of heat, weakness, dizziness, headache, coughing, rhinitis, sweating, sneezing, lacrimation, visual disturbances, pruritus, salivary gland enlargement, pallor, cardiac disorders, haemodynamic disturbances and hypotension; disseminated intravascular coagulation; fibrinolysis and depression of blood coagulation factors; rarely, convulsions, paralysis, coma, rigors, arrhythmias, pulmonary oedema, circulatory failure and cardiac arrest; occasionally anaphylactoid or hypersensitivity reactions; hyperthyroidism; pain on injection; extravasation may result in tissue damage, thrombophlebitis, thrombosis, venospasm and embolism.

Dose: *Diagnostic radiography*, ADULT and CHILD, route and dosage depend on procedure and preparation used (consult manufacturer's literature).

ADMINISTRATION: ONLY BY SPECIALIST RADIOGRAPHERS, ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Amidotrizoates** *(WMF 14.2)*
Injection (Solution for injection), Iodine (as sodium and/or meglumine amidotrizoate) 140–420 mg/ml, 20-ml ampoules.

POM **Meglumine Diatrizoate** *(EDL 15.4.7)*
Injection, Meglumine diatrizoate 60% in 25 ml amp. and 30 ml vial; 76% in 20 ml amp. and vial; 85% in 50 ml vial.
Injection, Meglumine diatrizoate 34.3%, sodium diatrizoate 35% in 25 ml and 50 ml vials; 50% and 25% in 20 ml and 50 ml vials; 60% and 30% in 20 ml and 50 ml vials.

POM **Sodium Diatrizoate** *(EDL 15.4.7)*
Injection, Meglumine diatrizoate 50%; in 20 ml amp.

POM **Meglumine Iothalamate** *(EDL 15.4.2)*
Injection, Meglumine iothalamate 60%; in 30 ml amp. and in 20 ml, 30 ml vials.

POM **Sodium Iothalamate** *(EDL 15.4.2)*
Injection, Sodium iothalamate 80%; in 20 ml, 50 ml vials.

POM **UROGRAFIN®** *(CHI/Schering)*
Injection, Amidotrizoate 0.1 g, meglumine diatrizoate 0.6 g per ml.
Pack - 10 x 20 ml.

BARIUM SULFATE

Indications: Radiographic examination of the gastrointestinal tract (see notes above).

Contra-indications: Intestinal obstruction, conditions such as pyloric stenosis or lesions which predispose to obstruction; intestinal perforation or conditions with risk of perforation, such as acute ulcerative colitis, diverticulitis, or after rectal or colonic biopsy, sigmoidoscopy or radiotherapy.

Precautions: Adequate hydration after procedure to prevent severe constipation.

Adverse effects: Constipation or diarrhoea, abdominal cramps and bleeding; perforation of bowel resulting in peritonitis, adhesions, granulomas and high mortality rate; electrocardiographical changes—may occur with rectal administration; pneumonitis or granuloma formation—following accidental aspiration into lungs.

Dose: Radiographic examination of gastrointestinal tract, ADULT and CHILD , route and dosage depend on procedure and preparation used (consult manufacturer's literature).

ADMINISTRATION: ONLY BY SPECIALIST RADIOGRAPHERS, ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Barium sulfate** *(14.2)*
Oral suspension (or Rectal suspension), Barium sulfate 30 to 200% w/v.

POM **Barium Sulphate** *(EDL 15.4.1)*
Suspension, Barium sulphate 75-100%.

IOHEXOL

Iohexol is a representative iodinated non-ionic contrast medium. Various media can serve as

alternatives.

Indications: Urography, venography, angiography, ventriculography, operative cholangiography, splenoportography, arthrography, diskography; computer-assisted axial tomography.

Contra-indications: Hypersensitivity to iodine-containing compounds.

Precautions: History of allergy, atopy or asthma; severe hepatic impairment; renal impairment (Appendix 4); dehydration—correct fluid and electrolyte balance before administration; multiple myeloma (risk if dehydrated, may precipitate fatal renal failure); cardiac disease, hypertension, phaeochromocytoma, sickle-cell disease, hyperthyroidism, elderly, debilitated or children—increased risk of adverse effects; pregnancy; breastfeeding; may interfere with thyroid-function tests; biguanides (withdraw 48 hours before administration; restart when renal function stabilized); **important**: because of risk of hypersensitivity reactions, adequate resuscitation facilities must be immediately available when radiographic procedures are carried out.

Adverse effects: (See also notes above); nausea, vomiting, metallic taste, flushing, sensations of heat, weakness, dizziness, headache, coughing, rhinitis, sweating, sneezing, lacrimation, visual disturbances, pruritus, salivary gland enlargement, pallor, cardiac disorders, haemodynamic disturbances and hypotension; rarely, convulsions, paralysis, coma, rigors, arrhythmias, pulmonary oedema, circulatory failure and cardiac arrest; occasionally anaphylactoid or hypersensitivity reactions; hyperthyroidism; pain on injection; extravasation may result in tissue damage, thrombophlebitis, thrombosis, venospasm and embolism.

Dose: *Diagnostic radiography*, ADULT and CHILD, route and dosage depend on procedure and preparation used (consult manufacturer's literature).

ADMINISTRATION: ONLY BY SPECIALIST RADIOGRAPHERS, ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Iohexol** *(WMF 14.2)*
Injection (Solution for injection), Iodine (as iohexol) 140–350 mg/ml, 5-ml, 10-ml, and 20-ml ampoules.

POM **Iohexol** *(EDL 15.4.7)*
Injection, Iodine 140-350 mg per ml; in amp.

IOPANOIC ACID

Iopanoic acid is a representative iodinated ionic monomeric contrast medium. Various media can serve as alternatives.

Indications: Examination of the gallbladder and biliary tract.

Contra-indications: Severe renal disease and hepatic disease (Appendices 4 and 5); jaundice caused by biliary-tract obstruction; impaired absorption due to acute gastrointestinal disorders.

Precautions: Hypersensitivity to iodine-containing compounds or other contrast media; severe hyperthyroidism, hyperuricaemia or cholangitis; may interfere with thyroid-function tests; **important**: because of risk of hypersensitivity reactions, adequate resuscitation facilities must be immediately available when radiographic procedures are carried out.

Adverse effects: Nausea and vomiting, abdominal pain and diarrhoea; mild stinging on micturition, rashes and flushing; acute renal failure, thrombocytopenia and hypersensitivity reactions reported; also uricosuric and anticholinesterase effects.

Dose: *Examination of gallbladder and biliary tract*, by mouth, ADULT 3 g with plenty of water 10–14 hours before examination; if examination needs to be repeated, a further 3 g on the same day; alternatively, repeat examination carried out after 5–7 days with single 6-g dose (maximum dose; 6 g over 24 hours; avoid doses over 3 g in renal impairment).

ADMINISTRATION: ONLY BY SPECIALIST RADIOGRAPHERS, ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Iopanoic acid** *(WMF 14.2)*
Tablets, Iopanoic acid 500 mg.

POM **Iopanoic acid** *(EDL 15.4.4)*
Tablet, Iopanoic acid 500 mg.

IOPHENDYLATE

An absorbable iodized fatty acid compound designed specially for myelography and particularly for the study of the lumbar region.

Indications: As a contrast medium in myelography.

Contra-indications: Avoid use when lumbar puncture is contra-indicated and within 10 days

of a previous lumbar puncture.
Precautions: Ensure that the needle point is in the subarachnoid space.
Adverse effects: Headache, transient fever.
Dose: By slow intrathecal injection, 2-5 ml; using lumbar puncture technique usually between 3rd and 4th lumbar segments.

POM **Iophendylate** *(EDL 15.4.6)*
Injection, Iophendylate in 1 ml, 3 ml amps.

IOPROMIDE

Indications: Non-ionic contrast medium for contrast enhancement in C.T. scan; for myelogaphy, onterography, I.V.U., phlebography of the extremeties, etc.

POM **ULTRAVIST 300®** *(CHI/Schering)*
Injection, Iopromide 0.63 g per ml in aqueous solution.
Pack - 10 x 20 ml.

MEGLUMINE IODIPAMIDE

Pharmacology: A radio-opaque organic iodine compound containing 49.4% iodine. Freely soluble in water and rapidly excreted by the liver.
Indications: For cholecystography and cholangiography.
Contra-indications: Hypersensitivity to iodides; hyperthyroidism; severe renal impairment.
Precautions: A test dose of 1ml of the solution should be given by slow i.v. before the full dose is given.
Adverse effects: Anaphylactic reaction.
Dose: By slow i.v. injection, Adult, 20 ml of a 52% solution.

POM **Meglumine Iodipamide** *(EDL 15.4.5)*
Injection, Meglumine iodipamide 52%; in 20 ml amp.

MEGLUMINE IOTROXATE

Meglumine iotroxate is a representative iodinated ionic dimeric contrast medium. Various media can serve as alternatives. It is a complementary drug.
Indications: Examination of the gallbladder and biliary tract.
Contra-indications: Hypersensitivity to iodine-containing compounds.
Precautions: History of allergy, atopy or asthma; severe hepatic impairment; renal impairment (Appendix 4); dehydration—correct fluid and electrolyte balance before administration; multiple myeloma (risk if dehydrated, may precipitate fatal renal failure); cardiac disease, hypertension, phaeochromocytoma, sickle-cell disease, hyperthyroidism, elderly, debilitated or children—increased risk of adverse effects; pregnancy; breastfeeding; may interfere with thyroid-function tests; biguanides (withdraw 48 hours before administration; restart when renal function stabilized); **important**: because of risk of hypersensitivity reactions, adequate resuscitation facilities must be immediately available during radiographic procedures.
Adverse effects: Nausea, vomiting, metallic taste, flushing, sensations of heat, weakness, dizziness, headache, cough, rhinitis, sweating, sneezing, lacrimation, visual disturbances, pruritus, salivary gland enlargement, pallor, cardiac disorders, haemodynamic disturbances and hypotension or hypertension; rarely, convulsions, paralysis, coma, rigors, arrhythmias, pulmonary oedema, circulatory failure and cardiac arrest; occasionally anaphylactoid or hypersensitivity reactions; hyperthyroidism; pain on injection; extravasation may result in tissue damage, thrombophlebitis, thrombosis, venospasm and embolism.
Dose: *Examination of gallbladder and biliary tract*, by intravenous injection, ADULT 100 ml of meglumine iotroxate 10.5% solution over at least 15 minutes (consult manufacturer's literature).
ADMINISTRATION: ONLY BY SPECIALIST RADIOGRAPHERS, ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Meglumine iotroxate** *(WMF 14.2)*
Injection (Solution for injection), Iodine 50 mg/ml (as meglumine iotroxate 105 mg/ml), 100-ml bottle.

METRIZAMIDE

Pharmacology: After intrathecal administration into the subarachnoid space, diffusion in the CSF allows the visualisation of the different regions of the bain and spinal cord.
Indications: Myelography as well as cisternography, ventriculography and epidurography.
Contra-indications: Severe cardiovascular disease, epilepsy, severe renal and hepatic disease, allergy to iodine, asthma.
Precautions: Children (increased risk of side effects); elderly (more sensitive); hepatorenal

disease; pregnancy, breast-feeding.
Adverse effects: Headache, backache, blurred vision, confusion; rarely anaphylaxis, nausea, vomiting, hallucinations, local or generalised seizures, hemiparesis.
Dose: As determined by the expert user.

POM **Metrizamide** *(EDL 15.4.6)*
Injection, Metrizamide 3.75 g per 20 ml, 6.75 g per 50 ml; with diluents.

PROPYLIODONE

Propyliodone is a representative iodinated organic contrast medium. Various drugs can serve as alternatives.
Indications: Examination of the bronchial tree (use only if no other alternative available).
Contra-indications: Hypersensitivity to iodine-containing compounds; severe heart disease.
Precautions: Asthma, bronchiectasis, pulmonary emphysema or reduced pulmonary function; use of excessive volume or too rapid administration may result in lobar collapse; may interfere with thyroid-function tests; **important**: because of risk of hypersensitivity reactions, adequate resuscitation facilities must be immediately available when radiographic procedures are carried out.
Adverse effects: Pyrexia, malaise, arthralgia, cough; occasionally, dyspnoea, atelectasis, pneumonia; rarely, hypersensitivity reactions.
Dose: *Examination of bronchial tree*, by instillation into the lungs, ADULT dose, consult manufacturer's literature.
ADMINISTRATION: ONLY BY SPECIALIST RADIOGRAPHERS, ACCORDING TO MANUFACTURER'S DIRECTIONS.

POM **Propyliodone** *(WMF 14.2)*
Oily suspension, Propyliodone 600 mg/ml, 20-ml ampoule.

POM **Propyliodone** *(EDL 15.4.3)*
Injection, Propyliodone 50% (aqueous suspension), 60% (oily suspension); in 20 ml vial.

20.3.5 Tuberculosis

TUBERCULIN PURIFIED PROTEIN DERIVATIVE (Tuberculin PPD)

See under section 17.3

POM **Tuberculin PPD** *(WMF 19.1)*
Injection, Tuberculin purified protein derivative 100 units/ml, 10 units/ml.

POM **Tuberculin PPD** *(EDL 15.5)*
Injection, Tuberculin PPD 10 units, 100 units, 100,000 units per ml; in ml amp.

POM **Tuberculin PPD** *(May and Baker)*
Injection, Purified tuberculin 10 i.u. per 0.1ml.
1 vial x 10 doses x 1 amp. of 1ml diluent.
10 vials x 10 doses x 10 amps of Iml diluent.
1 vial x 50 doses x 1 vial of 5ml diluent.

20.3.6 Endocrine Disorders

LUTEINIZING HORMONE RELEASING HORMONE

Synonym: LH-RH; Gonadorelin
Pharmacology: It stimulates the release of luteinizing hormone from theanterior pituitary, and follicle-stimulating hormone to a lesser exrent.
Indications: Mainly to distinguish between hypogonadism due to anterior pituitary defect and that due to hypothalamic impairment.
Precautions: Repeated high use may lead to inhibition of spermatogenesis.
Adverse effects: Abdominal pain, nausea, headache, increased menstrual bleeding, skin rash.
Dose: By i.v. or s.c. injection, see lit.

POM **Luteinising Hormone-Releasing Hormone (LH-RH)** *(EDL 15.6)*
Injection, LH-RH 100mcg per ml; in 1ml amp.

METYRAPONE

Pharmacology: Metyrapone inhibits the enzyme responsible for the 5-hydroxylation of 11-deoxycortisol in the biosynthesis of cortisol. The fall in blood concentration of hydrocortisone stimulates increased ACTH production which in turn leads to accumulation of 11-deoxycortisol in the blood. This subatance unlike cortisol, does not inhibit ACTH production. It is metabolised in the liver and the metabolites are excreted in the urine where their concentration can be measured.
Indications: To distinguish between primary and ACTH-dependent Cushing's syndrome.
Contra-indications: Adrenocortical insufficiency.
Precautions: The results of the test may be affected by thyroid hypofunction, liver disease, and by anticoagulants, antidepressants, neuroleptics and hormones which affect the

RETURN

hypothalamo-pituitary axis.
Adverse effects: Nausea, vomiting, dizziness, headache, hypotension, allergic reaction.
Dose: By mouth, 750 mg 4 hourly for 6 doses; after a 2-day urine collection and followed by a further 2-day urine collection.

POM **Metyrapone** *(EDL 15.6)*
Tablet or capsule, Metyrapone 250mg.

THYROTROPHIN-RELEASING HORMONE

Synonym: TRH; Protirelin
Pharmacology: It stimulates the release of thyroid stimulating hormone (TSH) from the anterior pituitary.
Indications: Assessement of the hypothalamic-pituitary-thyroid axis in the diagnosis of mild hyperthyroidism, primary hypothyroidism and ophthalmic Graves disease. It gives the following responses:

1) Normal person - increase in plasma TSH which reaches a peak in 20 - 30 minutes.
2) Hyperthyroidism - no rise in serum TSH or thyroid hormone levels.
3) Primary hypothyroidism - increase in TSH but no change in thyroid hormone levels.

Adverse effects: Nausea, a desire to urinate, flushing, dizziness, a peculiar taste; a transient increase in pulse rate and BP may also occur.
Dose: By i.v. bolus injection, 0.2 mg as a single dose; blood sample is taken 20 minutes later for TSH assay. A control sample is taken before the injection.

POM **Thyrotrophin-Releasing Hormone (TRH)** *(EDL 15.6)*
Injection, TRH 200 mcg per ml.

20.3.7 HIV Test Kits

POM **COULTER® Manual CD4 Count Kit** *(GSK)*
Test Kit, COULTER® CD4 Cyto - Spheres Reagent, inert latex spheres coated with murine monoclonal antibody.
Indications: For *in vitro* diagnostic use: to identify and manually enumerate by visible light microscopy the absolute count of CD4+ lymphocytes in fresh whole human blood. Enumeration of CD4+ lymphocytes may aid in the diagnosis and/or prognosis of immunodeficiency diseases such as AIDS.

Appendix 1: Interactions

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Two or more drugs given at the same time may interact with each other. The interaction may be potentiation or antagonism of one drug by another, or occasionally some other effect. Drug interactions may be pharmacodynamic or pharmacokinetic.

Pharmacodynamic interactions occur between drugs which have similar or antagonistic pharmacological effects or adverse effects. They are usually predictable from a knowledge of the pharmacology of the interacting drugs and an interaction occurring with one drug is likely to occur with a related drug. Pharmacodynamic interactions may be due to

- competition at receptor sites
- drugs acting on the same physiological system

Pharmacodynamic interactions occur to some extent in most patients who receive the interacting drugs.

Pharmacokinetic interactions occur when one drug increases or reduces the amount of another drug available to produce its pharmacological action. They are not easily predicted and an interaction occurring with one drug cannot be assumed to occur with a related drug unless their pharmacokinetic properties are similar. Pharmacokinetic interactions may be due to

- interference with absorption
- changes in protein binding
- modification of drug metabolism
- interference with renal excretion

Many pharmacokinetic interactions affect only a small proportion of patients taking the combination of drugs.

Many drug interactions do not have serious consequences and many which are potentially harmful occur only in a small proportion of patients. A known interaction will not necessarily occur to the same extent in all patients. Drugs with a small therapeutic ratio (such as phenytoin) and drugs which require careful dose control (such as anticoagulants, antihypertensives or antidiabetics) are most often involved.

Patients at increased risk from drug interactions include the elderly and those with impaired renal or liver function.

In the following table the symbol ***** indicates a **potentially hazardous interaction** and the combined administration of the drugs involved should be **avoided**, or only taken with caution and appropriate monitoring. Interactions with no symbol do not usually have serious consequences.

Acetazolamide

Acetylsalicylic acid: Reduced excretion of acetazolamide (risk of toxicity)
Alcohol: Enhanced hypotensive effect
Amitriptyline: Increased risk of postural hypotension
Atenolol: Enhanced hypotensive effect
* Carbamazepine: Increased risk of hyponatraemia; acetazolamide increases plasma-carbamazepine concentration
Chlorpromazine: Enhanced hypotensive effect
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of diuretic effect
Dexamethasone: Increased risk of hypokalaemia; antagonism of diuretic effect
Diazepam: Enhanced hypotensive effect
* Digoxin: Cardiac toxicity of digoxin increased if hypokalaemia occurs
Enalapril: Enhanced hypotensive effect (can be extreme)
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Increased risk of hypokalaemia
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect

Acetazolamide *(continued)*

Hydrochlorothiazide: Increased risk of hypokalaemia
Hydrocortisone: Increased risk of hypokalaemia; antagonism of diuretic effect
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Lidocaine: Action of lidocaine antagonised by hypokalaemia
* Lithium: Excretion of lithium increased
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Phenytoin: Increased risk of osteomalacia
Prednisolone: Increased risk of hypokalaemia; antagonism of diuretic effect
Propranolol: Enhanced hypotensive effect
* Quinidine: Cardiac toxicity of quinidine increased if hypokalaemia occurs; acetazolamide reduces excretion of quinidine (occasionally increased plasma concentration)
Salbutamol: Increased risk of hypokalaemia with high doses of salbutamol
Sodium nitroprusside: Enhanced hypotensive effect
Theophylline: Increased risk of hypokalaemia
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Acetylsalicylic acid

Acetazolamide: Reduced excretion of acetazolamide (risk of toxicity)
Antacids (Aluminium hydroxide; Magnesium hydroxide): Excretion of acetylsalicylic acid increased in alkaline urine
Dexamethasone: Increased risk of gastrointestinal bleeding and ulceration; dexamethasone reduces plasma-salicylate concentration
Enalapril: Antagonism of hypotensive effect; increased risk of renal impairment
* Heparin: Enhanced anticoagulant effect
Hydrocortisone: Increased risk of gastrointestinal bleeding and ulceration; hydrocortisone reduces plasma-salicylate concentration
* Ibuprofen: Avoid concurrent administration (increased adverse effects, including gastrointestinal damage); antiplatelet effect of acetylsalicyclic acid possibly reduced
* Methotrexate: Reduced excretion of methotrexate (increased toxicity)
Metoclopramide: Enhanced effect of acetylsalicylic acid (increased rate of absorption)
Phenytoin: Enhancement of effect of phenytoin
Prednisolone: Increased risk of gastrointestinal bleeding and ulceration; prednisolone reduces plasma-salicylate concentration
Spironolactone: Antagonism of diuretic effect
Valproic acid: Enhancement of effect of valproic acid
* Warfarin: Increased risk of bleeding due to antiplatelet effect

Albendazole

Dexamethasone: Plasma-albendazole concentration possibly increased
Praziquantel: Increased plasma concentration of active metabolite of albendazole

Alcohol

Acetazolamide: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
* Amitriptyline: Enhanced sedative effect
Atenolol: Enhanced hypotensive effect
Carbamazepine: Possibly enhanced CNS adverse effects of carbamazepine
Chlorphenamine: Enhanced sedative effect
Chlorpromazine: Enhanced sedative effect
* Clomipramine: Enhanced sedative effect
Clonazepam: Enhanced sedative effect
Codeine: Enhanced sedative and hypotensive effect
Diazepam: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
Fluphenazine: Enhanced sedative effect
Furosemide: Enhanced hypotensive effect
Glibenclamide: Enhanced hypoglycaemic effect

Alcohol *(continued)*

Glyceryl trinitrate: Enhanced hypotensive effect
Haloperidol: Enhanced sedative effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Insulins: Enhanced hypoglycaemic effect
Isosorbide dinitrate: Enhanced hypotensive effect
Levamisole: Disulfiram-like reaction
Metformin: Enhanced hypoglycaemic effect; increased risk of lactic acidosis
Methyldopa: Enhanced hypotensive effect
Metronidazole: Disulfiram-like reaction
Morphine: Enhanced sedative and hypotensive effect
Nifedipine: Enhanced hypotensive effect
Paracetamol: Increased risk of liver damage with regular large amounts of alcohol
Phenobarbital: Enhanced sedative effect
Phenytoin: Plasma-phenytoin concentration reduced with regular large amounts of alcohol
Procarbazine: Disulfiram-like reaction
Promethazine: Enhanced sedative effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect; plasma concentration of alcohol possibly increased by verapamil
* Warfarin: Enhanced anticoagulant effect with large amounts of alcohol; major changes in alcohol consumption may affect anticoagulant control

Alcuronium

Carbamazepine: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)
Clindamycin: Enhanced muscle relaxant effect
Ether, Anaesthetic: Effects of alcuronium enhanced
* Gentamicin: Enhanced muscle relaxant effect
Halothane: Effects of alcuronium enhanced
Lithium: Enhanced muscle relaxant effect
Magnesium (parenteral): Enhanced muscle relaxant effect
Neostigmine: Antagonism of muscle relaxant effect
Nifedipine: Enhanced muscle relaxant effect
Phenytoin: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)
* Procainamide: Enhanced muscle relaxant effect
Propranolol: Enhanced muscle relaxant effect
Pyridostigmine: Antagonism of muscle relaxant effect
* Quinidine: Enhanced muscle relaxant effect
* Streptomycin: Enhanced muscle relaxant effect
Verapamil: Enhanced muscle relaxant effect

Allopurinol

Amoxicillin: Increased risk of rash
Ampicillin: Increased risk of rash
* Azathioprine: Effects of azathioprine enhanced with increased toxicity, reduce dose when given with allopurinol
Ciclosporin: Plasma-ciclosporin concentration possibly increased (risk of nephrotoxicity)
* Mercaptopurine: Effects of mercaptopurine enhanced with increased toxicity, reduce dose when given with allopurinol
Theophylline: Plasma-theophylline concentration possibly increased
Warfarin: Anticoagulant effect possibly enhanced

Aluminium hydroxide *see* Antacids

Amiloride

Alcohol: Enhanced hypotensive effect
Amitriptyline: Increased risk of postural hypotension
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs
Atenolol: Enhanced hypotensive effect

Amiloride *(continued)*

Carbamazepine: Increased risk of hyponatraemia
Chlorpromazine: Enhanced hypotensive effect
* Ciclosporin: Increased risk of hyperkalaemia
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of diuretic effect
Dexamethasone: Antagonism of diuretic effect
Diazepam: Enhanced hypotensive effect
* Enalapril: Enhanced hypotensive effect (can be extreme); risk of severe hyperkalaemia
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrocortisone: Antagonism of diuretic effect
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Lithium: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
* Potassium salts: Risk of hyperkalaemia
Prednisolone: Antagonism of diuretic effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Aminophylline *see* Theophylline

Amitriptyline

Acetazolamide: Increased risk of postural hypotension
* Alcohol: Enhanced sedative effect
Amiloride: Increased risk of postural hypotension
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
Atropine: Increased antimuscarinic adverse effects
Biperiden: Increased antimuscarinic adverse effects
* Carbamazepine: Antagonism (convulsive threshold lowered); possibly accelerated metabolism of amitriptyline (reduced plasma concentration; reduced antidepressant effect)
Chlorphenamine: Increased antimuscarinic and sedative effects
* Chlorpromazine: Increased antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias
Clonazepam: Enhanced sedative effect
Codeine: Possibly increased sedation
Contraceptives, Oral: Antagonism of antidepressant effect but adverse effects possibly increased due to increased plasma concentration of amitriptyline
Diazepam: Enhanced sedative effect
* Epinephrine: Hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)
Ether, Anaesthetic: Increased risk of arrhythmias and hypotension
* Ethosuximide: Antagonism (convulsive threshold lowered)
* Fluphenazine: Increased antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias
Furosemide: Increased risk of postural hypotension

Amitriptyline *(continued)*

Glyceryl trinitrate: Enhanced hypotensive effect; reduced effect of sublingual glyceryl trinitrate (owing to dry mouth)

* Haloperidol: Increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias

Halothane: Increased risk of arrhythmias and hypotension

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Increased risk of postural hypotension

Isosorbide dinitrate: Enhanced hypotensive effect; reduced effect of sublingual isosorbide dinitrate (owing to dry mouth)

Ketamine: Increased risk of arrhythmias and hypotension

Methyldopa: Enhanced hypotensive effect

Morphine: Possibly increased sedation

Nitrous oxide: Increased risk of arrhythmias and hypotension

* Phenobarbital: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of amitriptyline possibly accelerated (reduced plasma concentration)
* Phenytoin: Antagonism (convulsive threshold lowered); possibly reduced plasma-amitriptyline concentration
* Procainamide: Increased risk of ventricular arrhythmias

Promethazine: Increased antimuscarinic and sedative effects

* Quinidine: Increased risk of ventricular arrhythmias

Rifampicin: Plasma concentration of amitriptyline possibly reduced (reduced antidepressant effect)

* Ritonavir: Plasma concentration possibly increased by ritonavir

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Increased risk of postural hypotension

Thiopental: Increased risk of arrhythmias and hypotension

* Valproic acid: Antagonism (convulsive threshold lowered)

Verapamil: Possibly increased plasma concentration of amitriptyline

Amodiaquine

Chlorpromazine: Plasma concentration of chlorpromazine increased (consider reducing chlorpromazine dose)

Amoxicillin

Allopurinol: Increased risk of rash

Contraceptives, Oral: Possibility of reduced contraceptive effect of estrogen-containing preparations

Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)

Warfarin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of amoxicillin

Amoxicillin + Clavulanic acid *see* Amoxicillin

Amphotericin B

NOTE: Close monitoring required with concomitant administration of nephrotoxic drugs or cytotoxics

* Ciclosporin: Increased risk of nephrotoxicity
* Dexamethasone: Increased risk of hypokalaemia (avoid concomitant use unless dexamethasone needed to control reactions)
* Digoxin: Increased digoxin toxicity if hypokalaemia occurs

Fluconazole: Possible antagonism of effect of amphotericin B

Flucytosine: Renal excretion of flucytosine decreased and cellular uptake increased (flucytosine toxicity possibly increased)

Furosemide: Increased risk of hypokalaemia

Gentamicin: Increased risk of nephrotoxicity

Hydrochlorothiazide: Increased risk of hypokalaemia

* Hydrocortisone: Increased risk of hypokalaemia (avoid concomitant use unless hydrocortisone needed to control reactions)
* Prednisolone: Increased risk of hypokalaemia (avoid concomitant use unless prednisolone needed to control reactions)

Streptomycin: Increased risk of nephrotoxicity

Ampicillin

Allopurinol: Increased risk of rash

Contraceptives, Oral: Possibility of reduced contraceptive effect of estrogen-containing preparations

Ampicillin *(continued)*

Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)

Warfarin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of ampicillin

Antacids (Aluminium hydroxide; Magnesium hydroxide)

NOTE: ANTACIDS SHOULD PREFERABLY NOT BE TAKEN AT THE SAME TIME AS OTHER DRUGS SINCE THEY MAY IMPAIR ABSORPTION

Acetylsalicylic acid: Excretion of acetylsalicylic acid increased in alkaline urine

Azithromycin: Reduced absorption of azithromycin

Chloroquine: Reduced absorption of chloroquine

Chlorpromazine: Reduced absorption of chlorpromazine

Ciprofloxacin: Reduced absorption of ciprofloxacin

Digoxin: Possibly reduced absorption of digoxin

Doxycycline: Reduced absorption of doxycycline

Enalapril: Absorption of enalapril reduced

Isoniazid: Reduced absorption of isoniazid

Ofloxacin: Reduced absorption of ofloxacin

Penicillamine: Reduced absorption of penicillamine

Phenytoin: Reduced absorption of phenytoin

Quinidine: Reduced quinidine excretion in alkaline urine (plasma-quinidine concentration occasionally increased)

Rifampicin: Reduced absorption of rifampicin

Artemether + Lumefantrine

* Amiloride: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs
* Amitriptyline: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Azithromycin: Avoid concomitant use
* Chloroquine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Chlorpromazine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Ciprofloxacin: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Clomipramine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Erythromycin: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Fluconazole: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Fluphenazine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Furosemide: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs
* Grapefruit Juice: Metabolism of artemether and lumefantrine may be inhibited (avoid concomitant use)
* Hydrochlorothiazide: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs
* Mefloquine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Nalidixic acid: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Ofloxacin: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Procainamide: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Pyrimethamine: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Quinidine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Quinine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Spironolactone: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs

Sulfadoxine + Pyrimethamine: Manufacturer of artemether with lumefantrine advises avoid concomitant use

Asparaginase

Vaccine, Live: Avoid use of live vaccines with asparaginase (impairment of immune response)

Atenolol

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Digoxin: Increased AV block and bradycardia
Enalapril: Enhanced hypotensive effect
* Epinephrine: Severe hypertension
Ergotamine: Increased peripheral vasoconstriction
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glibenclamide: Masking of warning signs of hypoglycaemia such as tremor
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Insulins: Enhanced hypoglycaemic effect; masking of warning signs of hypoglycaemia such as tremor
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Lidocaine: Increased risk of myocardial depression
Mefloquine: Increased risk of bradycardia
Metformin: Masking of warning signs of hypoglycaemia such as tremor
Methyldopa: Enhanced hypotensive effect
* Nifedipine: Severe hypotension and heart failure occasionally
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
* Procainamide: Increased risk of myocardial depression
* Quinidine: Increased risk of myocardial depression
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
* Verapamil: Asystole, severe hypotension and heart failure

Atropine

NOTE: MANY DRUGS HAVE ANTIMUSCARINIC EFFECTS; CONCOMITANT USE OF 2 OR MORE SUCH DRUGS CAN INCREASE ADVERSE EFFECTS SUCH AS DRY MOUTH, URINE RETENTION, AND CONSTIPATION, AND CAN ALSO LEAD TO CONFUSION IN THE ELDERLY

Amitriptyline: Increased antimuscarinic adverse effects
Chlorphenamine: Increased antimuscarinic adverse effects
Chlorpromazine: Increased antimuscarinic adverse effects of chlorpromazine (but reduced plasma concentration)
Clomipramine: Increased antimuscarinic adverse effects
Fluphenazine: Increased antimuscarinic adverse effects of fluphenazine (but reduced plasma concentration)
Glyceryl trinitrate: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Isosorbide dinitrate: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Levodopa: Absorption of levodopa possibly reduced
Metoclopramide: Antagonism of effect on gastrointestinal activity
Neostigmine: Antagonism of effect
Promethazine: Increased antimuscarinic adverse effects

Atropine *(continued)*
Pyridostigmine: Antagonism of effect

Azathioprine
* Allopurinol: Effects of azathioprine enhanced with increased toxicity, reduce dose when given with allopurinol
Phenytoin: Reduced absorption of phenytoin
* Rifampicin: Manufacturer reports interaction (transplants possibly rejected)
* Sulfamethoxazole + Trimethoprim: Increased risk of haematological toxicity
Sulfasalazine: Possibly increased risk of leukopenia
* Trimethoprim: Increased risk of haematological toxicity
* Vaccine, Live: Avoid use of live vaccines with azathioprine (impairment of immune response)
* Warfarin: Anticoagulant effect possibly reduced

Azithromycin
Antacids: Reduced absorption of azithromycin
* Artemether with lumefantrine: Avoid concomitant use
* Ciclosporin: Plasma concentration of ciclosporin possibly increased
Digoxin: Effect of digoxin possibly enhanced
* Ergotamine: Increased risk of ergotism—avoid concomitant use
Ritonavir: Plasma concentration of azithromycin possibly increased
* Warfarin: Possibly enhanced anticoagulant effect of warfarin

Benzathine benzylpenicillin *see* Benzylpenicillin

Benzylpenicillin
Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)

BCG vaccine *see* Vaccine, live

Biperiden
NOTE: MANY DRUGS HAVE ANTIMUSCARINIC EFFECTS; CONCOMITANT USE OF 2 OR MORE SUCH DRUGS CAN INCREASE ADVERSE EFFECTS SUCH AS DRY MOUTH, URINE RETENTION, AND CONSTIPATION, AND CAN ALSO LEAD TO CONFUSION IN THE ELDERLY
Amitriptyline: Increased antimuscarinic adverse effects
Chlorphenamine: Increased antimuscarinic adverse effects
Chlorpromazine: Increased antimuscarinic adverse effects of chlorpromazine (but reduced plasma concentration)
Clomipramine: Increased antimuscarinic adverse effects
Fluphenazine: Increased antimuscarinic adverse effects of fluphenazine (but reduced plasma concentration)
Glyceryl trinitrate: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Isosorbide dinitrate: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Levodopa: Absorption of levodopa possibly reduced
Metoclopramide: Antagonism of effect on gastrointestinal activity
Neostigmine: Antagonism of effect
Promethazine: Increased antimuscarinic adverse effects
Pyridostigmine: Antagonism of effect

Bleomycin
* Oxygen: Increased risk of pulmonary toxicity
Vaccine, Live: Avoid use of live vaccines with bleomycin (impairment of immune response)
* Vinblastine: Increased risk of cardiovascular toxicity

Bupivacaine
Lidocaine: Increased myocardial depression
Procainamide: Increased myocardial depression
* Propranolol: Increased risk of bupivacaine toxicity
Quinidine: Increased myocardial depression

Calcium folinate *see* Folic acid and Folinic acid

Calcium gluconate *see* Calcium salts

Calcium salts
Digoxin: Large intravenous doses of calcium can precipitate arrhythmias
Hydrochlorothiazide: Increased risk of hypercalcaemia

Carbamazepine
* Acetazolamide: Increased risk of hyponatraemia; acetazolamide increases plasma-carbamazepine concentration
Alcohol: Possibly enhanced CNS adverse effects of carbamazepine

Carbamazepine *(continued)*

Alcuronium: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)
Amiloride: Increased risk of hyponatraemia
* Amitriptyline: Antagonism (convulsive threshold lowered); possibly accelerated metabolism of amitriptyline (reduced plasma concentration; reduced antidepressant effect)
* Chloroquine: Convulsive threshold occasionally lowered
* Chlorpromazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Ciclosporin: Accelerated metabolism (reduced plasma-ciclosporin concentration)
* Clomipramine: Antagonism (convulsive threshold lowered); possibly accelerated metabolism of clomipramine (reduced plasma concentration; reduced antidepressant effect)
* Clonazepam: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of clonazepam often lowered
* Contraceptives, Oral: Accelerated metabolism (reduced contraceptive effect)
* Dexamethasone: Accelerated metabolism of dexamethasone (reduced effect)
Doxycycline: Accelerated doxycycline metabolism (reduced effect)
Ergocalciferol: Ergocalciferol requirements possibly increased
* Erythromycin: Increased plasma-carbamazepine concentration
* Ethosuximide: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide sometimes lowered
* Fluphenazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
Furosemide: Increased risk of hyponatraemia
* Haloperidol: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)
Hydrochlorothiazide: Increased risk of hyponatraemia
* Hydrocortisone: Accelerated metabolism of hydrocortisone (reduced effect)
Indinavir: Possibly reduced plasma-indinavir concentration
* Isoniazid: Increased plasma-carbamazepine concentration (also isoniazid hepatotoxicity possibly increased)
* Levonorgestrel: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
Levothyroxine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)
Lithium: Neurotoxicity may occur without increased plasma-lithium concentration
* Lopinavir: Possibly reduced plasma-lopinavir concentration
Mebendazole: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)
* Medroxyprogesterone: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Mefloquine: Antagonism of anticonvulsant effect
Nelfinavir: Possibly reduced plasma-nelfinavir concentration
Nifedipine: Probably reduced effect of nifedipine
* Norethisterone: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of carbamazepine often lowered
* Phenytoin: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; plasma concentration of carbamazepine often lowered
Praziquantel: Plasma-praziquantel concentration reduced
* Prednisolone: Accelerated metabolism of prednisolone (reduced effect)
* Ritonavir: Plasma concentration possibly increased by ritonavir
Saquinavir: Possibly reduced plasma-saquinavir concentration
Spironolactone: Increased risk of hyponatraemia
Theophylline: Accelerated metabolism of theophylline (reduced effect)
* Valproic acid: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproic acid often lowered; plasma concentration of active metabolite of carbamazepine often raised
Vecuronium: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)
* Verapamil: Enhanced effect of carbamazepine

Carbamazepine *(continued)*
* Warfarin: Accelerated metabolism of warfarin (reduced anticoagulant effect)

Ceftazidime
Contraceptives, Oral: Possibility of reduced contraceptive effect of estrogen-containing preparations
Furosemide: Nephrotoxicity of ceftazidime possibly increased
* Warfarin: Possibly enhanced anticoagulant effect

Ceftriaxone
Contraceptives, Oral: Possibility of reduced contraceptive effect of estrogen-containing preparations
Furosemide: Nephrotoxicity of ceftriaxone possibly increased
* Warfarin: Possibly enhanced anticoagulant effect

Chlorambucil
Vaccine, Live: Avoid use of live vaccines with chlorambucil (impairment of immune response)

Chloramphenicol
* Ciclosporin: Plasma concentration of ciclosporin possibly increased
* Glibenclamide: Enhanced effect of glibenclamide
* Phenobarbital: Metabolism of chloramphenicol accelerated (reduced chloramphenicol concentration)
* Phenytoin: Plasma-phenytoin concentration increased (risk of toxicity)
Rifampicin: Accelerated metabolism of chloramphenicol (reduced plasma-chloramphenicol concentration)
* Warfarin: Enhanced anticoagulant effect

Chlormethine
Vaccine, Live: Avoid use of live vaccines with chlormethine (impairment of immune response)

Chloroquine
Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of chloroquine
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Carbamazepine: Convulsive threshold occasionally lowered
* Ciclosporin: Increased plasma-ciclosporin concentration (increased risk of toxicity)
* Digoxin: Plasma-digoxin concentration possibly increased
* Ethosuximide: Convulsive threshold occasionally lowered
* Mefloquine: Increased risk of convulsions
Neostigmine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of neostigmine
* Phenytoin: Convulsive threshold occasionally lowered
Praziquantel: Plasma-praziquantel concentration possibly reduced
Pyridostigmine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of pyridostigmine
Quinidine: Increased risk of ventricular arrhythmias
Quinine: Increased risk of ventricular arrhythmias
* Valproic acid: Convulsive threshold occasionally lowered

Chlorphenamine
Alcohol: Enhanced sedative effect
Amitriptyline: Increased antimuscarinic and sedative effects
Atropine: Increased antimuscarinic adverse effects
Biperiden: Increased antimuscarinic adverse effects
Clomipramine: Increased antimuscarinic and sedative effects
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect

Chlorpromazine
Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced sedative effect
Amiloride: Enhanced hypotensive effect
* Amitriptyline: Increased antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias
Amodiaquine: Plasma concentration of chlorpromazine increased (consider reducing chlorpromazine dose)

Chlorpromazine *(continued)*

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of chlorpromazine
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
Atenolol: Enhanced hypotensive effect
Atropine: Increased antimuscarinic adverse effects of chlorpromazine (but reduced plasma concentration)
Biperiden: Increased antimuscarinic adverse effects of chlorpromazine (but reduced plasma concentration)
* Carbamazepine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Clomipramine: Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias
Clonazepam: Enhanced sedative effect
Codeine: Enhanced sedative and hypotensive effect
Diazepam: Enhanced sedative effect
Dopamine: Antagonism of pressor action
Enalapril: Enhanced hypotensive effect
Ephedrine: Antagonism of pressor action
Epinephrine: Antagonism of pressor action
* Ether, Anaesthetic: Enhanced hypotensive effect
* Ethosuximide: Antagonism (convulsive threshold lowered)
Furosemide: Enhanced hypotensive effect
Glibenclamide: Possible antagonism of hypoglycaemic effect
Glyceryl trinitrate: Enhanced hypotensive effect
* Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoprenaline: Antagonism of pressor action
Isosorbide dinitrate: Enhanced hypotensive effect
* Ketamine: Enhanced hypotensive effect
Levodopa: Antagonism of effects of levodopa
Lithium: Increased risk of extrapyramidal effects and possibility of neurotoxicity
Methyldopa: Enhanced hypotensive effect; increased risk of extrapyramidal effects
Metoclopramide: Increased risk of extrapyramidal effects
Morphine: Enhanced sedative and hypotensive effect
Nifedipine: Enhanced hypotensive effect
* Nitrous oxide: Enhanced hypotensive effect
* Phenobarbital: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Phenytoin: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Procainamide: Increased risk of ventricular arrhythmias
* Propranolol: Concomitant administration may increase plasma concentration of both drugs; enhanced hypotensive effect
* Quinidine: Increased risk of ventricular arrhythmias
* Ritonavir: Plasma concentration possibly increased by ritonavir
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
* Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
* Valproic acid: Antagonism of anticonvulsant effect (convulsive threshold lowered)
Verapamil: Enhanced hypotensive effect

Ciclosporin

Allopurinol: Plasma-ciclosporin concentration possibly increased (risk of nephrotoxicity)
* Amiloride: Increased risk of hyperkalaemia
* Amphotericin B: Increased risk of nephrotoxicity
* Azithromycin: Plasma concentration of ciclosporin possibly increased
* Carbamazepine: Accelerated metabolism (reduced plasma-ciclosporin concentration)
* Chloramphenicol: Plasma concentration of ciclosporin possibly increased
* Chloroquine: Increased plasma-ciclosporin concentration (increased risk of toxicity)
* Ciprofloxacin: Increased risk of nephrotoxicity
* Colchicine: Possibly increased risk of nephrotoxicity and myotoxicity (increased plasma-ciclosporin concentration)

Ciclosporin *(continued)*

* Contraceptives, Oral: Increased plasma-ciclosporin concentration
* Digoxin: Reduced clearance of digoxin (risk of toxicity)
* Doxorubicin: Increased risk of neurotoxicity
* Doxycycline: Possibly increased plasma-ciclosporin concentration
* Enalapril: Increased risk of hyperkalaemia
* Erythromycin: Increased plasma-ciclosporin concentration (inhibition of metabolism)
* Fluconazole: Metabolism of ciclosporin inhibited (increased plasma concentration)
* Gentamicin: Increased risk of nephrotoxicity
* Grapefruit Juice: Increased plasma-ciclosporin concentration (risk of toxicity)

Griseofulvin: Plasma-ciclosporin concentration possibly reduced

* Ibuprofen: Increased risk of nephrotoxicity
* Levonorgestrel: Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
* Medroxyprogesterone: Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
* Methotrexate: Increased toxicity
* Metoclopramide: Plasma-ciclosporin concentration increased
* Nalidixic acid: Increased risk of nephrotoxicity

Nelfinavir: Possibly increased plasma-ciclosporin concentration

Nifedipine: Possibly increased plasma-nifedipine concentration (increased risk of adverse effects such as gingival hyperplasia)

* Norethisterone: Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
* Ofloxacin: Increased risk of nephrotoxicity
* Phenobarbital: Metabolism of ciclosporin accelerated (reduced effect)
* Phenytoin: Accelerated metabolism (reduced plasma-ciclosporin concentration)
* Potassium salts: Increased risk of hyperkalaemia

Prednisolone: Increased plasma concentration of prednisolone

* Rifampicin: Accelerated metabolism (reduced plasma-ciclosporin concentration)
* Ritonavir: Plasma concentration possibly increased by ritonavir
* Spironolactone: Increased risk of hyperkalaemia
* Streptomycin: Increased risk of nephrotoxicity
* Sulfadiazine: Plasma-ciclosporin concentration possibly reduced; increased risk of nephrotoxicity
* Sulfadoxine + Pyrimethamine: Increased risk of nephrotoxicity
* Sulfamethoxazole + Trimethoprim: Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim
* Trimethoprim: Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim
* Vaccine, Live: Avoid use of live vaccines with ciclosporin (impairment of immune response)
* Vancomycin: Increased risk of nephrotoxicity
* Verapamil: Increased plasma-ciclosporin concentration

Ciprofloxacin

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of ciprofloxacin

* Artemether + Lumefantrine: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Ciclosporin: Increased risk of nephrotoxicity

Ferrous salts: Absorption of ciprofloxacin reduced by oral ferrous salts

Glibenclamide: Possibly enhanced effect of glibenclamide

* Ibuprofen: Possibly increased risk of convulsions

Morphine: Manufacturer of ciprofloxacin advises avoid premedication with morphine (reduced plasma-ciprofloxacin concentration)

Phenytoin: Plasma-phenytoin concentration possibly altered by ciprofloxacin

* Theophylline: Increased plasma-theophylline concentration; possible increased risk of convulsions
* Warfarin: Enhanced anticoagulant effect

Cisplatin

Acetazolamide: Increased risk of nephrotoxicity and ototoxicity

Amiloride: Increased risk of nephrotoxicity and ototoxicity

Cisplatin *(continued)*

Furosemide: Increased risk of nephrotoxicity and ototoxicity
* Gentamicin: Increased risk of nephrotoxicity and possibly of ototoxicity
Hydrochlorothiazide: Increased risk of nephrotoxicity and ototoxicity
Phenytoin: Reduced absorption of phenytoin
Spironolactone: Increased risk of nephrotoxicity and ototoxicity
* Streptomycin: Increased risk of nephrotoxicity and possibly of ototoxicity
Vaccine, Live: Avoid use of live vaccines with cisplatin (impairment of immune response)
Vancomycin: Increased risk of nephrotoxicity and possibly of ototoxicity

Clindamycin

Alcuronium: Enhanced muscle relaxant effect
Neostigmine: Antagonism of effects of neostigmine
Pyridostigmine: Antagonism of effects of pyridostigmine
Vecuronium: Enhanced muscle relaxant effect

Clomipramine

Acetazolamide: Increased risk of postural hypotension
* Alcohol: Enhanced sedative effect
Amiloride: Increased risk of postural hypotension
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
Atropine: Increased antimuscarinic adverse effects
Biperiden: Increased antimuscarinic adverse effects
* Carbamazepine: Antagonism (convulsive threshold lowered); possibly accelerated metabolism of clomipramine (reduced plasma concentration; reduced antidepressant effect)
Chlorphenamine: Increased antimuscarinic and sedative effects
* Chlorpromazine: Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias
Clonazepam: Enhanced sedative effect
Codeine: Possibly increased sedation
Contraceptives, Oral: Antagonism of antidepressant effect but adverse effects possibly increased due to increased plasma concentration of clomipramine
Diazepam: Enhanced sedative effect
* Epinephrine: Hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)
Ether, Anaesthetic: Increased risk of arrhythmias and hypotension
* Ethosuximide: Antagonism (convulsive threshold lowered)
* Fluphenazine: Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias
Furosemide: Increased risk of postural hypotension
Glyceryl trinitrate: Enhanced hypotensive effect; reduced effect of sublingual glyceryl trinitrate (owing to dry mouth)
* Haloperidol: Increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias
Halothane: Increased risk of arrhythmias and hypotension
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Increased risk of postural hypotension
Isosorbide dinitrate: Enhanced hypotensive effect; reduced effect of sublingual isosorbide dinitrate (owing to dry mouth)
Ketamine: Increased risk of arrhythmias and hypotension
Methyldopa: Enhanced hypotensive effect
Morphine: Possibly increased sedation
Nitrous oxide: Increased risk of arrhythmias and hypotension
* Phenobarbital: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of clomipramine possibly accelerated (reduced plasma concentration)
* Phenytoin: Antagonism (convulsive threshold lowered); possibly reduced plasma-clomipramine concentration
* Procainamide: Increased risk of ventricular arrhythmias
Promethazine: Increased antimuscarinic and sedative effects
* Quinidine: Increased risk of ventricular arrhythmias
Rifampicin: Plasma concentration of clomipramine possibly reduced (reduced antidepressant effect)

Clomipramine *(continued)*

* Ritonavir: Plasma concentration possibly increased by ritonavir
  Sodium nitroprusside: Enhanced hypotensive effect
  Spironolactone: Increased risk of postural hypotension
  Thiopental: Increased risk of arrhythmias and hypotension
* Valproic acid: Antagonism (convulsive threshold lowered)
  Verapamil: Possibly increased plasma concentration of clomipramine

Clonazepam

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced sedative effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Enhanced sedative effect
Atenolol: Enhanced hypotensive effect
* Carbamazepine: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of clonazepam often lowered
  Chlorphenamine: Enhanced sedative effect
  Chlorpromazine: Enhanced sedative effect
  Clomipramine: Enhanced sedative effect
  Codeine: Enhanced sedative effect
  Enalapril: Enhanced hypotensive effect
  Ether, Anaesthetic: Enhanced sedative effect
  Fluphenazine: Enhanced sedative effect
  Furosemide: Enhanced hypotensive effect
  Glyceryl trinitrate: Enhanced hypotensive effect
  Haloperidol: Enhanced sedative effect
  Halothane: Enhanced sedative effect
  Hydralazine: Enhanced hypotensive effect
  Hydrochlorothiazide: Enhanced hypotensive effect
  Isosorbide dinitrate: Enhanced hypotensive effect
  Ketamine: Enhanced sedative effect
  Levodopa: Possibly occasional antagonism of levodopa effects
  Methyldopa: Enhanced hypotensive effect
  Morphine: Enhanced sedative effect
  Nifedipine: Enhanced hypotensive effect
  Nitrous oxide: Enhanced sedative effect
* Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of clonazepam often lowered
* Phenytoin: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of clonazepam often lowered
  Promethazine: Enhanced sedative effect
  Propranolol: Enhanced hypotensive effect
  Rifampicin: Metabolism of clonazepam possibly accelerated (possibly reduced plasma concentration)
* Ritonavir: Plasma concentration possibly increased by ritonavir
  Sodium nitroprusside: Enhanced hypotensive effect
  Spironolactone: Enhanced hypotensive effect
  Thiopental: Enhanced sedative effect
  Timolol: Enhanced hypotensive effect
  Verapamil: Enhanced hypotensive effect

Cloxacillin *see* Benzylpenicillin

Codeine

Alcohol: Enhanced sedative and hypotensive effect
Amitriptyline: Possibly increased sedation
Chlorpromazine: Enhanced sedative and hypotensive effect
Clomipramine: Possibly increased sedation
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect
Fluphenazine: Enhanced sedative and hypotensive effect
Haloperidol: Enhanced sedative and hypotensive effect
Metoclopramide: Antagonism of effect of metoclopramide on gastrointestinal activity
* Ritonavir: Ritonavir possibly increases plasma concentration of codeine

Colchicine

* Ciclosporin: Possibly increased risk of nephrotoxicity and myotoxicity (increased plasma-ciclosporin concentration)

Contraceptives, Oral

NOTE: Interactions also apply to ethinylestradiol taken alone. In hormone replacement therapy low dose unlikely to induce interactions

Acetazolamide: Antagonism of diuretic effect
Amiloride: Antagonism of diuretic effect
Amitriptyline: Antagonism of antidepressant effect but adverse effects possibly increased due to increased plasma concentration of amitriptyline
Amoxicillin: Possibility of reduced contraceptive effect of estrogen-containing preparations
Ampicillin: Possibility of reduced contraceptive effect of estrogen-containing preparations
Atenolol: Antagonism of hypotensive effect
* Carbamazepine: Accelerated metabolism (reduced contraceptive effect)
Ceftazidime: Possibility of reduced contraceptive effect of estrogen-containing preparations
Ceftriaxone: Possibility of reduced contraceptive effect of estrogen-containing preparations
* Ciclosporin: Increased plasma-ciclosporin concentration
Clomipramine: Antagonism of antidepressant effect but adverse effects possibly increased due to increased plasma concentration of clomipramine
Dexamethasone: Oral contraceptives increase plasma concentration of dexamethasone
Doxycycline: Possibility of reduced contraceptive effect of estrogen-containing preparations
Efavirenz: Efficacy of oral contraceptives possibly reduced
Enalapril: Antagonism of hypotensive effect
Fluconazole: Anecdotal reports of contraceptive failure
Furosemide: Antagonism of diuretic effect
Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Antagonism of hypotensive effect
* Griseofulvin: Accelerated metabolism (reduced contraceptive effect)
Hydralazine: Antagonism of hypotensive effect
Hydrochlorothiazide: Antagonism of diuretic effect
Hydrocortisone: Oral contraceptives increase plasma concentration of hydrocortisone
Insulins: Antagonism of hypoglycaemic effect
Isosorbide dinitrate: Antagonism of hypotensive effect
Metformin: Antagonism of hypoglycaemic effect
Methyldopa: Antagonism of hypotensive effect
* Nelfinavir: Accelerated metabolism (reduced contraceptive effect)
* Nevirapine: Accelerated metabolism (reduced contraceptive effect)
Nifedipine: Antagonism of hypotensive effect
* Phenobarbital: Metabolism accelerated (reduced contraceptive effect)
* Phenytoin: Accelerated metabolism (reduced contraceptive effect)
Prednisolone: Oral contraceptives increase plasma concentration of prednisolone
Propranolol: Antagonism of hypotensive effect
* Rifampicin: Accelerated metabolism of oral contraceptives (reduced contraceptive effect)
* Ritonavir: Accelerated metabolism (reduced contraceptive effect)
Sodium nitroprusside: Antagonism of hypotensive effect
Spironolactone: Antagonism of diuretic effect
Theophylline: Delayed excretion of theophylline (increased plasma concentration)
Verapamil: Antagonism of hypotensive effect
* Warfarin: Antagonism of anticoagulant effect

Cyclophosphamide

Phenytoin: Reduced absorption of phenytoin
Suxamethonium: Enhanced effect of suxamethonium
Vaccine, Live: Avoid use of live vaccines with cyclophosphamide (impairment of immune response)

Cytarabine

Flucytosine: Plasma-flucytosine concentration possibly reduced
Phenytoin: educed absorption of phenytoin
Vaccine, Live: Avoid use of live vaccines with cytarabine (impairment of immune response)

Dacarbazine

Vaccine, Live: Avoid use of live vaccines with dacarbazine (impairment of immune response)

Dactinomycin

Vaccine, Live: Avoid use of live vaccines with dactinomycin (impairment of immune response)

Dapsone

Rifampicin: Reduced plasma-dapsone concentration
Sulfamethoxazole + Trimethoprim: Plasma concentration of both dapsone and trimethoprim increased with concomitant use
Trimethoprim: Plasma concentration of both dapsone and trimethoprim increased with concomitant use

Daunorubicin

Vaccine, Live: Avoid use of live vaccines with daunorubicin (impairment of immune response)

Dexamethasone

Acetazolamide: Increased risk of hypokalaemia; antagonism of diuretic effect
Acetylsalicylic acid: Increased risk of gastrointestinal bleeding and ulceration; dexamethasone reduces plasma-salicylate concentration
Albendazole: Plasma-albendazole concentration possibly increased
Amiloride: Antagonism of diuretic effect
* Amphotericin B: Increased risk of hypokalaemia (avoid concomitant use unless dexamethasone needed to control reactions)
Atenolol: Antagonism of hypotensive effect
* Carbamazepine: Accelerated metabolism of dexamethasone (reduced effect)
Contraceptives, Oral: Oral contraceptives increase plasma concentration of dexamethasone
Digoxin: Increased risk of hypokalaemia
Enalapril: Antagonism of hypotensive effect
Ephedrine: Metabolism of dexamethasone accelerated
Erythromycin: Erythromycin possibly inhibits metabolism of dexamethasone
Furosemide: Antagonism of diuretic effect; increased risk of hypokalaemia
Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Antagonism of hypotensive effect
Hydralazine: Antagonism of hypotensive effect
Hydrochlorothiazide: Antagonism of diuretic effect; increased risk of hypokalaemia
Ibuprofen: Increased risk of gastrointestinal bleeding and ulceration
Indinavir: Possibly reduced plasma-indinavir concentration
Insulins: Antagonism of hypoglycaemic effect
Isosorbide dinitrate: Antagonism of hypotensive effect
Levonorgestrel: Levonorgestrel increases plasma concentration of dexamethasone
* Lopinavir: Possibly reduced plasma-lopinavir concentration
Medroxyprogesterone: Medroxyprogesterone increases plasma concentration of dexamethasone
Metformin: Antagonism of hypoglycaemic effect
Methotrexate: Increased risk of haematological toxicity
Methyldopa: Antagonism of hypotensive effect
Nifedipine: Antagonism of hypotensive effect
Norethisterone: Norethisterone increases plasma concentration of dexamethasone
* Phenobarbital: Metabolism of dexamethasone accelerated (reduced effect)
* Phenytoin: Metabolism of dexamethasone accelerated (reduced effect)
Praziquantel: Plasma-praziquantel concentration reduced
Propranolol: Antagonism of hypotensive effect
* Rifampicin: Accelerated metabolism of dexamethasone (reduced effect)
Ritonavir: Plasma concentration possibly increased by ritonavir
Salbutamol: Increased risk of hypokalaemia if high doses of dexamethasone given with high doses of salbutamol
Saquinavir: Possibly reduced plasma-saquinavir concentration
Sodium nitroprusside: Antagonism of hypotensive effect
Spironolactone: Antagonism of diuretic effect
Theophylline: Increased risk of hypokalaemia

Dexamethasone *(continued)*

* Vaccine, Live: High doses of dexamethasone impair immune response; avoid use of live vaccines
  Verapamil: Antagonism of hypotensive effect
* Warfarin: Anticoagulant effect possibly altered

Diazepam

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced sedative effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Enhanced sedative effect
Atenolol: Enhanced hypotensive effect
Chlorphenamine: Enhanced sedative effect
Chlorpromazine: Enhanced sedative effect
Clomipramine: Enhanced sedative effect
Codeine: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
Ether, Anaesthetic: Enhanced sedative effect
Fluphenazine: Enhanced sedative effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Haloperidol: Enhanced sedative effect
Halothane: Enhanced sedative effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoniazid: Metabolism of diazepam inhibited
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced sedative effect
Levodopa: Occasional antagonism of levodopa effects
Methyldopa: Enhanced hypotensive effect
Morphine: Enhanced sedative effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced sedative effect
Phenytoin: Plasma-phenytoin concentrations increased or decreased by diazepam
Promethazine: Enhanced sedative effect
Propranolol: Enhanced hypotensive effect
Rifampicin: Metabolism of diazepam accelerated (reduced plasma concentration)
* Ritonavir: Plasma concentration possibly increased by ritonavir (risk of extreme sedation and respiratory depression—avoid concomitant use)
  Sodium nitroprusside: Enhanced hypotensive effect
  Spironolactone: Enhanced hypotensive effect
  Thiopental: Enhanced sedative effect
  Timolol: Enhanced hypotensive effect
  Verapamil: Enhanced hypotensive effect

Didanosine

NOTE: ANTACIDS PRESENT IN BUFFERED TABLET FORMULATION MAY AFFECT ABSORPTION OF OTHER DRUGS; SEE ALSO ANTACIDS

Digoxin

* Acetazolamide: Cardiac toxicity of digoxin increased if hypokalaemia occurs
* Amphotericin B: Increased digoxin toxicity if hypokalaemia occurs
  Antacids (Aluminium hydroxide; Magnesium hydroxide): Possibly reduced absorption of digoxin
  Atenolol: Increased AV block and bradycardia
  Azithromycin: Effect of digoxin possibly enhanced
  Calcium salts: Large intravenous doses of calcium can precipitate arrhythmias
* Chloroquine: Plasma-digoxin concentration possibly increased
* Ciclosporin: Reduced clearance of digoxin (risk of toxicity)
  Dexamethasone: Increased risk of hypokalaemia
  Erythromycin: Enhanced effect of digoxin
* Furosemide: Cardiac toxicity of digoxin increased if hypokalaemia occurs
* Hydrochlorothiazide: Cardiac toxicity of digoxin increased if hypokalaemia occurs
  Hydrocortisone: Increased risk of hypokalaemia
  Ibuprofen: Possibly exacerbation of heart failure, reduced GFR, and increased plasma-digoxin concentration

Digoxin *(continued)*

Mefloquine: Possibly increased risk of bradycardia
* Nifedipine: Possibly increased plasma concentration of digoxin
Penicillamine: Plasma concentration of digoxin possibly reduced
Phenytoin: Plasma concentration of digoxin possibly reduced
Prednisolone: Increased risk of hypokalaemia
Propranolol: Increased AV block and bradycardia
* Quinidine: Plasma concentration of digoxin increased (halve maintenance dose of digoxin)
* Quinine: Plasma concentration of digoxin increased
Rifampicin: Plasma concentration of digoxin possibly reduced
* Spironolactone: Enhanced effect of digoxin
Sulfamethoxazole + Trimethoprim: Plasma concentration of digoxin possibly increased
Sulfasalazine: Absorption of digoxin possibly reduced
Suxamethonium: Risk of arrhythmias
Timolol: Increased AV block and bradycardia
Trimethoprim: Plasma concentration of digoxin possibly increased
* Verapamil: Increased plasma concentration of digoxin; increased AV block and bradycardia

Dopamine

Chlorpromazine: Antagonism of pressor action
Ergometrine: Increased risk of ergotism
Ergotamine: Increased risk of ergotism
Fluphenazine: Antagonism of pressor action
Haloperidol: Antagonism of pressor action

Doxorubicin

* Ciclosporin: Increased risk of neurotoxicity
Phenytoin: Reduced absorption of phenytoin
Stavudine: Doxorubicin may inhibit effect of stavudine
Vaccine, Live: Avoid use of live vaccines with doxorubicin (impairment of immune response)

Doxycycline

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of doxycycline
Carbamazepine: Accelerated doxycycline metabolism (reduced effect)
* Ciclosporin Possibly increased plasma-ciclosporin concentration
Contraceptives, Oral: Possibility of reduced contraceptive effect of estrogen-containing preparations
* Ergotamine: Increased risk of ergotism
Ferrous salts: Reduced absorption of oral ferrous salts by doxycycline; reduced absorption of doxycycline by oral ferrous salts
Phenobarbital: Metabolism of doxycycline accelerated (reduced plasma concentration)
Phenytoin: Increased metabolism of doxycycline (reduced plasma concentration)
Rifampicin: Plasma-doxycycline concentration possibly reduced
* Warfarin: Anticoagulant effect possibly enhanced

Efavirenz

Contraceptives, Oral: Efficacy of oral contraceptives possibly reduced
Grapefruit Juice: Plasma concentration of efavirenz may be affected
Indinavir: Efavirenz reduces plasma concentration of indinavir (increase indinavir dose)
* Lopinavir: Plasma concentration of lopinavir reduced
Nevirapine: Plasma-efavirenz concentration reduced
Rifampicin: Reduced plasma concentration of efavirenz (increase efavirenz dose)
Ritonavir: Increased risk of toxicity (monitor liver function)
Saquinavir: Efavirenz significantly reduces plasma concentration of saquinavir

Enalapril

Acetazolamide: Enhanced hypotensive effect (can be extreme)
Acetylsalicylic acid: Antagonism of hypotensive effect; increased risk of renal impairment
Alcohol: Enhanced hypotensive effect
* Amiloride: Enhanced hypotensive effect (can be extreme); risk of severe hyperkalaemia
Antacids (Aluminium hydroxide; Magnesium hydroxide): Absorption of enalapril reduced
Atenolol: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect

Enalapril *(continued)*

* Ciclosporin: Increased risk of hyperkalaemia
  Clonazepam: Enhanced hypotensive effect
  Contraceptives, Oral: Antagonism of hypotensive effect
  Dexamethasone: Antagonism of hypotensive effect
  Diazepam: Enhanced hypotensive effect
  Ether, Anaesthetic: Enhanced hypotensive effect
  Ethinylestradiol: Antagonism of hypotensive effect
  Fluphenazine: Enhanced hypotensive effect
  Furosemide: Enhanced hypotensive effect (can be extreme)
  Glibenclamide: Hypoglycaemic effect possibly enhanced
  Glyceryl trinitrate: Enhanced hypotensive effect
  Haloperidol: Enhanced hypotensive effect
  Halothane: Enhanced hypotensive effect
  Heparin: Increased risk of hyperkalaemia
  Hydralazine: Enhanced hypotensive effect
  Hydrochlorothiazide: Enhanced hypotensive effect (can be extreme)
  Hydrocortisone: Antagonism of hypotensive effect
  Ibuprofen: Antagonism of hypotensive effect, increased risk of renal impairment
  Insulins: Hypoglycaemic effect possibly enhanced
  Isosorbide dinitrate: Enhanced hypotensive effect
  Ketamine: Enhanced hypotensive effect
  Levodopa: Enhanced hypotensive effect
* Lithium: Enalapril reduces excretion of lithium (increased plasma-lithium concentration)
  Metformin: Hypoglycaemic effect possibly enhanced
  Methyldopa: Enhanced hypotensive effect
  Nifedipine: Enhanced hypotensive effect
  Nitrous oxide: Enhanced hypotensive effect
* Potassium salts: Risk of severe hyperkalaemia
  Prednisolone: Antagonism of hypotensive effect
  Propranolol: Enhanced hypotensive effect
  Sodium nitroprusside: Enhanced hypotensive effect
* Spironolactone: Enhanced hypotensive effect (can be extreme); risk of severe hyperkalaemia
  Thiopental: Enhanced hypotensive effect
  Timolol: Enhanced hypotensive effect
  Verapamil: Enhanced hypotensive effect

Ephedrine

Chlorpromazine: Antagonism of pressor action
Dexamethasone: Metabolism of dexamethasone accelerated
Ergotamine: Increased risk of ergotism
Fluphenazine: Antagonism of pressor action
Haloperidol: Antagonism of pressor action
Oxytocin: Hypertension due to enhanced vasopressor effect of ephedrine

Epinephrine (Adrenaline)

* Amitriptyline: Hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)
* Atenolol: Severe hypertension
  Chlorpromazine: Antagonism of pressor action
* Clomipramine: Hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)
  Ergotamine: Increased risk of ergotism
* Ether, Anaesthetic: Risk of arrhythmias
  Fluphenazine: Antagonism of pressor action
  Haloperidol: Antagonism of pressor action
* Halothane: Risk of arrhythmias
  Oxytocin: Hypertension due to enhanced vasopressor effect of epinephrine
* Propranolol: Severe hypertension
* Timolol: Severe hypertension

Ergocalciferol

Carbamazepine: Ergocalciferol requirements possibly increased
Hydrochlorothiazide: Increased risk of hypercalcaemia

Ergocalciferol *(continued)*
Phenobarbital: Ergocalciferol requirements possibly increased
Phenytoin: Ergocalciferol requirements possibly increased

Ergometrine
Dopamine: Increased risk of ergotism
Halothane: Reduced effect of ergometrine on parturient uterus

Ergotamine
Atenolol: Increased peripheral vasoconstriction
* Azithromycin: Increased risk of ergotism—avoid concomitant use
Dopamine: Increased risk of ergotism
* Doxycycline: Increased risk of ergotism
Ephedrine: Increased risk of ergotism
Epinephrine: Increased risk of ergotism
* Erythromycin: Increased risk of ergotism (avoid concomitant use)
* Indinavir: Increased risk of ergotism (avoid concomitant use)
Isoprenaline: Increased risk of ergotism
* Nelfinavir: Increased risk of ergotism (avoid concomitant use)
Propranolol: Increased peripheral vasoconstriction
* Ritonavir: Increased risk of ergotism (avoid concomitant use)
* Saquinavir: Possible increased risk of ergotism (avoid concomitant use)
Timolol: Increased peripheral vasoconstriction

Erythromycin
* Artemether + Lumefantrine: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Carbamazepine: Increased plasma-carbamazepine concentration
* Ciclosporin: Increased plasma-ciclosporin concentration (inhibition of metabolism)
Dexamethasone: Erythromycin possibly inhibits metabolism of dexamethasone
Digoxin: Enhanced effect of digoxin
* Ergotamine: Increased risk of ergotism (avoid concomitant use)
Hydrocortisone: Erythromycin possibly inhibits metabolism of hydrocortisone
Prednisolone: Erythromycin possibly inhibits metabolism of prednisolone
Ritonavir: Plasma concentration possibly increased by ritonavir
* Theophylline: Inhibition of theophylline metabolism (increased plasma-theophylline concentration); if erythromycin given by mouth, also decreased plasma-erythromycin concentration
Valproic acid: Metabolism of valproic acid possibly inhibited (increased plasma concentration)
* Warfarin: Enhanced anticoagulant effect

Ether, Anaesthetic
Acetazolamide: Enhanced hypotensive effect
Alcuronium: Effects of alcuronium enhanced
Amiloride: Enhanced hypotensive effect
Amitriptyline: Increased risk of arrhythmias and hypotension
Atenolol: Enhanced hypotensive effect
* Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Increased risk of arrhythmias and hypotension
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
* Epinephrine: Risk of arrhythmias
* Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
* Haloperidol: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoniazid: Possible potentiation of isoniazid hepatotoxicity
* Isoprenaline: Risk of arrhythmias
Isosorbide dinitrate: Enhanced hypotensive effect
* Levodopa: Risk of arrhythmias
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect

Ether, Anaesthetic *(continued)*

Oxytocin: Oxytocic effect possibly reduced; enhanced hypotensive effect and risk of arrhythmias

Propranolol: Enhanced hypotensive effect

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

* Verapamil: Enhanced hypotensive effect and AV delay

Ethinylestradiol *see* Contraceptives, Oral

Ethosuximide

* Amitriptyline: Antagonism (convulsive threshold lowered)
* Carbamazepine: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide sometimes lowered
* Chloroquine: Convulsive threshold occasionally lowered
* Chlorpromazine: Antagonism (convulsive threshold lowered)
* Clomipramine: Antagonism (convulsive threshold lowered)
* Fluphenazine: Antagonism (convulsive threshold lowered)
* Haloperidol: Antagonism (convulsive threshold lowered)
* Isoniazid: Metabolism of ethosuximide inhibited (increased plasma-ethosuximide concentration and risk of toxicity)
* Mefloquine: Antagonism of anticonvulsant effect
* Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide sometimes lowered
* Phenytoin: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin sometimes raised; plasma concentration of ethosuximide sometimes lowered
* Valproic acid: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide sometimes raised

Etoposide

Vaccine, Live: Avoid use of live vaccines with etoposide (impairment of immune response)

Ferrous salts

Ciprofloxacin: Absorption of ciprofloxacin reduced by oral ferrous salts

Doxycycline: Reduced absorption of oral ferrous salts by doxycycline; reduced absorption of doxycycline by oral ferrous salts

Levodopa: Absorption of levodopa may be reduced

Methyldopa: Reduced hypotensive effect of methyldopa

Ofloxacin: Absorption of ofloxacin reduced by oral ferrous salts

Penicillamine: Reduced absorption of penicillamine

Ferrous salt and Folic acid *see* Ferrous salts; Folic acid

Fluconazole

Amphotericin B: Possible antagonism of effect of amphotericin

* Artemether + Lumefantrine Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Ciclosporin: Metabolism of ciclosporin inhibited (increased plasma concentration)

Contraceptives, Oral: Anecdotal reports of contraceptive failure

* Glibenclamide: Plasma concentration of glibenclamide increased

Hydrochlorothiazide: Plasma concentration of fluconazole increased

* Phenytoin: Effect of phenytoin enhanced; plasma concentration increased
* Rifampicin: Accelerated metabolism of fluconazole (reduced plasma concentration)
* Ritonavir: Plasma concentration possibly increased by ritonavir

Saquinavir: Plasma concentration of saquinavir possibly increased

* Theophylline: Plasma-theophylline concentration possibly increased
* Warfarin: Enhanced anticoagulant effect
* Zidovudine: Increased plasma concentration of zidovudine (increased risk of toxicity)

Flucytosine

Amphotericin B: Renal excretion of flucytosine decreased and cellular uptake increased (flucytosine toxicity possibly increased)

Cytarabine: Plasma-flucytosine concentration possibly reduced

Fluorouracil

Metronidazole: Metabolism of fluorouracil inhibited (increased toxicity)

Fluorouracil *(continued)*

Phenytoin: Reduced absorption of phenytoin
Vaccine, Live: Avoid use of live vaccines with fluorouracil (impairment of immune response)
* Warfarin: Anticoagulant effect possibly enhanced

Fluphenazine

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced sedative effect
Amiloride: Enhanced hypotensive effect
* Amitriptyline: Increased antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
Atenolol: Enhanced hypotensive effect
Atropine: Increased antimuscarinic adverse effects of fluphenazine (but reduced plasma concentration)
Biperiden: Increased antimuscarinic adverse effects of fluphenazine (but reduced plasma concentration)
* Carbamazepine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Clomipramine: Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias
Clonazepam: Enhanced sedative effect
Codeine: Enhanced sedative and hypotensive effect
Diazepam: Enhanced sedative effect
Dopamine: Antagonism of pressor action
Enalapril: Enhanced hypotensive effect
Ephedrine: Antagonism of pressor action
Epinephrine: Antagonism of pressor action
* Ether, Anaesthetic: Enhanced hypotensive effect
* Ethosuximide: Antagonism (convulsive threshold lowered)
Furosemide: Enhanced hypotensive effect
Glibenclamide: Possible antagonism of hypoglycaemic effect
Glyceryl trinitrate: Enhanced hypotensive effect
* Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoprenaline: Antagonism of pressor action
Isosorbide dinitrate: Enhanced hypotensive effect
* Ketamine: Enhanced hypotensive effect
Levodopa: Antagonism of effects of levodopa
Lithium: Increased risk of extrapyramidal effects and possibility of neurotoxicity
Methyldopa: Enhanced hypotensive effect; increased risk of extrapyramidal effects
Metoclopramide: Increased risk of extrapyramidal effects
Morphine: Enhanced sedative and hypotensive effect
Nifedipine: Enhanced hypotensive effect
* Nitrous oxide: Enhanced hypotensive effect
* Phenobarbital: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Phenytoin: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Procainamide: Increased risk of ventricular arrhythmias
Propranolol: Enhanced hypotensive effect
* Quinidine: Increased risk of ventricular arrhythmias
* Ritonavir: Plasma concentration possibly increased by ritonavir
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
* Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
* Valproic acid: Antagonism of anticonvulsant effect (convulsive threshold lowered)
Verapamil: Enhanced hypotensive effect

Folic acid and Folinic acid

Phenobarbital: Plasma concentration of phenobarbital possibly reduced
Phenytoin: Plasma-phenytoin concentration possibly reduced

Furosemide

Acetazolamide: Increased risk of hypokalaemia
Alcohol: Enhanced hypotensive effect
Amitriptyline: Increased risk of postural hypotension
Amphotericin B: Increased risk of hypokalaemia
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs
Atenolol: Enhanced hypotensive effect
Carbamazepine: Increased risk of hyponatraemia
Ceftazidime: Nephrotoxicity of ceftazidime possibly increased
Ceftriaxone: Nephrotoxicity of ceftriaxone possibly increased
Chlorpromazine: Enhanced hypotensive effect
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of diuretic effect
Dexamethasone: Antagonism of diuretic effect; increased risk of hypokalaemia
Diazepam: Enhanced hypotensive effect
* Digoxin: Cardiac toxicity of digoxin increased if hypokalaemia occurs
Enalapril: Enhanced hypotensive effect (can be extreme)
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
* Gentamicin: Increased risk of ototoxicity
Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Increased risk of hypokalaemia
Hydrocortisone: Antagonism of diuretic effect; increased risk of hypokalaemia
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
Insulins: Antagonism of hypoglycaemic effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Lidocaine: Action of lidocaine antagonised by hypokalaemia
* Lithium: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide
Metformin: Antagonism of hypoglycaemic effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of diuretic effect; increased risk of hypokalaemia
Propranolol: Enhanced hypotensive effect
* Quinidine: Cardiac toxicity of quinidine increased if hypokalaemia occurs
Salbutamol: Increased risk of hypokalaemia with high doses of salbutamol
Sodium nitroprusside: Enhanced hypotensive effect
* Streptomycin: Increased risk of ototoxicity
Theophylline: Increased risk of hypokalaemia
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
* Vancomycin: Increased risk of ototoxicity
Verapamil: Enhanced hypotensive effect

Gentamicin

* Alcuronium: Enhanced muscle relaxant effect
Amphotericin B: Increased risk of nephrotoxicity
* Ciclosporin: Increased risk of nephrotoxicity
* Cisplatin: Increased risk of nephrotoxicity and possibly of ototoxicity
* Furosemide: Increased risk of ototoxicity
* Neostigmine: Antagonism of effect of neostigmine
Polygeline: Increased risk of nephrotoxicity
* Pyridostigmine: Antagonism of effect of pyridostigmine
* Suxamethonium: Enhanced muscle relaxant effect

Gentamicin *(continued)*

Vancomycin: Increased risk of nephrotoxicity and ototoxicity
* Vecuronium: Enhanced muscle relaxant effect

Glibenclamide

Alcohol: Enhanced hypoglycaemic effect
Atenolol: Masking of warning signs of hypoglycaemia such as tremor
* Chloramphenicol; Enhanced effect of glibenclamide
Chlorpromazine: Possible antagonism of hypoglycaemic effect
Ciprofloxacin: Possibly enhanced effect of glibenclamide
Contraceptives, Oral: Antagonism of hypoglycaemic effect
Dexamethasone: Antagonism of hypoglycaemic effect
Enalapril: Hypoglycaemic effect possibly enhanced
* Fluconazole: Plasma concentration of glibenclamide increased
Fluphenazine: Possible antagonism of hypoglycaemic effect
Furosemide: Antagonism of hypoglycaemic effect
Hydrochlorothiazide: Antagonism of hypoglycaemic effect
Hydrocortisone: Antagonism of hypoglycaemic effect
* Ibuprofen: Possibly enhanced effect of glibenclamide
Levonorgestrel: Antagonism of hypoglycaemic effect
Lithium: May occasionally impair glucose tolerance
Medroxyprogesterone: Antagonism of hypoglycaemic effect
Norethisterone: Antagonism of hypoglycaemic effect
Prednisolone: Antagonism of hypoglycaemic effect
Propranolol: Masking of warning signs of hypoglycaemia such as tremor
* Rifampicin: Possibly accelerated metabolism (reduced effect) of glibenclamide
Sulfadiazine: Effect of glibenclamide rarely enhanced
Sulfadoxine + Pyrimethamine: Effect of glibenclamide rarely enhanced
Sulfamethoxazole + Trimethoprim: Effect of glibenclamide rarely enhanced
Testosterone: Hypoglycaemic effect possibly enhanced
Timolol: Masking of warning signs of hypoglycaemia such as tremor
* Warfarin: Possibly enhanced hypoglycaemic effects and changes to anticoagulant effect

Glyceryl trinitrate

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Enhanced hypotensive effect; reduced effect of sublingual glyceryl trinitrate (owing to dry mouth)
Atenolol: Enhanced hypotensive effect
Atropine: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Biperiden: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Enhanced hypotensive effect; reduced effect of sublingual glyceryl trinitrate (owing to dry mouth)
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect

Glyceryl trinitrate *(continued)*

Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Grapefruit Juice

Artemether + Lumefantrine: Metabolism of artemether and lumefantrine may be inhibited (manufacturer advises avoid)
* Ciclosporin: Increased plasma-ciclosporin concentration (risk of toxicity)
Efavirenz: Plasma concentration of efavirenz may be affected
Nifedipine: Significantly increased plasma-nifedipine concentration
Verapamil: Significantly increased plasma-verapamil concentration

Griseofulvin

Ciclosporin: Plasma-ciclosporin concentration possibly reduced
* Contraceptives, Oral: Accelerated metabolism (reduced contraceptive effect)
* Levonorgestrel Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Medroxyprogesterone Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Norethisterone Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone entantate for contraception
Phenobarbital: Reduction in absorption of griseofulvin (reduced effect)
* Warfarin: Metabolism of warfarin accelerated (reduced anticoagulant effect)

Haloperidol

Alcohol: Enhanced sedative effect
* Amitriptyline: Increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias
* Carbamazepine: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)
* Clomipramine: Increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias
Clonazepam: Enhanced sedative effect
Codeine: Enhanced sedative and hypotensive effect
Diazepam: Enhanced sedative effect
Dopamine: Antagonism of pressor action
Enalapril: Enhanced hypotensive effect
Ephedrine: Antagonism of pressor action
Epinephrine: Antagonism of pressor action
* Ether, Anaesthetic: Enhanced hypotensive effect
* Ethosuximide: Antagonism (convulsive threshold lowered)
* Halothane: Enhanced hypotensive effect
Isoprenaline: Antagonism of pressor action
* Ketamine: Enhanced hypotensive effect
Levodopa: Antagonism of effects of levodopa
Lithium: Increased risk of extrapyramidal effects and possibility of neurotoxicity
Methyldopa: Enhanced hypotensive effect; increased risk of extrapyramidal effects
Metoclopramide: Increased risk of extrapyramidal effects
Morphine: Enhanced sedative and hypotensive effect
Nifedipine: Enhanced hypotensive effect
* Nitrous oxide: Enhanced hypotensive effect
* Phenobarbital: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)
* Phenytoin: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Procainamide: Increased risk of ventricular arrhythmias
* Quinidine: Increased risk of ventricular arrhythmias
* Rifampicin: Accelerated metabolism of haloperidol (reduced plasma-haloperidol concentration)
* Ritonavir: Plasma concentration possibly increased by ritonavir

Haloperidol *(continued)*

* Thiopental: Enhanced hypotensive effect
* Valproic acid: Antagonism of anticonvulsant effect (convulsive threshold lowered)
  Verapamil: Enhanced hypotensive effect

Halothane

Acetazolamide: Enhanced hypotensive effect
Alcuronium: Effects of alcuronium enhanced
Amiloride: Enhanced hypotensive effect
Amitriptyline: Increased risk of arrhythmias and hypotension
Atenolol: Enhanced hypotensive effect
* Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Increased risk of arrhythmias and hypotension
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
* Epinephrine: Risk of arrhythmias
Ergometrine: Reduced effect of ergometrine on parturient uterus
* Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
* Haloperidol: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoniazid: Possible potentiation of isoniazid hepatotoxicity
* Isoprenaline: Risk of arrhythmias
Isosorbide dinitrate: Enhanced hypotensive effect
* Levodopa: Risk of arrhythmias
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Oxytocin: Oxytocic effect possibly reduced; enhanced hypotensive effect and risk of arrhythmias
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Theophylline: Increased risk of arrhythmias
Timolol: Enhanced hypotensive effect
Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
* Verapamil: Enhanced hypotensive effect and AV delay

Heparin

* Acetylsalicylic acid: Enhanced anticoagulant effect
Enalapril: Increased risk of hyperkalaemia
Ibuprofen: Possibly increased risk of bleeding

Hydralazine

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Enhanced hypotensive effect
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect

Hydralazine *(continued)*

Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Isosorbide: dinitrate Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Hydrochlorothiazide

Acetazolamide: Increased risk of hypokalaemia
Alcohol; Enhanced hypotensive effect
Amitriptyline: Increased risk of postural hypotension
Amphotericin B: Increased risk of hypokalaemia
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs
Atenolol: Enhanced hypotensive effect
Calcium salts: Increased risk of hypercalcaemia
Carbamazepine: Increased risk of hyponatraemia
Chlorpromazine: Enhanced hypotensive effect
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of diuretic effect
Dexamethasone: Antagonism of diuretic effect; increased risk of hypokalaemia
Diazepam: Enhanced hypotensive effect
* Digoxin: Cardiac toxicity of digoxin increased if hypokalaemia occurs
Enalapril: Enhanced hypotensive effect (can be extreme)
Ergocalciferol: Increased risk of hypercalcaemia
Ether, Anaesthetic: Enhanced hypotensive effect
Fluconazole: Plasma concentration of fluconazole increased
Fluphenazine: Enhanced hypotensive effect
Furosemide: Increased risk of hypokalaemia
Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrocortisone: Antagonism of diuretic effect; increased risk of hypokalaemia
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
Insulins: Antagonism of hypoglycaemic effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Lidocaine: Action of lidocaine antagonised by hypokalaemia
* Lithium: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide
Metformin: Antagonism of hypoglycaemic effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of diuretic effect; increased risk of hypokalaemia
Propranolol: Enhanced hypotensive effect
* Quinidine: Cardiac toxicity of quinidine increased if hypokalaemia occurs
Salbutamol: Increased risk of hypokalaemia with high doses of salbutamol
Sodium nitroprusside: Enhanced hypotensive effect

Hydrochlorothiazide *(continued)*

Theophylline: Increased risk of hypokalaemia
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Hydrocortisone

NOTE: INTERACTIONS DO NOT GENERALLY APPLY TO HYDROCORTISONE USED FOR TOPICAL APPLICATION

Acetazolamide: Increased risk of hypokalaemia; antagonism of diuretic effect
Acetylsalicylic acid: Increased risk of gastrointestinal bleeding and ulceration; hydrocortisone reduces plasma-salicylate concentration
Amiloride: Antagonism of diuretic effect
* Amphotericin B: Increased risk of hypokalaemia (avoid concomitant use unless hydrocortisone needed to control reactions)
Atenolol: Antagonism of hypotensive effect
* Carbamazepine: Accelerated metabolism of hydrocortisone (reduced effect)
Contraceptives, Oral: Oral contraceptives increase plasma concentration of hydrocortisone
Digoxin: Increased risk of hypokalaemia
Enalapril: Antagonism of hypotensive effect
Erythromycin: Erythromycin possibly inhibits metabolism of hydrocortisone
Furosemide: Antagonism of diuretic effect; increased risk of hypokalaemia
Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Antagonism of hypotensive effect
Hydralazine: Antagonism of hypotensive effect
Hydrochlorothiazide: Antagonism of diuretic effect; increased risk of hypokalaemia
Ibuprofen: Increased risk of gastrointestinal bleeding and ulceration
Insulins: Antagonism of hypoglycaemic effect
Isosorbide: dinitrate Antagonism of hypotensive effect
Levonorgestrel: Levonorgestrel increases plasma concentration of hydrocortisone
Medroxyprogesterone: Medroxyprogesterone increases plasma concentration of hydrocortisone
Metformin: Antagonism of hypoglycaemic effect
Methotrexate: Increased risk of haematological toxicity
Methyldopa: Antagonism of hypotensive effect
Nifedipine: Antagonism of hypotensive effect
Norethisterone: Norethisterone increases plasma concentration of hydrocortisone
* Phenobarbital: Metabolism of hydrocortisone accelerated (reduced effect)
* Phenytoin: Metabolism of hydrocortisone accelerated (reduced effect)
Propranolol: Antagonism of hypotensive effect
* Rifampicin: Accelerated metabolism of hydrocortisone (reduced effect)
Ritonavir: Plasma concentration possibly increased by ritonavir
Salbutamol: Increased risk of hypokalaemia if high doses of hydrocortisone given with high doses of salbutamol
Sodium nitroprusside: Antagonism of hypotensive effect
Spironolactone: Antagonism of diuretic effect
Theophylline: Increased risk of hypokalaemia
* Vaccine, Live: High doses of hydrocortisone impair immune response; avoid use of live vaccines
Verapamil: Antagonism of hypotensive effect
* Warfarin: Anticoagulant effect possibly altered

Ibuprofen

Acetazolamide: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
* Acetylsalicylic acid: Avoid concurrent administration (increased adverse effects, including gastrointestinal damage); antiplatelet effect of acetylsalicylic acid possibly reduced
Amiloride: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia
Atenolol: Antagonism of hypotensive effect
* Ciclosporin: Increased risk of nephrotoxicity
* Ciprofloxacin: Possibly increased risk of convulsions
Dexamethasone: Increased risk of gastrointestinal bleeding and ulceration

Ibuprofen *(continued)*

Digoxin: Possibly exacerbation of heart failure, reduced GFR, and increased plasma-digoxin concentration
Enalapril: Antagonism of hypotensive effect, increased risk of renal impairment
Furosemide: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
* Glibenclamide: Possibly enhanced effect of glibenclamide
Glyceryl trinitrate: Antagonism of hypotensive effect
Heparin: Possibly increased risk of bleeding
Hydralazine: Antagonism of hypotensive effect
Hydrochlorothiazide: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
Hydrocortisone: Increased risk of gastrointestinal bleeding and ulceration
Isosorbide dinitrate: Antagonism of hypotensive effect
* Lithium: Reduced excretion of lithium (risk of toxicity)
* Methotrexate: Excretion of methotrexate reduced (increased risk of toxicity)
Methyldopa: Antagonism of hypotensive effect
* Nalidixic acid: Possibly increased risk of convulsions
Nifedipine: Antagonism of hypotensive effect
* Ofloxacin: Possible increased risk of convulsions
* Phenytoin: Effect of phenytoin possibly enhanced
Prednisolone: Increased risk of gastrointestinal bleeding and ulceration
Propranolol: Antagonism of hypotensive effect
Ritonavir: Plasma concentration possibly increased by ritonavir
Sodium nitroprusside: Antagonism of hypotensive effect
Spironolactone: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia
Verapamil: Antagonism of hypotensive effect
* Warfarin: Anticoagulant effect possibly enhanced
Zidovudine: Increased risk of haematological toxicity

Immunoglobulin, Anti-D

* Vaccine, Live: Avoid use of live virus vaccine during 4 weeks before or during 3 months after injection of anti-D immunoglobulin (impairment of immune response) but rubella vaccine (either as MMR or as single antigen rubella vaccine) may be given at the same time as anti-D immunoglobulin

Indinavir

Carbamazepine: Possibly reduced plasma-indinavir concentration
Dexamethasone: Possibly reduced plasma-indinavir concentration
Efavirenz: Efavirenz reduces plasma concentration of indinavir (increase indinavir dose)
* Ergotamine: Increased risk of ergotism (avoid concomitant use)
Nelfinavir: Combination may lead to increased plasma concentration of either drug (or both)
Nevirapine: Nevirapine reduces plasma concentration of indinavir
* Phenobarbital: Plasma concentration of indinavir possibly reduced
Phenytoin: Plasma-indinavir concentration possibly reduced
* Rifampicin: Metabolism enhanced by rifampicin (plasma-indinavir concentration significantly reduced—avoid concomitant use)
Ritonavir: Ritonavir increases plasma concentration of indinavir
Saquinavir: Indinavir increases plasma concentration of saquinavir

Insulins

Alcohol: Enhanced hypoglycaemic effect
Atenolol: Enhanced hypoglycaemic effect; masking of warning signs of hypoglycaemia such as tremor
Contraceptives, Oral: Antagonism of hypoglycaemic effect
Dexamethasone: Antagonism of hypoglycaemic effect
Enalapril: Hypoglycaemic effect possibly enhanced
Furosemide: Antagonism of hypoglycaemic effect
Hydrochlorothiazide: Antagonism of hypoglycaemic effect
Hydrocortisone: Antagonism of hypoglycaemic effect
Levonorgestrel: Antagonism of hypoglycaemic effect
Lithium: May occasionally impair glucose tolerance
Medroxyprogesterone: Antagonism of hypoglycaemic effect
Nifedipine: Occasionally impaired glucose tolerance

Insulins *(continued)*

Norethisterone: Antagonism of hypoglycaemic effect
Prednisolone: Antagonism of hypoglycaemic effect
Propranolol: Enhanced hypoglycaemic effect; masking of warning signs of hypoglycaemia such as tremor
Testosterone: Hypoglycaemic effect possibly enhanced
Timolol: Enhanced hypoglycaemic effect; masking of warning signs of hypoglycaemia such as tremor

Isoniazid

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of isoniazid
* Carbamazepine: Increased plasma-carbamazepine concentration (also isoniazid hepatotoxicity possibly increased)
Diazepam: Metabolism of diazepam inhibited
Ether, Anaesthetic: Possible potentiation of isoniazid hepatotoxicity
* Ethosuximide: Metabolism of ethosuximide inhibited (increased plasma-ethosuximide concentration and risk of toxicity)
Halothane: Possible potentiation of isoniazid hepatotoxicity
Ketamine: Possible potentiation of isoniazid hepatotoxicity
Nitrous oxide: Possible potentiation of isoniazid hepatotoxicity
* Phenytoin: Metabolism of phenytoin inhibited (enhanced effect)
Theophylline: Plasma-theophylline concentration possibly increased
Thiopental: Possible potentiation of isoniazid hepatotoxicity

Isophane insulin *see* Insulins

Isoprenaline

Chlorpromazine: Antagonism of pressor action
Ergotamine: Increased risk of ergotism
* Ether, Anaesthetic: Risk of arrhythmias
Fluphenazine: Antagonism of pressor action
Haloperidol: Antagonism of pressor action
* Halothane: Risk of arrhythmias

Isosorbide dinitrate

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Enhanced hypotensive effect; reduced effect of sublingual isosorbide dinitrate (owing to dry mouth)
Atenolol: Enhanced hypotensive effect
Atropine: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Biperiden: Possibly reduced effect of sublingual nitrates (failure to dissolve under the tongue owing to dry mouth)
Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Enhanced hypotensive effect; reduced effect of sublingual isosorbide dinitrate (owing to dry mouth)
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect

Isosorbide dinitrate *(continued)*

Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Ketamine

Acetazolamide: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Increased risk of arrhythmias and hypotension
Atenolol: Enhanced hypotensive effect
* Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Increased risk of arrhythmias and hypotension
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
* Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
* Haloperidol: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoniazid: Possible potentiation of isoniazid hepatotoxicity
Isosorbide dinitrate: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Theophylline: Increased risk of convulsions
Timolol: Enhanced hypotensive effect
Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
* Verapamil: Enhanced hypotensive effect and AV delay

Lamivudine

Sulfamethoxazole + Trimethoprim: Plasma concentration of lamivudine increased (avoid concomitant use of high-dose sulfamethoxazole + trimethoprim)
Trimethoprim: Plasma concentration of lamivudine increased (avoid concomitant use of high-dose trimethoprim)

Levamisole

Alcohol: Disulfiram-like reaction
Phenytoin: Plasma-phenytoin concentration possibly increased
Warfarin: Anticoagulant effect possibly enhanced

Levodopa

Acetazolamide: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Atropine: Absorption of levodopa possibly reduced
Biperiden: Absorption of levodopa possibly reduced
Chlorpromazine: Antagonism of effects of levodopa
Clonazepam: Possibly occasional antagonism of levodopa effects
Diazepam: Occasional antagonism of levodopa effects
Enalapril: Enhanced hypotensive effect
* Ether, Anaesthetic: Risk of arrhythmias
Ferrous salts: Absorption of levodopa may be reduced
Fluphenazine: Antagonism of effects of levodopa
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Haloperidol: Antagonism of effects of levodopa
* Halothane: Risk of arrhythmias

Levodopa *(continued)*

Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isosorbide dinitrate: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect; antagonism of antiparkinsonian effect
Nifedipine: Enhanced hypotensive effect
Propranolol: Enhanced hypotensive effect
Pyridoxine: Antagonism of levodopa unless carbidopa also given
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Levonorgestrel *see also* Contraceptives, Oral

* Carbamazepine: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Ciclosporin: Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
Dexamethasone: Levonorgestrel increases plasma concentration of dexamethasone
Glibenclamide: Antagonism of hypoglycaemic effect
* Griseofulvin: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
Hydrocortisone: Levonorgestrel increases plasma concentration of hydrocortisone
Insulins: Antagonism of hypoglycaemic effect
Metformin: Antagonism of hypoglycaemic effect
* Nelfinavir: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Nevirapine: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Phenobarbital: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Phenytoin: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
Prednisolone: Levonorgestrel increases plasma concentration of prednisolone
* Rifampicin: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Ritonavir: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Warfarin: Antagonism of anticoagulant effect

Levothyroxine

Carbamazepine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)
Phenobarbital: Metabolism of levothyroxine accelerated (may increase levothyroxine requirements in hypothyroidism)
Phenytoin: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism); plasma concentration of phenytoin possibly increased
Propranolol: Metabolism of propranolol accelerated (reduced effect)
Rifampicin: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)
* Warfarin: Enhanced anticoagulant effect

Lidocaine

* Acetazolamide: Action of lidocaine antagonised by hypokalaemia
* Atenolol: Increased risk of myocardial depression
Bupivacaine: Increased myocardial depression
* Furosemide: Action of lidocaine antagonised by hypokalaemia
* Hydrochlorothiazide: Action of lidocaine antagonised by hypokalaemia
* Procainamide: Increased myocardial depression
* Propranolol: Increased risk of myocardial depression; increased risk of lidocaine toxicity
* Quinidine: Increased myocardial depression
Suxamethonium: Action of suxamethonium prolonged
* Timolol: Increased risk of myocardial depression
* Verapamil: Increased risk of myocardial depression

Lithium

* Acetazolamide: Excretion of lithium increased
Alcuronium: Enhanced muscle relaxant effect
* Amiloride: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)
Carbamazepine: Neurotoxicity may occur without increased plasma-lithium concentration
Chlorpromazine: Increased risk of extrapyramidal effects and possibility of neurotoxicity
* Enalapril: Enalapril reduces excretion of lithium (increased plasma-lithium concentration)

Lithium *(continued)*

Fluphenazine: Increased risk of extrapyramidal effects and possibility of neurotoxicity
* Furosemide: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide
Glibenclamide: May occasionally impair glucose tolerance
Haloperidol: Increased risk of extrapyramidal effects and possibility of neurotoxicity
* Hydrochlorothiazide: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide
* Ibuprofen: Reduced excretion of lithium (risk of toxicity)
Insulins: May occasionally impair glucose tolerance
Metformin: May occasionally impair glucose tolerance
* Methyldopa: Neurotoxicity may occur without increased plasma-lithium concentration
Metronidazole: Increased lithium toxicity reported
Neostigmine: Antagonism of effect of neostigmine
Phenytoin: Neurotoxicity may occur without increased plasma-lithium concentration
Pyridostigmine: Antagonism of effect of pyridostigmine
Sodium hydrogen carbonate: Increased excretion; reduced plasma-lithium concentration
* Spironolactone: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)
Suxamethonium: Enhanced muscle relaxant effect
Theophylline: Increased lithium excretion (reduced plasma-lithium concentration)
Vecuronium: Enhanced muscle relaxant effect
Verapamil: Neurotoxicity may occur without increased plasma-lithium concentration

Lopinavir

* Carbamazepine: Possibly reduced plasma-lopinavir concentration
* Dexamethasone: Possibly reduced plasma-lopinavir concentration
* Efavirenz: Plasma concentration of lopinavir reduced
* Nevirapine: Plasma concentration of lopinavir possibly reduced
* Phenobarbital: Plasma concentration of lopinavir possibly reduced
* Phenytoin: Plasma-lopinavir concentration possibly reduced
* Rifampicin: Reduced plasma concentration of lopinavir (avoid concomitant use)

Magnesium hydroxide *see* Antacids

Magnesium (parenteral)

Alcuronium: Enhanced muscle relaxant effect
* Nifedipine: Profound hypotension reported with nifedipine and intravenous magnesium sulfate in pre-eclampsia
Suxamethonium: Enhanced muscle relaxant effect
Vecuronium: Enhanced muscle relaxant effect

Magnesium sulfate *see* Magnesium (parenteral)

Measles vaccine *see* Vaccine, live

Mebendazole

Carbamazepine: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)
Phenytoin: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)

Medroxyprogesterone *see also* Contraceptives, Oral

* Carbamazepine: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Ciclosporin: Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
Dexamethasone: Medroxyprogesterone increases plasma concentration of dexamethasone
Glibenclamide: Antagonism of hypoglycaemic effect
* Griseofulvin: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
Hydrocortisone: Medroxyprogesterone increases plasma concentration of hydrocortisone
Insulins: Antagonism of hypoglycaemic effect
Metformin: Antagonism of hypoglycaemic effect
* Nelfinavir: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Nevirapine: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

Medroxyprogesterone *(continued)*

* Phenobarbital: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Phenytoin: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Prednisolone: Medroxyprogesterone increases plasma concentration of prednisolone
* Rifampicin: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Ritonavir: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Warfarin: Antagonism of anticoagulant effect

Mefloquine

* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
  Atenolol: Increased risk of bradycardia
* Carbamazepine: Antagonism of anticonvulsant effect
* Chloroquine: Increased risk of convulsions
  Digoxin: Possibly increased risk of bradycardia
* Ethosuximide: Antagonism of anticonvulsant effect
  Nifedipine: Possibly increased risk of bradycardia
* Phenytoin: Antagonism of anticonvulsant effect
  Propranolol: Increased risk of bradycardia
* Quinidine: Increased risk of ventricular arrhythmias
* Quinine: Increased risk of convulsions, but should not prevent the use of intravenous quinine in severe cases
  Timolol: Increased risk of bradycardia
* Valproic acid: Antagonism of anticonvulsant effect
  Verapamil: Possibly increased risk of bradycardia

Mercaptopurine

* Allopurinol: Effects of mercaptopurine enhanced with increased toxicity, reduce dose when given with allopurinol
  Phenytoin: Reduced absorption of phenytoin
* Sulfamethoxazole + Trimethoprim: Increased risk of haematological toxicity
  Sulfasalazine: Possibly increased risk of leukopenia
* Trimethoprim: Increased risk of haematological toxicity
  Vaccine, Live: Avoid use of live vaccines with mercaptopurine (impairment of immune response)
* Warfarin: Anticoagulant effect possibly reduced

Metformin

Alcohol: Enhanced hypoglycaemic effect; increased risk of lactic acidosis
Atenolol: Masking of warning signs of hypoglycaemia such as tremor
Contraceptives, Oral: Antagonism of hypoglycaemic effect
Dexamethasone: Antagonism of hypoglycaemic effect
Enalapril: Hypoglycaemic effect possibly enhanced
Furosemide: Antagonism of hypoglycaemic effect
Hydrochlorothiazide: Antagonism of hypoglycaemic effect
Hydrocortisone: Antagonism of hypoglycaemic effect
Levonorgestrel: Antagonism of hypoglycaemic effect
Lithium: May occasionally impair glucose tolerance
Medroxyprogesterone: Antagonism of hypoglycaemic effect
Norethisterone: Antagonism of hypoglycaemic effect
Prednisolone: Antagonism of hypoglycaemic effect
Propranolol: Masking of warning signs of hypoglycaemia such as tremor
Testosterone: Hypoglycaemic effect possibly enhanced
Timolol: Masking of warning signs of hypoglycaemia such as tremor

Methotrexate

* Acetylsalicylic acid: Reduced excretion of methotrexate (increased toxicity)
  Amoxicillin: Reduced excretion of methotrexate (increased risk of toxicity)
  Ampicillin: Reduced excretion of methotrexate (increased risk of toxicity)
  Benzylpenicillin: Reduced excretion of methotrexate (increased risk of toxicity)
* Ciclosporin: Increased toxicity
  Dexamethasone: Increased risk of haematological toxicity

Methotrexate *(continued)*

Hydrocortisone: Increased risk of haematological toxicity
* Ibuprofen: Excretion of methotrexate reduced (increased risk of toxicity)
* Nitrous oxide: Increased antifolate effect (avoid concomitant use)
Phenoxymethylpenicillin: Reduced excretion of methotrexate (increased risk of toxicity)
Phenytoin: Reduced absorption of phenytoin; antifolate effect of methotrexate increased
Prednisolone: Increased risk of haematological toxicity
* Pyrimethamine: Antifolate effect of methotrexate increased
Sulfadiazine: Risk of methotrexate toxicity increased
* Sulfadoxine + Pyrimethamine: Antifolate effect of methotrexate increased; risk of methotrexate toxicity increased
* Sulfamethoxazole + Trimethoprim: Antifolate effect of methotrexate increased (avoid concomitant use); risk of methotrexate toxicity increased
* Trimethoprim: Antifolate effect of methotrexate increased (avoid concomitant use)
Vaccine, Live: Avoid use of live vaccines with methotrexate (impairment of immune response)

Methyldopa

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect; increased risk of extrapyramidal effects
Clomipramine: Enhanced hypotensive effect
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Ether, Anaesthetic: Enhanced hypotensive effect
Ferrous salts: Reduced hypotensive effect of methyldopa
Fluphenazine: Enhanced hypotensive effect; increased risk of extrapyramidal effects
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Haloperidol: Enhanced hypotensive effect; increased risk of extrapyramidal effects
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect; antagonism of antiparkinsonian effect
* Lithium: Neurotoxicity may occur without increased plasma-lithium concentration
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
* Salbutamol: Acute hypotension reported with salbutamol infusion
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Metoclopramide

Acetylsalicylic acid: Enhanced effect of acetylsalicylic acid (increased rate of absorption)
Atropine: Antagonism of effect on gastrointestinal activity
Biperiden: Antagonism of effect on gastrointestinal activity
Chlorpromazine: Increased risk of extrapyramidal effects
* Ciclosporin: Plasma-ciclosporin concentration increased
Codeine: Antagonism of effect of metoclopramide on gastrointestinal activity
Fluphenazine: Increased risk of extrapyramidal effects

Metoclopramide *(continued)*
Haloperidol: Increased risk of extrapyramidal effects
Morphine: Antagonism of effect of metoclopramide on gastrointestinal activity
Paracetamol: Increased absorption of paracetamol (enhanced effect)

Metronidazole
Alcohol: Disulfiram-like reaction
Fluorouracil: Metabolism of fluorouracil inhibited (increased toxicity)
Lithium: Increased lithium toxicity reported
Phenobarbital: Metabolism of metronidazole accelerated (reduced plasma concentration)
* Phenytoin: Metabolism of phenytoin inhibited (increased plasma-phenytoin concentration)
* Warfarin: Enhanced anticoagulant effect

MMR vaccine *see* Vaccine, live

Morphine
Alcohol: Enhanced sedative and hypotensive effect
Amitriptyline: Possibly increased sedation
Chlorpromazine: Enhanced sedative and hypotensive effect
Ciprofloxacin: Manufacturer of ciprofloxacin advises avoid premedication with morphine (reduced plasma-ciprofloxacin concentration)
Clomipramine: Possibly increased sedation
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect
Fluphenazine: Enhanced sedative and hypotensive effect
Haloperidol: Enhanced sedative and hypotensive effect
Metoclopramide: Antagonism of effect of metoclopramide on gastrointestinal activity
* Ritonavir: Ritonavir possibly increases plasma concentration of morphine

Nalidixic acid
* Artemether + Lumefantrine: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Ciclosporin: Increased risk of nephrotoxicity
* Ibuprofen: Possibly increased risk of convulsions
* Theophylline: Possible increased risk of convulsions
* Warfarin: Enhanced anticoagulant effect

Nelfinavir
Carbamazepine: Possibly reduced plasma-nelfinavir concentration
Ciclosporin: Possibly increased plasma-ciclosporin concentration
* Contraceptives, Oral: Accelerated metabolism (reduced contraceptive effect)
* Ergotamine: Increased risk of ergotism (avoid concomitant use)
Indinavir: Combination may lead to increased plasma concentration of either drug (or both)
* Levonorgestrel: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Medroxyprogesterone: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Norethisterone: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Phenobarbital: Plasma concentration of nelfinavir possibly reduced
Phenytoin: Reduced plasma-phenytoin concentration
* Quinidine: Increased risk of ventricular arrhythmias (avoid concomitant use)
* Rifampicin: Plasma concentration of nelfinavir significantly reduced (avoid concomitant use)
Ritonavir: Combination may lead to increased plasma concentration of either drug (or both)
Saquinavir: Combination may lead to increased plasma concentration of either drug (or both)

Neostigmine
Alcuronium: Antagonism of muscle relaxant effect
Atropine: Antagonism of effect
Biperiden: Antagonism of effect
Chloroquine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of neostigmine
Clindamycin: Antagonism of effects of neostigmine
* Gentamicin: Antagonism of effect of neostigmine
Lithium: Antagonism of effect of neostigmine

Neostigmine *(continued)*

Procainamide: Antagonism of effect of neostigmine
Propranolol: Antagonism of effect of neostigmine
Quinidine: Antagonism of effect of neostigmine
* Streptomycin: Antagonism of effect of neostigmine
Suxamethonium: Effect of suxamethonium enhanced
Vecuronium: Antagonism of muscle relaxant effect

Nevirapine

* Contraceptives, Oral: Accelerated metabolism (reduced contraceptive effect)
Efavirenz: Plasma-efavirenz concentration reduced
Indinavir: Nevirapine reduces plasma concentration of indinavir
* Levonorgestrel: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Lopinavir: Plasma concentration of lopinavir possibly reduced
* Medroxyprogesterone: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Norethisterone: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Rifampicin: Reduced plasma concentration of nevirapine (avoid concomitant use)
* Saquinavir: Plasma concentration of saquinavir reduced (avoid concomitant use)

Nifedipine

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Alcuronium: Enhanced muscle relaxant effect
Amiloride: Enhanced hypotensive effect
* Atenolol: Severe hypotension and heart failure occasionally
Carbamazepine: Probably reduced effect of nifedipine
Chlorpromazine: Enhanced hypotensive effect
Ciclosporin: Possibly increased plasma-nifedipine concentration (increased risk of adverse effects such as gingival hyperplasia)
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
* Digoxin: Possibly increased plasma concentration of digoxin
Enalapril: Enhanced hypotensive effect
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Grapefruit juice: Significantly increased plasma-nifedipine concentration
Haloperidol: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Insulins: Occasionally impaired glucose tolerance
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Magnesium (parenteral): Profound hypotension reported with nifedipine and intravenous magnesium sulfate in pre-eclampsia
Mefloquine: Possibly increased risk of bradycardia
Methyldopa: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
* Phenobarbital: Effect of nifedipine probably reduced
* Phenytoin: Probably reduced effect of nifedipine
Prednisolone: Antagonism of hypotensive effect
* Propranolol: Severe hypotension and heart failure occasionally
Quinidine: Reduced plasma-quinidine concentration
* Ritonavir: Plasma concentration possibly increased by ritonavir

Nifedipine *(continued)*

* Rifampicin: Accelerated metabolism of nifedipine (plasma concentration significantly reduced)
  Sodium nitroprusside: Enhanced hypotensive effect
  Spironolactone: Enhanced hypotensive effect
* Theophylline: Possibly enhanced theophylline effect (possibly increased plasma-theophylline concentration)
  Thiopental: Enhanced hypotensive effect
* Timolol: Severe hypotension and heart failure occasionally
  Vecuronium: Enhanced muscle relaxant effect
  Vincristine: Possibly reduced metabolism of vincristine

Nitrous oxide

  Acetazolamide: Enhanced hypotensive effect
  Amiloride: Enhanced hypotensive effect
  Amitriptyline: Increased risk of arrhythmias and hypotension
  Atenolol: Enhanced hypotensive effect
* Chlorpromazine: Enhanced hypotensive effect
  Clomipramine: Increased risk of arrhythmias and hypotension
  Clonazepam: Enhanced sedative effect
  Diazepam: Enhanced sedative effect
  Enalapril: Enhanced hypotensive effect
* Fluphenazine: Enhanced hypotensive effect
  Furosemide: Enhanced hypotensive effect
  Glyceryl trinitrate: Enhanced hypotensive effect
* Haloperidol: Enhanced hypotensive effect
  Hydralazine: Enhanced hypotensive effect
  Hydrochlorothiazide: Enhanced hypotensive effect
  Isoniazid: Possible potentiation of isoniazid hepatotoxicity
  Isosorbide dinitrate: Enhanced hypotensive effect
* Methotrexate: Increased antifolate effect (avoid concomitant use)
  Methyldopa: Enhanced hypotensive effect
  Nifedipine: Enhanced hypotensive effect
  Propranolol: Enhanced hypotensive effect
  Sodium nitroprusside: Enhanced hypotensive effect
  Spironolactone: Enhanced hypotensive effect
  Timolol: Enhanced hypotensive effect
  Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
* Verapamil: Enhanced hypotensive effect and AV delay

Norethisterone *see also* Contraceptives, Oral

* Carbamazepine: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Ciclosporin: Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
  Dexamethasone: Norethisterone increases plasma concentration of dexamethasone
  Glibenclamide: Antagonism of hypoglycaemic effect
* Griseofulvin: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
  Hydrocortisone: Norethisterone increases plasma concentration of hydrocortisone
  Insulins: Antagonism of hypoglycaemic effect
  Metformin: Antagonism of hypoglycaemic effect
* Nelfinavir: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Nevirapine: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Phenobarbital: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Phenytoin: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Prednisolone: Norethisterone increases plasma concentration of prednisolone
* Rifampicin: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception

Norethisterone *(continued)*

* Ritonavir: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Warfarin: Antagonism of anticoagulant effect

Ofloxacin

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of ofloxacin
* Artemether + Lumefantrine: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Ciclosporin: Increased risk of nephrotoxicity

Ferrous salts: Absorption of ofloxacin reduced by oral ferrous salts
* Ibuprofen: Possible increased risk of convulsions
* Theophylline: Possible increased risk of convulsions
* Warfarin: Enhanced anticoagulant effect

Oxygen

* Bleomycin: Increased risk of pulmonary toxicity

Oxytocin

Ephedrine: Hypertension due to enhanced vasopressor effect of ephedrine
Epinephrine: Hypertension due to enhanced vasopressor effect of epinephrine
Ether, Anaesthetic: Oxytocic effect possibly reduced; enhanced hypotensive effect and risk of arrhythmias
Halothane: Oxytocic effect possibly reduced; enhanced hypotensive effect and risk of arrhythmias

Paracetamol

Alcohol: Increased risk of liver damage with regular large amounts of alcohol
Metoclopramide: Increased absorption of paracetamol (enhanced effect)
Warfarin: Prolonged regular use of paracetamol possibly enhances anticoagulant effect

Penicillamine

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of penicillamine
Digoxin: Plasma concentration of digoxin possibly reduced
Ferrous salts: Reduced absorption of penicillamine

Phenobarbital

Alcohol: Enhanced sedative effect
* Amitriptyline: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of amitriptyline possibly accelerated (reduced plasma concentration)
* Carbamazepine: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of carbamazepine often lowered
* Chloramphenicol: Metabolism of chloramphenicol accelerated (reduced chloramphenicol concentration)
* Chlorpromazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Ciclosporin: Metabolism of ciclosporin accelerated (reduced effect)
* Clomipramine: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of clomipramine possibly accelerated (reduced plasma concentration)
* Clonazepam: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of clonazepam often lowered
* Contraceptives, Oral: Metabolism accelerated (reduced contraceptive effect)
* Dexamethasone: Metabolism of dexamethasone accelerated (reduced effect)

Doxycycline: Metabolism of doxycycline accelerated (reduced plasma concentration)
Ergocalciferol: Ergocalciferol requirements possibly increased
* Ethosuximide: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide sometimes lowered
* Fluphenazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)

Folic acid and Folinic acid: Plasma concentration of phenobarbital possibly reduced
Griseofulvin: Reduction in absorption of griseofulvin (reduced effect)
* Haloperidol: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)
* Hydrocortisone: Metabolism of hydrocortisone accelerated (reduced effect)
* Indinavir: Plasma concentration of indinavir possibly reduced
* Levonorgestrel: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

Levothyroxine: Metabolism of levothyroxine accelerated (may increase levothyroxine requirements in hypothyroidism)
* Lopinavir: Plasma concentration of lopinavir possibly reduced

Phenobarbital *(continued)*

* Medroxyprogesterone: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
Metronidazole: Metabolism of metronidazole accelerated (reduced plasma concentration)
* Nelfinavir: Plasma concentration of nelfinavir possibly reduced
* Nifedipine: Effect of nifedipine probably reduced
* Norethisterone: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Phenytoin: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; plasma concentration of phenobarbital often raised
* Prednisolone: Metabolism of prednisolone accelerated (reduced effect)
Quinidine: Metabolism of quinidine accelerated (reduced plasma concentration)
* Saquinavir: Plasma concentration of saquinavir possibly reduced
Theophylline: Metabolism of theophylline accelerated (reduced effect)
* Valproic acid: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproic acid often lowered; phenobarbital concentration often raised
* Verapamil: Effect of verapamil probably reduced
* Warfarin: Metabolism of warfarin accelerated (reduced anticoagulant effect)

Phenoxymethylpenicillin

Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)

Phenytoin

Acetazolamide: Increased risk of osteomalacia
Acetylsalicylic acid: Enhancement of effect of phenytoin
Alcohol: Plasma-phenytoin concentration reduced with regular large amounts of alcohol
Alcuronium: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)
* Amitriptyline: Antagonism (convulsive threshold lowered); possibly reduced plasma-amitriptyline concentration
Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of phenytoin
Azathioprine: Reduced absorption of phenytoin
* Carbamazepine: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; plasma concentration of carbamazepine often lowered
* Chloramphenicol: Plasma-phenytoin concentration increased (risk of toxicity)
* Chloroquine: Convulsive threshold occasionally lowered
* Chlorpromazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Ciclosporin: Accelerated metabolism (reduced plasma-ciclosporin concentration)
Ciprofloxacin: Plasma-phenytoin concentration possibly altered by ciprofloxacin
Cisplatin: Reduced absorption of phenytoin
* Clomipramine: Antagonism (convulsive threshold lowered); possibly reduced plasma-clomipramine concentration
* Clonazepam: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of clonazepam often lowered
* Contraceptives, Oral: Accelerated metabolism (reduced contraceptive effect)
Cyclophosphamide: Reduced absorption of phenytoin
Cytarabine: Reduced absorption of phenytoin
* Dexamethasone: Metabolism of dexamethasone accelerated (reduced effect)
Diazepam: Plasma-phenytoin concentrations increased or decreased by diazepam
Digoxin: Plasma concentration of digoxin possibly reduced
Doxorubicin: Reduced absorption of phenytoin
Doxycycline: Increased metabolism of doxycycline (reduced plasma concentration)
Ergocalciferol: Ergocalciferol requirements possibly increased
* Ethosuximide: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin sometimes raised; plasma concentration of ethosuximide sometimes lowered
* Fluconazole: Effect of phenytoin enhanced; plasma concentration increased
Fluorouracil: Reduced absorption of phenytoin
* Fluphenazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
Folic acid and Folinic acid: Plasma-phenytoin concentration possibly reduced

Phenytoin *(continued)*

* Haloperidol: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Hydrocortisone: Metabolism of hydrocortisone accelerated (reduced effect)
* Ibuprofen: Effect of phenytoin possibly enhanced
  Indinavir: Plasma-indinavir concentration possibly reduced
* Isoniazid: Metabolism of phenytoin inhibited (enhanced effect)
  Levamisole: Plasma-phenytoin concentration possibly increased
* Levonorgestrel: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
  Levothyroxine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism); plasma concentration of phenytoin possibly increased
  Lithium: Neurotoxicity may occur without increased plasma-lithium concentration
* Lopinavir: Plasma-lopinavir concentration possibly reduced
  Mebendazole: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infections)
* Medroxyprogesterone: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Mefloquine: Antagonism of anticonvulsant effect
  Mercaptopurine: Reduced absorption of phenytoin
  Methotrexate: Reduced absorption of phenytoin; antifolate effect of methotrexate increased
* Metronidazole: Metabolism of phenytoin inhibited (increased plasma-phenytoin concentration)
  Nelfinavir: Reduced plasma-phenytoin concentration
* Nifedipine: Probably reduced effect of nifedipine
* Norethisterone: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; plasma concentration of phenobarbital often raised
  Praziquantel: Plasma-praziquantel concentration reduced
* Prednisolone: Metabolism of prednisolone accelerated (reduced effect)
  Procarbazine: Reduced absorption of phenytoin
* Pyrimethamine: Antagonism of anticonvulsant effect; increased antifolate effect
* Quinidine: Accelerated metabolism (reduced plasma-quinidine concentration)
* Rifampicin: Accelerated metabolism of phenytoin (reduced plasma concentration)
  Saquinavir: Plasma-saquinavir concentration possibly reduced
  Sulfadiazine: Plasma-phenytoin concentration possibly increased
* Sulfadoxine + Pyrimethamine: Plasma-phenytoin concentration possibly increased; increased antifolate effect
* Sulfamethoxazole + Trimethoprim: Antifolate effect and plasma-phenytoin concentration increased
  Theophylline: Accelerated metabolism of theophylline (reduced plasma-theophylline concentration), also plasma-phenytoin concentration possibly reduced
* Trimethoprim: Antifolate effect and plasma-phenytoin concentration increased
  Vaccine, Influenza: Enhanced effect of phenytoin
* Valproic acid: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproic acid often lowered; plasma concentration of phenytoin often raised (but may also be lowered)
  Vecuronium: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)
  Verapamil: Reduced effect of verapamil
* Warfarin: Accelerated metabolism of warfarin (possibility of reduced anticoagulant effect, but enhancement also reported)
  Zidovudine: Plasma-phenytoin concentration increased or decreased by zidovudine

Phytomenadione

* Warfarin: Antagonism of anticoagulant effect by phytomenadione

Poliomyelitis, oral vaccine *see* Vaccine, live

Polygeline

Gentamicin: Increased risk of nephrotoxicity

Potassium chloride *see* Potassium salts

Potassium salts

* Amiloride: Risk of hyperkalaemia

Potassium salts *(continued)*

* Ciclosporin: Increased risk of hyperkalaemia
* Enalapril: Risk of severe hyperkalaemia
* Spironolactone: Risk of hyperkalaemia

Praziquantel

Albendazole: Increased plasma concentration of active metabolite of albendazole
Carbamazepine: Plasma-praziquantel concentration reduced
Chloroquine: Plasma-praziquantel concentration possibly reduced
Dexamethasone: Plasma-praziquantel concentration reduced
Phenytoin: Plasma-praziquantel concentration reduced

Prednisolone

Acetazolamide: Increased risk of hypokalaemia; antagonism of diuretic effect
Acetylsalicylic acid: Increased risk of gastrointestinal bleeding and ulceration; prednisolone reduces plasma-salicylate concentration
Amiloride: Antagonism of diuretic effect
* Amphotericin B: Increased risk of hypokalaemia (avoid concomitant use unless prednisolone needed to control reactions)
Atenolol: Antagonism of hypotensive effect
* Carbamazepine: Accelerated metabolism of prednisolone (reduced effect)
Ciclosporin: Increased plasma concentration of prednisolone
Contraceptives, Oral: Oral contraceptives increase plasma concentration of prednisolone
Digoxin: Increased risk of hypokalaemia
Enalapril: Antagonism of hypotensive effect
Erythromycin: Erythromycin possibly inhibits metabolism of prednisolone
Furosemide: Antagonism of diuretic effect; increased risk of hypokalaemia
Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Antagonism of hypotensive effect
Hydralazine: Antagonism of hypotensive effect
Hydrochlorothiazide: Antagonism of diuretic effect; increased risk of hypokalaemia
Ibuprofen: Increased risk of gastrointestinal bleeding and ulceration
Insulins: Antagonism of hypoglycaemic effect
Isosorbide dinitrate: Antagonism of hypotensive effect
Levonorgestrel: Levonorgestrel increases plasma concentration of prednisolone
* Medroxyprogesterone: Medroxyprogesterone increases plasma concentration of prednisolone
Metformin: Antagonism of hypoglycaemic effect
Methotrexate: Increased risk of haematological toxicity
Methyldopa: Antagonism of hypotensive effect
Nifedipine: Antagonism of hypotensive effect
* Norethisterone: Norethisterone increases plasma concentration of prednisolone
* Phenobarbital: Metabolism of prednisolone accelerated (reduced effect)
* Phenytoin: Metabolism of prednisolone accelerated (reduced effect)
Propranolol: Antagonism of hypotensive effect
* Rifampicin: Accelerated metabolism of prednisolone (reduced effect)
Ritonavir: Plasma concentration possibly increased by ritonavir
Salbutamol: Increased risk of hypokalaemia if high doses of prednisolone given with high doses of salbutamol
Sodium nitroprusside: Antagonism of hypotensive effect
Spironolactone: Antagonism of diuretic effect
Theophylline: Increased risk of hypokalaemia
* Vaccine, Live: High doses of prednisolone impair immune response; avoid use of live vaccines
Verapamil: Antagonism of hypotensive effect
* Warfarin: Anticoagulant effect possibly altered

Procainamide

* Alcuronium: Enhanced muscle relaxant effect
* Amitriptyline: Increased risk of ventricular arrhythmias
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Atenolol: Increased risk of myocardial depression
Bupivacaine: Increased myocardial depression
* Chlorpromazine: Increased risk of ventricular arrhythmias

Procainamide *(continued)*
* Clomipramine: Increased risk of ventricular arrhythmias
* Fluphenazine: Increased risk of ventricular arrhythmias
* Haloperidol: Increased risk of ventricular arrhythmias
* Lidocaine: Increased myocardial depression
  Neostigmine: Antagonism of effect of neostigmine
* Propranolol: Increased risk of myocardial depression
  Pyridostigmine: Antagonism of effect of pyridostigmine
* Quinidine: Increased myocardial depression
  Sulfamethoxazole + Trimethoprim: Increased plasma-procainamide concentration
* Suxamethonium: Enhanced muscle relaxant effect
* Timolol: Increased risk of myocardial depression
  Trimethoprim: Increased plasma-procainamide concentration
* Vecuronium: Enhanced muscle relaxant effect

Procaine benzylpenicillin *see* Benzylpenicillin

Procarbazine
Alcohol: Disulfiram-like reaction
Phenytoin: Reduced absorption of phenytoin
Vaccine, Live: Avoid use of live vaccines with procarbazine (impairment of immune response)

Proguanil
Warfarin: Isolated reports of enhanced anticoagulant effect

Promethazine
Alcohol: Enhanced sedative effect
Amitriptyline: Increased antimuscarinic and sedative effects
Atropine: Increased antimuscarinic adverse effects
Biperiden: Increased antimuscarinic adverse effects
Clomipramine: Increased antimuscarinic and sedative effects
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect

Propranolol
Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Alcuronium: Enhanced muscle relaxant effect
Amiloride: Enhanced hypotensive effect
* Bupivacaine: Increased risk of bupivacaine toxicity
* Chlorpromazine: Concomitant administration may increase plasma concentration of both drugs; enhanced hypotensive effect
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Digoxin: Increased AV block and bradycardia
Enalapril: Enhanced hypotensive effect
* Epinephrine: Severe hypertension
Ergotamine: Increased peripheral vasoconstriction
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glibenclamide: Masking of warning signs of hypoglycaemia such as tremor
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Insulins: Enhanced hypoglycaemic effect; masking of warning signs of hypoglycaemia such as tremor
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Levothyroxine: Metabolism of propranolol accelerated (reduced effect)

Propranolol *(continued)*

* Lidocaine: Increased risk of myocardial depression; increased risk of lidocaine toxicity
  Mefloquine: Increased risk of bradycardia
  Metformin: Masking of warning signs of hypoglycaemia such as tremor
  Methyldopa: Enhanced hypotensive effect
  Neostigmine: Antagonism of effect of neostigmine
* Nifedipine: Severe hypotension and heart failure occasionally
  Nitrous oxide: Enhanced hypotensive effect
  Prednisolone: Antagonism of hypotensive effect
* Procainamide: Increased risk of myocardial depression
  Pyridostigmine: Antagonism of effect of pyridostigmine
* Quinidine: Increased risk of myocardial depression
  Rifampicin: Metabolism of propranolol accelerated (significantly reduced plasma concentration)
  Sodium nitroprusside: Enhanced hypotensive effect
  Spironolactone: Enhanced hypotensive effect
  Suxamethonium: Enhanced muscle relaxant effect
  Thiopental: Enhanced hypotensive effect
  Vecuronium: Enhanced muscle relaxant effect
* Verapamil: Asystole, severe hypotension and heart failure

Pyridostigmine

Alcuronium: Antagonism of muscle relaxant effect
Atropine: Antagonism of effect
Biperiden: Antagonism of effect
Chloroquine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of pyridostigmine
Clindamycin: Antagonism of effects of pyridostigmine
* Gentamicin: Antagonism of effect of pyridostigmine
  Lithium: Antagonism of effect of pyridostigmine
  Procainamide: Antagonism of effect of pyridostigmine
  Propranolol: Antagonism of effect of pyridostigmine
  Quinidine: Antagonism of effect of pyridostigmine
* Streptomycin: Antagonism of effect of pyridostigmine
  Suxamethonium: Effect of suxamethonium enhanced
  Vecuronium: Antagonism of muscle relaxant effect

Pyridoxine

Levodopa: Antagonism of levodopa unless carbidopa also given

Pyrimethamine

* Artemether + Lumefantrine: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Methotrexate: Antifolate effect of methotrexate increased
* Phenytoin: Antagonism of anticonvulsant effect; increased antifolate effect
* Sulfadiazine: Increased risk of antifolate effect
* Sulfamethoxazole + Trimethoprim: Increased antifolate effect
* Trimethoprim: Increased antifolate effect

Pyrimethamine + Sulfadoxine *see* Sulfadoxine + Pyrimethamine

Quinidine

* Acetazolamide: Cardiac toxicity of quinidine increased if hypokalaemia occurs; acetazolamide reduces excretion of quinidine (occasionally increased plasma concentration)
* Alcuronium: Enhanced muscle relaxant effect
* Amitriptyline: Increased risk of ventricular arrhythmias
  Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced quinidine excretion in alkaline urine (plasma-quinidine concentration occasionally increased)
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
* Atenolol: Increased risk of myocardial depression
  Bupivacaine: Increased myocardial depression
  Chloroquine: Increased risk of ventricular arrhythmias
* Chlorpromazine: Increased risk of ventricular arrhythmias
* Clomipramine: Increased risk of ventricular arrhythmias
* Digoxin: Plasma concentration of digoxin increased (halve maintenance dose of digoxin)

Quinidine *(continued)*

* Fluphenazine: Increased risk of ventricular arrhythmias
* Furosemide: Cardiac toxicity of quinidine increased if hypokalaemia occurs
* Haloperidol: Increased risk of ventricular arrhythmias
* Hydrochlorothiazide: Cardiac toxicity of quinidine increased if hypokalaemia occurs
* Lidocaine: Increased myocardial depression
* Mefloquine: Increased risk of ventricular arrhythmias
* Nelfinavir: Increased risk of ventricular arrhythmias (avoid concomitant use)

Neostigmine: Antagonism of effect of neostigmine
Nifedipine: Reduced plasma-quinidine concentration
Phenobarbital: Metabolism of quinidine accelerated (reduced plasma concentration)

* Phenytoin: Accelerated metabolism (reduced plasma-quinidine concentration)
* Procainamide: Increased myocardial depression
* Propranolol: Increased risk of myocardial depression

Pyridostigmine: Antagonism of effect of pyridostigmine

* Rifampicin: Accelerated metabolism (reduced plasma-quinidine concentration)
* Ritonavir: Increased plasma-quinidine concentration (increased risk of ventricular arrhythmias—avoid concomitant use)
* Suxamethonium: Enhanced muscle relaxant effect
* Timolol: Increased risk of myocardial depression
* Vecuronium: Enhanced muscle relaxant effect
* Verapamil: Increased plasma-quinidine concentration (extreme hypotension may occur)
* Warfarin: Anticoagulant effect may be enhanced

Quinine

* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)

Chloroquine: Increased risk of ventricular arrhythmias

* Digoxin: Plasma concentration of digoxin increased
* Mefloquine: Increased risk of convulsions, but should not prevent the use of intravenous quinine in severe cases

Ranitidine

Saquinavir: Plasma-saquinavir concentration increased

Rifampicin

Amitriptyline: Plasma concentration of amitriptyline possibly reduced (reduced antidepressant effect)
Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of rifampicin

* Azathioprine: Manufacturer reports interaction (transplants possibly rejected)

Chloramphenicol: Accelerated metabolism of chloramphenicol (reduced plasma-chloramphenicol concentration)

* Ciclosporin: Accelerated metabolism (reduced plasma-ciclosporin concentration)

Clomipramine: Plasma concentration of clomipramine possibly reduced (reduced antidepressant effect)
Clonazepam: Metabolism of clonazepam possibly accelerated (possibly reduced plasma concentration)

* Contraceptives, Oral: Accelerated metabolism of oral contraceptives (reduced contraceptive effect)

Dapsone: Reduced plasma-dapsone concentration

* Dexamethasone: Accelerated metabolism of dexamethasone (reduced effect)

Diazepam: Metabolism of diazepam accelerated (reduced plasma concentration)
Digoxin: Plasma concentration of digoxin possibly reduced
Doxycycline: Plasma-doxycycline concentration possibly reduced
Efavirenz: Reduced plasma concentration of efavirenz (increase efavirenz dose)

* Fluconazole: Accelerated metabolism of fluconazole (reduced plasma concentration)
* Glibenclamide: Possibly accelerated metabolism (reduced effect) of glibenclamide
* Haloperidol: Accelerated metabolism of haloperidol (reduced plasma-haloperidol concentration)
* Hydrocortisone: Accelerated metabolism of hydrocortisone (reduced effect)
* Indinavir: Metabolism enhanced by rifampicin (plasma-indinavir concentration significantly reduced—avoid concomitant use)
* Rifampicin: Levonorgestrel Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

Rifampicin *(continued)*

Levothyroxine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)
* Lopinavir: Reduced plasma concentration of lopinavir (avoid concomitant use)
* Medroxyprogesterone: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Nelfinavir: Plasma concentration of nelfinavir significantly reduced (avoid concomitant use)
* Nevirapine: Reduced plasma concentration of nevirapine (avoid concomitant use)
* Nifedipine: Accelerated metabolism of nifedipine (plasma concentration significantly reduced)
* Norethisterone: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception
* Phenytoin: Accelerated metabolism of phenytoin (reduced plasma concentration)
* Prednisolone: Accelerated metabolism of prednisolone (reduced effect)

Propranolol: Metabolism of propranolol accelerated (significantly reduced plasma concentration)
* Quinidine: Accelerated metabolism (reduced plasma-quinidine concentration)
* Saquinavir: Accelerated metabolism of saquinavir (reduced plasma concentration—avoid concomitant use unless another protease inhibitor for example ritonavir also given)

Theophylline: Accelerated metabolism of theophylline (reduced plasma-theophylline concentration)
* Verapamil: Accelerated metabolism of verapamil (plasma concentration significantly reduced)
* Warfarin: Accelerated metabolism of warfarin (reduced anticoagulant effect)

Ritonavir

* Amitriptyline: Plasma concentration possibly increased by ritonavir

Azithromycin: Plasma concentration of azithromycin possibly increased
* Carbamazepine: Plasma concentration possibly increased by ritonavir
* Chlorpromazine: Plasma concentration possibly increased by ritonavir
* Ciclosporin: Plasma concentration possibly increased by ritonavir
* Clomipramine: Plasma concentration possibly increased by ritonavir
* Clonazepam: Plasma concentration possibly increased by ritonavir
* Codeine: Ritonavir possibly increases plasma concentration of codeine
* Contraceptives, Oral: Accelerated metabolism (reduced contraceptive effect)

Dexamethasone: Plasma concentration possibly increased by ritonavir
* Diazepam: Plasma concentration possibly increased by ritonavir (risk of extreme sedation and respiratory depression—avoid concomitant use)

Efavirenz: Increased risk of toxicity (monitor liver function)
* Ergotamine: Increased risk of ergotism (avoid concomitant use)

Erythromycin: Plasma concentration possibly increased by ritonavir
* Fluconazole: Plasma concentration possibly increased by ritonavir
* Fluphenazine: Plasma concentration possibly increased by ritonavir
* Haloperidol: Plasma concentration possibly increased by ritonavir

Hydrocortisone: Plasma concentration possibly increased by ritonavir

Ibuprofen: Plasma concentration possibly increased by ritonavir

Indinavir: Ritonavir increases plasma concentration of indinavir
* Levonorgestrel: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
* Medroxyprogesterone: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
* Morphine: Ritonavir possibly increases plasma concentration of morphine

Nelfinavir: Combination may lead to increased plasma concentration of either drug (or both)
* Nifedipine: Plasma concentration possibly increased by ritonavir
* Norethisterone: Accelerated metabolism of norethisterone (reduced contraceptive effect)—does not apply to injectable norethisterone enantate for contraception

Prednisolone: Plasma concentration possibly increased by ritonavir
* Quinidine: Increased plasma-quinidine concentration (increased risk of ventricular arrhythmias—avoid concomitant use)
* Saquinavir: Ritonavir increases plasma concentration of saquinavir
* Theophylline: Accelerated theophylline metabolism (reduced plasma concentration)
* Verapamil: Plasma concentration possibly increased by ritonavir

Ritonavir *(continued)*
* Warfarin: Plasma concentration possibly increased by ritonavir

Rubella vaccine *see* Vaccine, live

Salbutamol
Acetazolamide: Increased risk of hypokalaemia with high doses of salbutamol
Dexamethasone: Increased risk of hypokalaemia if high doses of dexamethasone given with high doses of salbutamol
Furosemide: Increased risk of hypokalaemia with high doses of salbutamol
Hydrochlorothiazide: Increased risk of hypokalaemia with high doses of salbutamol
Hydrocortisone: Increased risk of hypokalaemia if high doses of hydrocortisone given with high doses of salbutamol
* Methyldopa: Acute hypotension reported with salbutamol infusion
Prednisolone: Increased risk of hypokalaemia if high doses of prednisolone given with high doses of salbutamol
Theophylline: Increased risk of hypokalaemia with concomitant use of high doses of salbutamol

Saquinavir
Carbamazepine: Possibly reduced plasma-saquinavir concentration
Dexamethasone: Possibly reduced plasma-saquinavir concentration
Efavirenz: Efavirenz significantly reduces plasma concentration of saquinavir
* Ergotamine: Possible increased risk of ergotism (avoid concomitant use)
Fluconazole: Plasma concentration of saquinavir possibly increased
Indinavir: Indinavir increases plasma concentration of saquinavir
Nelfinavir: Combination may lead to increased plasma concentration of either drug (or both)
* Nevirapine: Plasma concentration of saquinavir reduced (avoid concomitant use)
* Phenobarbital: Plasma concentration of saquinavir possibly reduced
Phenytoin: Plasma-saquinavir concentration possibly reduced
Ranitidine: Plasma-saquinavir concentration increased
* Rifampicin: Accelerated metabolism of saquinavir (reduced plasma concentration—avoid concomitant use unless another protease inhibitor for example ritonavir also given)
* Ritonavir: Ritonavir increases plasma concentration of saquinavir

Sodium hydrogen carbonate (Sodium bicarbonate)
Lithium: Increased excretion; reduced plasma-lithium concentration

Sodium lactate compound solution *see* Potassium salts; Sodium hydrogen carbonate

Sodium nitroprusside
Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Enhanced hypotensive effect
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect

Sodium nitroprusside *(continued)*
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Sodium valproate *see* Valproic acid

Soluble insulin *see* Insulins

Spironolactone
Acetylsalicylic acid: Antagonism of diuretic effect
Alcohol: Enhanced hypotensive effect
Amitriptyline: Increased risk of postural hypotension
* Artemether + Lumefantrine: Increased risk of ventricular arrhythmias if electrolyte disturbance occurs
Atenolol: Enhanced hypotensive effect
Carbamazepine: Increased risk of hyponatraemia
Chlorpromazine: Enhanced hypotensive effect
* Ciclosporin: Increased risk of hyperkalaemia
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Clonazepam: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of diuretic effect
Dexamethasone: Antagonism of diuretic effect
Diazepam: Enhanced hypotensive effect
* Digoxin: Enhanced effect of digoxin
* Enalapril: Enhanced hypotensive effect (can be extreme); risk of severe hyperkalaemia
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrocortisone: Antagonism of diuretic effect
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Lithium: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
* Potassium salts: Risk of hyperkalaemia
Prednisolone: Antagonism of diuretic effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Stavudine
Doxorubicin: Doxorubicin may inhibit effect of stavudine
* Zidovudine: May inhibit effect of stavudine (avoid concomitant use)

Streptomycin
* Alcuronium: Enhanced muscle relaxant effect
Amphotericin B: Increased risk of nephrotoxicity
* Ciclosporin: Increased risk of nephrotoxicity
* Cisplatin: Increased risk of nephrotoxicity and possibly of ototoxicity
* Furosemide: Increased risk of ototoxicity
* Neostigmine: Antagonism of effect of neostigmine
* Pyridostigmine: Antagonism of effect of pyridostigmine

Streptomycin *(continued)*

* Suxamethonium: Enhanced muscle relaxant effect
  Vancomycin: Increased risk of nephrotoxicity and ototoxicity
* Vecuronium: Enhanced muscle relaxant effect

Sulfadiazine

* Ciclosporin: Plasma-ciclosporin concentration possibly reduced; increased risk of nephrotoxicity
  Glibenclamide: Effect of glibenclamide rarely enhanced
  Methotrexate: Risk of methotrexate toxicity increased
  Phenytoin: Plasma-phenytoin concentration possibly increased
* Pyrimethamine: Increased risk of antifolate effect
* Sulfadoxine + Pyrimethamine: Increased risk of antifolate effect
  Thiopental: Enhanced effects of thiopental
* Warfarin: Enhanced anticoagulant effect

Sulfadoxine + Pyrimethamine

* Artemether + Lumefantrine: Manufacturer of artemether with lumefantrine advises avoid concomitant use
* Ciclosporin: Increased risk of nephrotoxicity
  Glibenclamide: Effect of glibenclamide rarely enhanced
* Methotrexate: Antifolate effect of methotrexate increased; risk of methotrexate toxicity increased
* Phenytoin: Plasma-phenytoin concentration possibly increased; increased antifolate effect
* Sulfadiazine: Increased risk of antifolate effect
* Sulfamethoxazole+Trimethoprim: Increased antifolate effect
  Thiopental: Enhanced effects of thiopental
* Trimethoprim: Increased antifolate effect
* Warfarin: Enhanced anticoagulant effect

Sulfamethoxazole + Trimethoprim

* Azathioprine: Increased risk of haematological toxicity
* Ciclosporin: Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim
  Dapsone: Plasma concentration of both dapsone and trimethoprim increased with concomitant use
  Digoxin: Plasma concentration of digoxin possibly increased
  Glibenclamide: Effect of glibenclamide rarely enhanced
  Lamivudine: Plasma concentration of lamivudine increased (avoid concomitant use of high-dose sulfamethoxazole + trimethoprim)
* Mercaptopurine: Increased risk of haematological toxicity
* Methotrexate: Antifolate effect of methotrexate increased (avoid concomitant use); risk of methotrexate toxicity increased
* Phenytoin: Antifolate effect and plasma-phenytoin concentration increased
  Procainamide: Increased plasma-procainamide concentration
* Pyrimethamine: Increased antifolate effect
* Sulfadoxine + Pyrimethamine: Increased antifolate effect
  Thiopental: Enhanced effects of thiopental
* Warfarin: Enhanced anticoagulant effect

Sulfasalazine

  Azathioprine: Possibly increased risk of leukopenia
  Digoxin: Absorption of digoxin possibly reduced
  Mercaptopurine: Possibly increased risk of leukopenia

Suxamethonium

  Cyclophosphamide: Enhanced effect of suxamethonium
  Digoxin: Risk of arrhythmias
* Gentamicin: Enhanced muscle relaxant effect
  Lidocaine: Action of suxamethonium prolonged
  Lithium: Enhanced muscle relaxant effect
  Magnesium (parenteral): Enhanced muscle relaxant effect
  Neostigmine: Effect of suxamethonium enhanced
* Procainamide: Enhanced muscle relaxant effect
  Propranolol: Enhanced muscle relaxant effect
  Pyridostigmine: Effect of suxamethonium enhanced

Suxamethonium *(continued)*
* Quinidine: Enhanced muscle relaxant effect
* Streptomycin: Enhanced muscle relaxant effect

Tamoxifen
* Warfarin: Enhanced anticoagulant effect

Testosterone
Glibenclamide: Hypoglycaemic effect possibly enhanced
Insulins: Hypoglycaemic effect possibly enhanced
Metformin: Hypoglycaemic effect possibly enhanced
* Warfarin: Enhanced anticoagulant effect

Theophylline
Acetazolamide: Increased risk of hypokalaemia
Allopurinol: Plasma-theophylline concentration possibly increased
Carbamazepine: Accelerated metabolism of theophylline (reduced effect)
* Ciprofloxacin: Increased plasma-theophylline concentration; possible increased risk of convulsions
Contraceptives, Oral: Delayed excretion of theophylline (increased plasma concentration)
Dexamethasone: Increased risk of hypokalaemia
* Erythromycin: Inhibition of theophylline metabolism (increased plasma-theophylline concentration); if erythromycin given by mouth, also decreased plasma-erythromycin concentration
* Fluconazole: Plasma-theophylline concentration possibly increased
Furosemide: Increased risk of hypokalaemia
Halothane: Increased risk of arrhythmias
Hydrochlorothiazide: Increased risk of hypokalaemia
Hydrocortisone: Increased risk of hypokalaemia
Isoniazid: Plasma-theophylline concentration possibly increased
Ketamine: Increased risk of convulsions
Lithium: Increased lithium excretion (reduced plasma-lithium concentration)
* Nalidixic acid: Possible increased risk of convulsions
* Nifedipine: Possibly enhanced theophylline effect (possibly increased plasma-theophylline concentration)
* Ofloxacin: Possible increased risk of convulsions
Phenobarbital: Metabolism of theophylline accelerated (reduced effect)
Phenytoin: Accelerated metabolism of theophylline (reduced plasma-theophylline concentration), also plasma-phenytoin concentration possibly reduced
Prednisolone: Increased risk of hypokalaemia
Rifampicin: Accelerated metabolism of theophylline (reduced plasma-theophylline concentration)
* Ritonavir: Accelerated theophylline metabolism (reduced plasma concentration)
Salbutamol: Increased risk of hypokalaemia with concomitant use of high doses of salbutamol
Tobacco: Tobacco smoking increases theophylline metabolism (reduced plasma-theophylline concentration)
Vaccine, Influenza: Plasma-theophylline concentration occasionally increased
* Verapamil: Enhanced theophylline effect (increased plasma-theophylline concentration)

Thioacetazone + Isoniazid *see* Isoniazid

Thiopental
Acetazolamide: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Increased risk of arrhythmias and hypotension
Atenolol: Enhanced hypotensive effect
* Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Increased risk of arrhythmias and hypotension
Clonazepam: Enhanced sedative effect
Diazepam: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
* Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
* Haloperidol: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect

Thiopental *(continued)*

Hydrochlorothiazide: Enhanced hypotensive effect
Isoniazid: Possible potentiation of isoniazid hepatotoxicity
Isosorbide dinitrate: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Sulfadiazine: Enhanced effects of thiopental
Sulfadoxine + Pyrimethamine: Enhanced effects of thiopental
Sulfamethoxazole + Trimethoprim: Enhanced effects of thiopental
Timolol: Enhanced hypotensive effect
Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
* Verapamil: Enhanced hypotensive effect and AV delay

Timolol

NOTE: Systemic absorption may follow topical application of timolol to the eye

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect
Clonazepam: Enhanced hypotensive effect
Diazepam: Enhanced hypotensive effect
Digoxin: Increased AV block and bradycardia
Enalapril: Enhanced hypotensive effect
* Epinephrine: Severe hypertension
Ergotamine: Increased peripheral vasoconstriction
Ether, Anaesthetic: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glibenclamide: Masking of warning signs of hypoglycaemia such as tremor
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Insulins: Enhanced hypoglycaemic effect; masking of warning signs of hypoglycaemia such as tremor
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
* Lidocaine: Increased risk of myocardial depression
Mefloquine: Increased risk of bradycardia
Metformin: Masking of warning signs of hypoglycaemia such as tremor
Methyldopa: Enhanced hypotensive effect
* Nifedipine: Severe hypotension and heart failure occasionally
Nitrous oxide: Enhanced hypotensive effect
* Procainamide: Increased risk of myocardial depression
* Quinidine: Increased risk of myocardial depression
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
* Verapamil: Asystole, severe hypotension and heart failure

Tobacco

Theophylline: Tobacco smoking increases theophylline metabolism (reduced plasma-theophylline concentration)

Trimethoprim

* Azathioprine: Increased risk of haematological toxicity
* Ciclosporin: Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim
Dapsone: Plasma concentration of both dapsone and trimethoprim possibly increased with concomitant use

Trimethoprim *(continued)*

Digoxin: Plasma concentration of digoxin possibly increased
Lamivudine: Plasma concentration of lamivudine increased (avoid concomitant use of high-dose trimethoprim)
* Mercaptopurine: Increased risk of haematological toxicity
* Methotrexate: Antifolate effect of methotrexate increased (avoid concomitant use)
* Phenytoin: Antifolate effect and plasma-phenytoin concentration increased
Procainamide: Increased plasma-procainamide concentration
* Pyrimethamine: Increased antifolate effect
* Sulfadoxine + Pyrimethamine: Increased antifolate effect
Warfarin: Possibly enhanced anticoagulant effect

Vaccine, Influenza

Phenytoin: Enhanced effect of phenytoin
Theophylline: Plasma-theophylline concentration occasionally increased
Warfarin: Effect of warfarin occasionally enhanced

Vaccine, Live

NOTE: VACCINE, LIVE INCLUDES BCG, MEASLES, MMR, POLIOMYELITIS (ORAL), RUBELLA, AND YELLOW FEVER VACCINES

Asparaginase: Avoid use of live vaccines with asparaginase (impairment of immune response)
* Azathioprine: Avoid use of live vaccines with azathioprine (impairment of immune response)
Bleomycin: Avoid use of live vaccines with bleomycin (impairment of immune response)
Chlorambucil: Avoid use of live vaccines with chlorambucil (impairment of immune response)
Chlormethine: Avoid use of live vaccines with chlormethine (impairment of immune response)
* Ciclosporin: Avoid use of live vaccines with ciclosporin (impairment of immune response)
Cisplatin: Avoid use of live vaccines with cisplatin (impairment of immune response)
Cyclophosphamide: Avoid use of live vaccines with cyclophosphamide (impairment of immune response)
Cytarabine: Avoid use of live vaccines with cytarabine (impairment of immune response)
Dacarbazine: Avoid use of live vaccines with dacarbazine (impairment of immune response)
Dactinomycin: Avoid use of live vaccines with dactinomycin (impairment of immune response)
Daunorubicin: Avoid use of live vaccines with daunorubicin (impairment of immune response)
* Dexamethasone: High doses of dexamethasone impair immune response; avoid use of live vaccines
Doxorubicin: Avoid use of live vaccines with doxorubicin (impairment of immune response)
Etoposide: Avoid use of live vaccines with etoposide (impairment of immune response)
Fluorouracil: Avoid use of live vaccines with fluorouracil (impairment of immune response)
* Hydrocortisone: High doses of hydrocortisone impair immune response; avoid use of live vaccines
* Immunoglobulin, Anti-D: Avoid use of live virus vaccine during 4 weeks before or during 3 months after injection of anti-D immunoglobulin (impairment of immune response) but rubella vaccine (either as MMR or single antigen rubella vaccine) may be given at the same time as anti-D immunoglobulin
Mercaptopurine: Avoid use of live vaccines with mercaptopurine (impairment of immune response)
Methotrexate: Avoid use of live vaccines with methotrexate (impairment of immune response)
* Prednisolone: High doses of prednisolone impair immune response; avoid use of live vaccines
Procarbazine: Avoid use of live vaccines with procarbazine (impairment of immune response)
Vinblastine: Avoid use of live vaccines with vinblastine (impairment of immune response)
Vincristine: Avoid use of live vaccines with vincristine (impairment of immune response)

Valproic acid

Acetylsalicylic acid: Enhancement of effect of valproic acid
* Amitriptyline: Antagonism (convulsive threshold lowered)

Valproic acid *(continued)*

* Carbamazepine: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproic acid often lowered; plasma concentration of active metabolite of carbamazepine often raised
* Chloroquine: Convulsive threshold occasionally lowered
* Chlorpromazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Clomipramine: Antagonism (convulsive threshold lowered)

Erythromycin: Metabolism of valproic acid possibly inhibited (increased plasma concentration)

* Ethosuximide: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide sometimes raised
* Fluphenazine: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Haloperidol: Antagonism of anticonvulsant effect (convulsive threshold lowered)
* Mefloquine: Antagonism of anticonvulsant effect
* Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproic acid often lowered; phenobarbital concentration often raised
* Phenytoin: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproic acid often lowered; plasma concentration of phenytoin often raised (but may also be lowered)

Warfarin: Anticoagulant effect possibly enhanced

Zidovudine: Plasma concentration of zidovudine possibly increased (risk of toxicity)

Vancomycin

* Ciclosporin: Increased risk of nephrotoxicity

Cisplatin: Increased risk of nephrotoxicity and possibly of ototoxicity

Ether, Anaesthetic: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

* Furosemide: Increased risk of ototoxicity

Gentamicin: Increased risk of nephrotoxicity and ototoxicity

Halothane: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Ketamine: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Nitrous oxide: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Streptomycin: Increased risk of nephrotoxicity and ototoxicity

Thiopental: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Vecuronium

Carbamazepine: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)

Clindamycin: Enhanced muscle relaxant effect

* Gentamicin: Enhanced muscle relaxant effect

Lithium: Enhanced muscle relaxant effect

Magnesium (parenteral): Enhanced muscle relaxant effect

Neostigmine: Antagonism of muscle relaxant effect

Nifedipine: Enhanced muscle relaxant effect

Phenytoin: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)

* Procainamide: Enhanced muscle relaxant effect

Propranolol: Enhanced muscle relaxant effect

Pyridostigmine: Antagonism of muscle relaxant effect

* Quinidine: Enhanced muscle relaxant effect
* Streptomycin: Enhanced muscle relaxant effect

Verapamil: Enhanced muscle relaxant effect

Verapamil

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced hypotensive effect; plasma concentration of alcohol possibly increased by verapamil

Alcuronium: Enhanced muscle relaxant effect

Amiloride: Enhanced hypotensive effect

Amitriptyline: Possibly increased plasma concentration of amitriptyline

Verapamil *(continued)*

* Atenolol: Asystole, severe hypotension and heart failure
* Carbamazepine: Enhanced effect of carbamazepine
  Chlorpromazine: Enhanced hypotensive effect
* Ciclosporin: Increased plasma-ciclosporin concentration
  Clomipramine: Possibly increased plasma concentration of clomipramine
  Clonazepam: Enhanced hypotensive effect
  Contraceptives, Oral: Antagonism of hypotensive effect
  Dexamethasone: Antagonism of hypotensive effect
  Diazepam: Enhanced hypotensive effect
* Digoxin: Increased plasma concentration of digoxin; increased AV block and bradycardia
  Enalapril: Enhanced hypotensive effect
* Ether, Anaesthetic: Enhanced hypotensive effect and AV delay
  Fluphenazine: Enhanced hypotensive effect
  Furosemide: Enhanced hypotensive effect
  Glyceryl trinitrate: Enhanced hypotensive effect
  Grapefruit juice: Significantly increased plasma-verapamil concentration
  Haloperidol: Enhanced hypotensive effect
* Halothane: Enhanced hypotensive effect and AV delay
  Hydralazine: Enhanced hypotensive effect
  Hydrochlorothiazide: Enhanced hypotensive effect
  Hydrocortisone: Antagonism of hypotensive effect
  Ibuprofen: Antagonism of hypotensive effect
  Isosorbide dinitrate: Enhanced hypotensive effect
* Ketamine: Enhanced hypotensive effect and AV delay
  Levodopa: Enhanced hypotensive effect
* Lidocaine: Increased risk of myocardial depression
  Lithium: Neurotoxicity may occur without increased plasma-lithium concentration
  Mefloquine: Possibly increased risk of bradycardia
  Methyldopa: Enhanced hypotensive effect
* Nitrous oxide: Enhanced hypotensive effect and AV delay
* Phenobarbital: Effect of verapamil probably reduced
  Phenytoin: Reduced effect of verapamil
  Prednisolone: Antagonism of hypotensive effect
* Propranolol: Asystole, severe hypotension and heart failure
* Quinidine: Increased plasma-quinidine concentration (extreme hypotension may occur)
* Rifampicin: Accelerated metabolism of verapamil (plasma concentration significantly reduced)
* Ritonavir: Plasma concentration possibly increased by ritonavir
  Sodium nitroprusside: Enhanced hypotensive effect
  Spironolactone: Enhanced hypotensive effect
* Theophylline: Enhanced theophylline effect (increased plasma-theophylline concentration)
* Thiopental: Enhanced hypotensive effect and AV delay
* Timolol: Asystole, severe hypotension and heart failure
  Vecuronium: Enhanced muscle relaxant effect

Vinblastine

* Bleomycin: Increased risk of cardiovascular toxicity
  Vaccine, Live: Avoid use of live vaccines with vinblastine (impairment of immune response)

Vincristine

Nifedipine: Possibly reduced metabolism of vincristine
Vaccine, Live: Avoid use of live vaccines with vincristine (impairment of immune response)

Vitamin D *see* Ergocalciferol

Warfarin

NOTE: Major changes in diet (especially involving salads and vegetables) and in alcohol consumption may affect anticoagulant control

* Acetylsalicylic acid: Increased risk of bleeding due to antiplatelet effect
* Alcohol: Enhanced anticoagulant effect with large amounts of alcohol; major changes in alcohol consumption may affect anticoagulant control
  Allopurinol: Anticoagulant effect possibly enhanced

Warfarin *(continued)*

Amoxicillin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of amoxicillin
Ampicillin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of ampicillin
* Azathioprine: Anticoagulant effect possibly reduced
* Azithromycin: Possibly enhanced anticoagulant effect of warfarin
* Carbamazepine: Accelerated metabolism of warfarin (reduced anticoagulant effect)
* Ceftazidime: Possibly enhanced anticoagulant effect
* Ceftriaxone: Possibly enhanced anticoagulant effect
* Chloramphenicol: Enhanced anticoagulant effect
* Ciprofloxacin: Enhanced anticoagulant effect
* Contraceptives, Oral: Antagonism of anticoagulant effect
* Dexamethasone: Anticoagulant effect possibly altered
* Doxycycline: Anticoagulant effect possibly enhanced
* Erythromycin: Enhanced anticoagulant effect
* Fluconazole: Enhanced anticoagulant effect
* Fluorouracil: Anticoagulant effect possibly enhanced
* Glibenclamide: Possibly enhanced hypoglycaemic effects and changes to anticoagulant effect
* Griseofulvin: Metabolism of warfarin accelerated (reduced anticoagulant effect)
* Hydrocortisone: Anticoagulant effect possibly altered
* Ibuprofen: Anticoagulant effect possibly enhanced
Levamisole: Anticoagulant effect possibly enhanced
* Levonorgestrel: Antagonism of anticoagulant effect
* Levothyroxine: Enhanced anticoagulant effect
* Medroxyprogesterone: Antagonism of anticoagulant effect
* Mercaptopurine: Anticoagulant effect possibly reduced
* Metronidazole: Enhanced anticoagulant effect
* Nalidixic acid: Enhanced anticoagulant effect
* Norethisterone: Antagonism of anticoagulant effect
* Ofloxacin: Enhanced anticoagulant effect
Paracetamol: Prolonged regular use of paracetamol possibly enhances anticoagulant effect
* Phenobarbital: Metabolism of warfarin accelerated (reduced anticoagulant effect)
* Phenytoin: Accelerated metabolism of warfarin (possibility of reduced anticoagulant effect, but enhancement also reported)
* Phytomenadione: Antagonism of anticoagulant effect by phytomenadione
* Prednisolone: Anticoagulant effect possibly altered
Proguanil: Isolated reports of enhanced anticoagulant effect
* Quinidine: Anticoagulant effect may be enhanced
* Rifampicin: Accelerated metabolism of warfarin (reduced anticoagulant effect)
* Ritonavir: Plasma concentration possibly increased by ritonavir
* Sulfadiazine: Enhanced anticoagulant effect
* Sulfadoxine + Pyrimethamine: Enhanced anticoagulant effect
* Sulfamethoxazole + Trimethoprim: Enhanced anticoagulant effect
* Tamoxifen: Enhanced anticoagulant effect
* Testosterone: Enhanced anticoagulant effect
Trimethoprim: Possibly enhanced anticoagulant effect
Vaccine, Influenza: Effect of warfarin occasionally enhanced
Valproic acid: Anticoagulant effect possibly enhanced

Yellow fever vaccine *see* Vaccine, live

Zidovudine

NOTE: INCREASED RISK OF TOXICITY WITH NEPHROTOXIC AND MYELOSUPPRESSIVE DRUGS
* Fluconazole: Increased plasma concentration of zidovudine (increased risk of toxicity)
Ibuprofen: Increased risk of haematological toxicity
Phenytoin: Plasma-phenytoin concentration increased or decreased by zidovudine
* Stavudine: May inhibit effect of stavudine (avoid concomitant use)
Valproic acid: Plasma concentration of zidovudine possibly increased (risk of toxicity)

Appendix 2: Pregnancy

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During pregnancy the mother and the fetus form a non-separable functional unit. Maternal well-being is an absolute prerequisite for the optimal functioning and development of both parts of this unit. Consequently, it is important to treat the mother whenever needed while protecting the unborn to the greatest possible extent.

Drugs can have harmful effects on the fetus at any time during pregnancy. It is important to remember this when prescribing for a woman of childbearing age. However, irrational fear of using drugs during pregnancy can also result in harm. This includes untreated illness, impaired maternal compliance, suboptimal treatment and treatment failures.

Such approaches may impose risk to maternal well-being, and may also affect the unborn child. It is important to know the 'background risk' in the context of the prevalence of drug-induced adverse pregnancy outcomes. Major congenital malformations occur in 2–4% of all live births. Up to 15% of all diagnosed pregnancies will result in fetal loss. The cause of these adverse pregnancy outcomes is understood in only a minority of the incidents.

During the *first trimester* drugs may produce congenital malformations (teratogenesis), and the greater risk is from third to the eleventh week of pregnancy. During the *second* and *third trimester* drugs may affect the growth and functional development of the fetus or have toxic effects on fetal tissues. Drugs given shortly before term or during labour may have adverse effects on labour or on the neonate after delivery. Few drugs have been shown conclusively to be teratogenic in man but no drug is safe beyond all doubt in early pregnancy. Screening procedures are available where there is a known risk of certain defects.

Prescribing in pregnancy

If possible counselling of women before a planned pregnancy should be carried out including discussion of risks associated with specific therapeutic agents, traditional medicines and abuse of substances such as smoking and alcohol. Folic acid supplements should be given during pregnancy planning because periconceptual use of folic acid reduces neural tube defects.

Drugs should be prescribed in pregnancy only if the expected benefits to the mother are thought to be greater than the risk to the fetus. All drugs should be avoided if possible during the first trimester. Drugs which have been used extensively in pregnancy and appear to be usually safe should be prescribed in preference to new or untried drugs and the smallest effective dose should be used. Well known single component drugs should usually be preferred to multi-component drugs.

The following list includes drugs which may have harmful effects in pregnancy and indicates the trimester of risk. It is based on human data but information on *animal* studies has been included for some newer drugs when its omission might be misleading.

Absence of a drug from the list does not imply safety.

Table of drugs to be avoided or used with caution in pregnancy

Drug	*Comment*
Abacavir	Toxicity in *animal* studies; *see* section 9.5.2
Acetazolamide	Not used to treat hypertension in pregnancy First trimester: Avoid (toxicity in *animal* studies)
Acetylsalicylic acid	Third trimester: Impaired platelet function and risk of haemorrhage; delayed onset and increased duration of labour with increased blood loss; avoid analgesic doses if possible in last few weeks (low doses probably not harmful); with high doses, closure of fetal ductus arteriosus *in utero* and possibly persistent pulmonary hypertension of newborn; kernicterus in jaundiced neonates
Aciclovir	Not known to be harmful; limited absorption from topical preparations
Albendazole	Contraindicated in cestode infections; *see* section 9.4.1.1 First trimester: avoid in nematode infections; *see* section 9.4.1.2

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Drug	*Comment*
Alcohol	First, second trimesters: Regular daily drinking is teratogenic (fetal alcohol syndrome) and may cause growth retardation; occasional single drinks are probably safe Third trimester: Withdrawal may occur in babies of alcoholic mothers
Alcuronium	Does not cross placenta in significant amounts; use only if potential benefit outweighs risk
Allopurinol	Toxicity not reported; use only if no safer alternative and disease carries risk for mother or child
Amiloride	Not used to treat hypertension in pregnancy
Aminophylline	Third trimester: Neonatal irritability and apnoea have been reported
Amitriptyline	Manufacturer advises avoid unless essential, particularly during first and third trimesters
Amodiaquine	Use only if no safer alternative
Amoxicillin	Not known to be harmful
Amoxicillin + Clavulanic acid	Not known to be harmful
Amphotericin B	Not known to be harmful but use only if potential benefit outweighs risk
Ampicillin	Not known to be harmful
Artemether	First trimester: Avoid
Artemether + Lumefantrine	Avoid. Toxicity in *animal* studies with artemether
Artesunate	First trimester: Avoid
Asparaginase	Avoid; *see also* section 12.1
Atenolol	May cause intrauterine growth restriction, neonatal hypoglycaemia, and bradycardia; risk greater in severe hypertension; *see also* section 5.3
Atropine	Not known to be harmful
Azathioprine	Transplant patients should not discontinue azathioprine on becoming pregnant; use in pregnancy should be supervised in specialist units; there is no evidence that azathioprine is teratogenic
Azithromycin	Use only if potential benefit outweighs risk
Beclometasone	Benefit of treatment, for example in asthma, outweighs risk
Benzathine benzylpenicillin	Not known to be harmful
Benznidazole	First trimester: avoid
Benzylpenicillin	Not known to be harmful
Betamethasone	Benefit of treatment, for example in asthma, outweighs risk
Bleomycin	Avoid (teratogenic and carcinogenic in *animal* studies); *see also* section 12.1
Bupivacaine	Third trimester: With large doses, neonatal respiratory depression, hypotonia, and bradycardia after paracervical or epidural block
Calcium folinate	Manufacturer advises use only if potential benefit outweighs risk
Carbamazepine	First trimester: Risk of teratogenesis including increased risk of neural tube defects (counselling and screening and adequate folate supplements advised, for example 5 mg daily); risk of teratogenicity greater if more than one antiepileptic used; *see also* section 1.7.1 Third trimester: May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding
Ceftazidime	Not known to be harmful
Ceftriaxone	Not known to be harmful
Chlorambucil	Avoid; use effective contraception during administration to men or women; *see also* section 12.1
Chloramphenicol	Third trimester: Neonatal 'grey' syndrome
Chlormethine	Avoid; *see also* section 12.1
Chloroquine	First, third trimesters: Benefit of prophylaxis and treatment in malaria outweighs risk; **important**: *see also* section 9.3.1
Chlorphenamine	No evidence of teratogenicity

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Drug	Comment
Chlorpromazine	Third trimester: Extrapyramidal effects in neonate occasionally reported
Ciclosporin	There is less experience of ciclosporin in pregnancy but it does not appear to be any more harmful than azathioprine; use in pregnancy should be supervised in specialist units
Ciprofloxacin	All trimesters: Avoid—arthropathy in *animal* studies; safer alternatives available
Cisplatin	Avoid (teratogenic and toxic in *animal* studies); *see also* section 12.1
Clindamycin	Not known to be harmful
Clomifene	Possible effects on fetal development
Clomipramine	Manufacturer advises avoid unless essential, particularly during first and third trimester
Clonazepam	Avoid regular use (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression)
Cloxacillin	Not known to be harmful
Codeine	Third trimester: Depresses neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour
Contraceptives, oral	Epidemiological evidence suggests no harmful effects on fetus
Cromoglicic acid	see Sodium cromoglicate
Cyclophosphamide	Avoid (use effective contraception during and for at least 3 months after administration to men or women); *see also* section 12.1
Cytarabine	Avoid (teratogenic in *animal* studies); *see also* section 12.1
Dacarbazine	Avoid (carcinogenic and teratogenic in *animal* studies); ensure effective contraception during and for at least 6 months after administration to men or women; *see also* section 12.1
Dactinomycin	Avoid (teratogenic in *animal* studies); *see also* section 12.1
Dapsone	Third trimester: Neonatal haemolysis and methaemoglobinaemia; folic acid 5 mg daily should be given to mother
Daunorubicin	Avoid (teratogenic and carcinogenic in *animal* studies); *see also* section 12.1
Deferoxamine	Teratogenic in *animal* studies; manufacturer advises use only if potential benefit outweighs risk
Dexamethasone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Diazepam	Avoid regular use (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression)
Didanosine	Avoid if possible in first trimester; increased risk of lactic acidosis and hepatic steatosis; *see* section 6.5.2
Diethylcarbamazine	Avoid: Delay treatment until after delivery
Digoxin	May need dosage adjustment
Diloxanide	Defer treatment until after first trimester
Doxorubicin	Avoid (teratogenic and toxic in *animal* studies); with liposomal product use effective contraception during and for at least 6 months after administration to men or women; *see also* section 8.2
Doxycycline	First trimester: Effects on skeletal development in *animal* studies Second, third trimesters: Dental discoloration; maternal hepatotoxicity with large doses
Efavirenz	Avoid (potential teratogenic effects); *see* section 9.5.2
Eflornithine	All trimesters: avoid
Enalapril	All trimesters: Avoid; may adversely affect fetal and neonatal blood pressure control and renal function; also possible skull defects and oligohydramnios; toxicity in *animal* studies

Drug	*Comment*
Ephedrine	Increased fetal heart rate reported with parenteral ephedrine
Ergocalciferol	High doses teratogenic in *animals* but therapeutic doses unlikely to be harmful
Ergotamine	All trimesters: Oxytocic effects on the pregnant uterus
Erythromycin	Not known to be harmful
Ethambutol	Not known to be harmful
Ether, anaesthetic	Third trimester: Depresses neonatal respiration
Ethinylestradiol	Epidemiological evidence suggests no harmful effects on fetus
Ethosuximide	First trimester: May possibly be teratogenic; risk of teratogenicity greater if more than one antiepileptic used; *see also* section 1.7.1
Etoposide	Avoid (teratogenic in *animal* studies); *see also* section 12.1
Fluconazole	Avoid (multiple congenital abnormalities reported with long-term high doses)
Flucytosine	Teratogenic in *animal* studies; manufacturer advises use only if potential benefit outweighs risk
Fluorouracil	Avoid (teratogenic); *see also* section 12.1
Fluphenazine	Third trimester: Extrapyramidal effects in neonate occasionally reported
Furosemide	Not used to treat hypertension in pregnancy
Gentamicin	Second, third trimesters: Auditory or vestibular nerve damage, risk probably very small with gentamicin, but avoid unless essential (if given, serum-gentamicin concentration monitoring essential)
Glibenclamide	Third trimester: Neonatal hypoglycaemia; insulin is normally substituted in all diabetics; if oral drugs are used therapy should be stopped at least 2 days before delivery
Griseofulvin	Avoid (fetotoxicity and teratogenicity in *animals*); effective contraception required during and for at least 1 month after administration (**important**: effectiveness of oral contraceptives reduced, *see* Appendix 1); also men should avoid fathering a child during and for at least 6 months after administration
Haloperidol	Third trimester: Extrapyramidal effects in neonate occasionally reported
Halothane	Third trimester: Depresses neonatal respiration
Heparin	All trimesters: Osteoporosis has been reported after prolonged use; multidose vials may contain benzyl alcohol—some manufacturers advise avoid
Hydralazine	Avoid during first and second trimesters; no reports of serious harm following use in third trimester
Hydrochlorothiazide	Not used to treat hypertension in pregnancy Third trimester: May cause neonatal thrombocytopenia
Hydrocortisone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Ibuprofen	Avoid unless potential benefit outweighs risk Third trimester: With regular use closure of fetal ductus arteriosus in utero and possibly persistent pulmonary hypertension of the newborn. Delayed onset and increased duration of labour
Idoxuridine	Teratogenic in *animal* studies
Imipenem+Cilastatin	Use only if potential benefit outweighs risk (toxicity in *animal* studies)
Indinavir	Avoid if possible in first trimester; theoretical risk of hyperbilirubinaemia and renal stones in neonate if used at term; *see* section 9.5.2
Insulin	All trimesters: Insulin requirements should be assessed frequently by an experienced diabetic clinician
Iodine	Second, third trimesters: Neonatal goitre and hypothyroidism
Isoniazid	Not known to be harmful
Ivermectin	Delay treatment until after delivery; *see also* section 9.4.2.3
Ketamine	Third trimester: Depresses neonatal respiration

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Drug	*Comment*
Lamivudine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters; *see* section 9.5.2
Levamisole	Third trimester: Avoid
Levodopa + Carbidopa	Toxicity in *animal* studies
Levonorgestrel	In oral contraceptives, epidemiological evidence suggests no harmful effects on fetus
Levothyroxine	Monitor maternal serum-thyrotrophin concentration—dosage adjustment may be necessary
Lidocaine	Third trimester: With large doses, neonatal respiratory depression, hypotonia, and bradycardia after paracervical or epidural block
Lithium	First trimester: Avoid if possible (risk of teratogenicity including cardiac abnormalities) Second and third trimesters: Dose requirements increased (but on delivery return to normal abruptly); close monitoring of serum-lithium concentration advised (risk of toxicity in neonate)
Lopinavir + Ritonavir	Avoid if possible in first trimester; avoid oral solution due to high propylene glycol content; *see* section 9.5.2
Magnesium sulfate	Third trimester: not known to be harmful for short-term intravenous administration in eclampsia but excessive doses may cause neonatal respiratory depression
Mebendazole	Toxicity in *animal* studies. Contraindicated in cestode infections; *see* section 9.4.1.1 First trimester: Avoid in nematode infections; *see* section 9.4.1.2
Medroxyprogesterone	Avoid (genital malformations and cardiac defects reported in male and female fetuses); inadvertent use of depot-medroxyprogesterone acetate contraceptive injection in pregnancy unlikely to harm fetus
Mefloquine	Use only if other antimalarials inappropriate, *see also* Prophylaxis and Treatment of Malaria, section 9.3.1
Melarsoprol	All trimesters: Avoid
Mercaptopurine	Avoid (teratogenic); *see also* section 12.1
Metformin	All trimesters: Avoid; insulin is normally substituted in all diabetics
Methotrexate	Avoid (teratogenic; fertility may be reduced during therapy but this may be reversible); use effective contraception during and for at least 6 months after administration to men or women; *see also* section 12.1
Methyldopa	Not known to be harmful
Metoclopramide	Not known to be harmful
Metronidazole	Avoid high-dose regimens
Morphine	Third trimester: Depresses neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour
Nalidixic acid	All trimesters: Avoid—arthropathy in *animal* studies; safer alternatives available
Naloxone	Use only if potential benefit outweighs risk
Nelfinavir	Avoid if possible in first trimester; potential benefit of treatment considered to outweigh risk in second and third trimesters; *see* section 9.5.2
Neostigmine	Third trimester: Neonatal myasthenia with large doses
Nevirapine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters; *see* section 9.5.2
Niclosamide	*T. solium* infections in pregnancy should be treated immediately; *see* section 9.4.1.1
Nifedipine	May inhibit labour; some dihydropyridines are teratogenic in *animals*, but risk to fetus should be balanced against risk of uncontrolled maternal hypertension
Nifurtimox	First trimester: Avoid
Nitrofurantoin	Third trimester: May produce neonatal haemolysis if used at term
Nitrous oxide	Third trimester: Depresses neonatal respiration

Drug	Comment
Norethisterone	In oral contraceptives, epidemiological evidence suggests no harmful effects on fetus In higher doses masculinization of female fetuses and other defects reported
Nystatin	No information available, but absorption from gastrointestinal tract negligible
Ofloxacin	All trimesters: Avoid—arthropathy in *animal* studies; safer alternatives available
Oxamniquine	If immediate treatment not required schistosomiasis treatment should be delayed until after delivery; *see* section 9.4.3.1
Paracetamol	Not known to be harmful
Penicillamine	All trimesters: Fetal abnormalities reported rarely; avoid if possible
Pentamidine isetionate	Potentially fatal visceral leishmaniasis must be treated without delay. Should not be withheld in trypanosomiasis even if evidence of meningoencephalitic involvement. Potentially fatal *P. carinii* pneumonia must be treated without delay
Pentavalent antimony compounds	Potentially fatal visceral leishmaniasis must be treated without delay
Phenobarbital	First, third trimesters: Congenital malformations; risk of teratogenicity greater if more than one antiepileptic used. May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding; *see* section 1.7.1
Phenoxymethylpenicillin	Not known to be harmful
Phenytoin	First, third trimesters: Congenital malformations (screening advised); adequate folate supplements should be given to mother (for example folic acid 5 mg daily); risk of teratogenicity greater if more than one antiepileptic used. May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding. Caution in interpreting plasma concentrations—bound may be reduced but free (or effective) unchanged; *see also* section 1.7.1
Phytomenadione	Use only if potential benefit outweighs risk—no specific information available
Podophyllum resin	All trimesters: Avoid—neonatal death and teratogenesis have been reported
Polyvidone–iodine	Second, third trimesters: Sufficient iodine may be absorbed to affect the fetal thyroid
Potassium iodide	Second, third trimesters: Neonatal goitre and hypothyroidism
Praziquantel	*T. solium* infections in pregnancy should be treated immediately; *see* section 9.4.1.1. Benefit of treatment in schistosomiasis outweighs risk If immediate treatment not considered essential for fluke infections, treatment should be delayed until after delivery
Prednisolone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Primaquine	Third trimester: Neonatal haemolysis and methaemoglobinaemia. Delay treatment until after delivery
Procarbazine	Avoid (teratogenic in *animal* studies and isolated reports in humans); *see also* section 12.1
Proguanil	Benefit of prophylaxis and of treatment outweighs risk. Adequate folate supplements should be given to mother
Promethazine	No evidence of teratogenicity
Propranolol	May cause intrauterine growth restriction, neonatal hypoglycaemia, and bradycardia; risk greater in severe hypertension; *see also* section 5.3

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Drug	*Comment*
Propylthiouracil	Second, third trimesters: Neonatal goitre and hypothyroidism
Pyrazinamide	Use only if potential benefit outweighs risk
Pyridostigmine	Third trimester: Neonatal myasthenia with large doses
Pyrimethamine	First trimester: Theoretical teratogenic risk (folate antagonist); adequate folate supplements should be given to the mother. First trimester: avoid in Pneumocystosis and toxoplasmosis; *see also* Sulfadiazine
Quinine	First trimester: High doses are teratogenic; but in malaria benefit of treatment outweighs risk
Ranitidine	Not known to be harmful
Retinol	First trimester: Excessive doses may be teratogenic; *see also* section 6.7 [text]
Rifampicin	First trimester: Very high doses teratogenic in *animal* studies Third trimester: Risk of neonatal bleeding may be increased
Ritonavir	*See* Lopinavir with Ritonavir
Salbutamol	For use in asthma *see* section 7.1 [text] Third trimester: For use in premature labour *see* section 11.1
Saquinavir	Avoid if possible in first trimester; potential benefit of treatment considered to outweigh risk in second and third trimesters; *see* section 9.5.2
Silver sulfadiazine	Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded
Sodium cromoglicate	Not known to be harmful; *see also* section 7.1 [text]
Sodium valproate	*see* Valproic acid
Spironolactone	Toxicity in *animal* studies
Stavudine	Avoid if possible in first trimester; increased risk of lactic acidosis and hepatic steatosis; *see* section 9.5.2
Streptokinase	All trimesters: Possibility of premature separation of placenta in first 18 weeks; theoretical possibility of fetal haemorrhage throughout pregnancy; risk of maternal haemorrhage on postpartum use
Streptomycin	Second, third trimesters: Auditory or vestibular nerve damage; avoid unless essential (if given, serum-streptomycin concentration monitoring essential)
Sulfadiazine	Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded In toxoplasmosis, avoid in first trimester, but may be given in second and third trimester if danger of congenital transmission
Sulfadoxine + Pyrimetha-mine	In malaria, benefit of prophylaxis and treatment outweigh risk. First trimester: Possible teratogenic risk (pyrimethamine a folate antagonist) Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded *See also* section 9.3.1
Sulfamethoxazole + Tri-methoprim	First trimester: Teratogenic risk (trimethoprim a folate antagonist) Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded
Sulfasalazine	Third trimester: Theoretical risk of neonatal haemolysis; adequate folate supplements should be given to mother
Suramin sodium	In onchocerciasis, delay treatment until after delivery. In *T. b. rhodesiense* treatment should be given even if evidence of meningoencephalopathic involvement
Suxamethonium	Mildly prolonged maternal paralysis may occur
Tamoxifen	Avoid—possible effects on fetal development; effective contraception must be used during treatment and for 2 months after stopping

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Drug	*Comment*
Testosterone	All trimesters: Masculinization of female fetus
Tetracycline	First trimester: Effects on skeletal development in *animal* studies Second, third trimesters: Dental discoloration; maternal hepatotoxicity with large doses
Theophylline	Third trimester: Neonatal irritability and apnoea have been reported
Thiopental	Third trimester: Depresses neonatal respiration
Trimethoprim	First trimester: Teratogenic risk (folate antagonist)
Vaccine, BCG	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus (*see also* section 17.1 [contraindications and precautions])
Vaccine, Measles	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus (*see also* section 17.1 [contraindications and precautions]); avoid MMR
Vaccine, MMR	Avoid; pregnancy should be avoided for 1 month after immunization
Vaccine, Poliomyelitis, live	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus (*see also* section 17.1 [contraindications and precautions])
Vaccine, Rubella	Avoid; pregnancy should be avoided for 1 month after immunization
Vaccine, Yellow fever	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus (*see also* section 17.1 [contraindications and precautions])
Valproic acid	First, third trimesters: Increased risk of neural tube defects (counselling and screening advised—folic acid supplement may reduce risk); risk of teratogenicity greater if more than one antiepileptic used; neonatal bleeding (related to hypofibrinaemia) and neonatal hepatotoxicity also reported; *see also* section 1.7.1 (sodium valproate)
Vancomycin	Use only if potential benefit outweighs risk—plasma-vancomycin concentration monitoring essential to reduce risk of fetal toxicity
Vecuronium	Use only if potential benefit outweighs risk—no information available
Verapamil	*Animal* studies have not shown teratogenic effect; possibility that verapamil can relax uterine muscles should be considered at term; risk to fetus should be balanced against risk of uncontrolled maternal hypertension
Vinblastine	Avoid (limited experience suggests fetal harm; teratogenic in *animal* studies); *see also* section 12.1
Vincristine	Avoid (teratogenicity and fetal loss in *animal* studies); *see also* section 12.1
Warfarin	All trimesters: Congenital malformations; fetal and neonatal haemorrhage *See also* section 6.2
Zidovudine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters; *see* section 9.5.2

Appendix 3: Breastfeeding

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Administration of sofme drugs (for example, ergotamine) to nursing mothers may harm the infant, whereas administration of others (for example, digoxin) has little effect. Some drugs inhibit lactation (for example, estrogens).

Toxicity to the infant can occur if the drug enters the milk in pharmacologically significant quantities. The concentration in milk of some drugs (for example, iodides) may exceed that in the maternal plasma so that therapeutic doses in the mother may cause toxicity to the infant. Some drugs inhibit the infant's sucking reflex (for example, phenobarbital). Drugs in breast milk may, at least theoretically, cause hypersensitivity in the infant even when the concentration is too low for a pharmacological effect.

The following table lists drugs:

- which should be used with caution or which are contraindicated in breastfeeding for the reasons given above;
- which, on present evidence, may be given to the mother during breastfeeding, because they appear in milk in amounts which are too small to be harmful to the infant;
- which are not known to be harmful to the infant although they are present in milk in significant amounts.

For many drugs insufficient evidence is available to provide guidance and it is advisable to administer only drugs essential to a mother during breastfeeding. Because of the inadequacy of information on drugs in breast milk the following table should be used only as a guide; absence from the table does not imply safety.

WHO POLICY

It is WHO policy to encourage breastfeeding whenever possible, particularly in situations where there is no safe alternative. Advice in the table may differ from other sources, including manufacturer's product literature.

For further information on use of drugs during breastfeeding, *see also* the WHO document 'Breastfeeding and Maternal Medication', WHO/CDR/95.11.

Table of drugs present in breast milk

Drug	*Comment*
Abacavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Acetazolamide	Amount too small to be harmful
Acetylsalicylic acid	Short course safe in usual dosage; monitor infant; regular use of high doses could impair platelet function and produce hypoprothrombinaemia in infant if neonatal vitamin K stores low; possible risk of Reye syndrome
Aciclovir	Significant amount in milk after systemic administration, but considered safe to use
Alcohol	Large amounts may affect infant and reduce milk consumption
Alcuronium	No information available
Allopurinol	Present in milk
Amiloride	Manufacturer advises avoid—no information available
Aminophylline	Present in milk—irritability in infant reported
Amitriptyline	Detectable in breast milk; continue breastfeeding; adverse effects possible, monitor infant for drowsiness
Amodiaquine	No information available
Amoxicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Amoxicillin + Clavulanic acid	Trace amounts in milk
Amphotericin B	No information available
Ampicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Artemether + Lumefantrine	Discontinue breastfeeding during and for 1 week after stopping treatment; present in milk in *animal* studies
Asparaginase	Breastfeeding contraindicated
Atenolol	Significant amounts in milk; safe in usual dosage; monitor infant
Atropine	Small amount present in milk; monitor infant

Drug	*Comment*
Azathioprine	Breastfeeding contraindicated
Azithromycin	No information available
Beclometasone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Benzathine benzylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Benzylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Betamethasone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Bleomycin	Breastfeeding contraindicated
Bupivacaine	Amount too small to be harmful
Carbamazepine	Continue breastfeeding; adverse effects possible (severe skin reaction reported in 1 infant); monitor infant for drowsiness; *see also* section 1.7.1
Ceftazidime	Excreted in low concentrations; safe in usual dosage; monitor infant
Ceftriaxone	Excreted in low concentrations; safe in usual dosage; monitor infant
Chlorambucil	Breastfeeding contraindicated
Chloramphenicol	Continue breastfeeding; use alternative drug if possible; may cause bone-marrow toxicity in infant; concentration in milk usually insufficient to cause 'grey syndrome'
Chlormethine	Breastfeeding contraindicated
Chloroquine	For malaria prophylaxis, amount probably too small to be harmful; inadequate for reliable protection against malaria, *see also* section 9.3.1; avoid breastfeeding when used for rheumatic disease
Chlorphenamine	Safe in usual dosage; monitor infant for drowsiness
Chlorpromazine	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Ciclosporin	Present in milk—manufacturer advises avoid
Ciprofloxacin	Continue breastfeeding; use alternative drug if possible; high concentrations in breast milk
Cisplatin	Breastfeeding contraindicated
Clindamycin	Amount probably too small to be harmful but bloody diarrhoea reported in 1 infant
Clomifene	May inhibit lactation
Clomipramine	Small amount present in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Clonazepam	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness; *see also* section 1.7.1
Cloxacillin	Trace amounts in milk; safe in usual dosage; monitor infant
Codeine	Amount too small to be harmful
Colchicine	Present in milk but no adverse effects reported; caution because of risk of cytotoxicity
Contraceptives, oral	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (start 3 weeks after birth or later)
Cromoglicic acid	*see* Sodium cromoglicate
Cyclophosphamide	Breastfeeding contraindicated during and for 36 hours after stopping treatment
Cytarabine	Breastfeeding contraindicated
Dacarbazine	Breastfeeding contraindicated
Dactinomycin	Breastfeeding contraindicated
Dapsone	Although significant amount in milk risk to infant very small; continue breastfeeding; monitor infant for jaundice
Daunorubicin	Breastfeeding contraindicated
Deferoxamine	Manufacturer advises use only if potential benefit outweighs risk—no information available

Drug	Comment
Dexamethasone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Diazepam	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness; *see also* section 1.7.1
Didanosine	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Digoxin	Amount too small to be harmful
Diloxanide	Manufacturer advises avoid
Doxorubicin	Breastfeeding contraindicated
Doxycycline	Continue breastfeeding; use alternative drug if possible (absorption and therefore discoloration of teeth in infant probably usually prevented by chelation with calcium in milk)
Efavirenz	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Eflornithine	Avoid
Enalapril	Amount probably too small to be harmful
Ephedrine	Irritability and disturbed sleep reported
Ergocalciferol	Caution with high doses; may cause hypercalcaemia in infant
Ergotamine	Use alternative drug; ergotism may occur in infant; repeated doses may inhibit lactation
Erythromycin	Only small amounts in milk; safe in usual dosage; monitor infant
Ethambutol	Amount too small to be harmful
Ethinylestradiol	Use alternative method of contraception; may inhibit lactation; *see also* Contraceptives, Oral
Ethosuximide	Significant amount in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness; *see also* section 1.7.1
Etoposide	Breastfeeding contraindicated
Fluconazole	Present in milk; safe in usual dosage; monitor infant
Flucytosine	Manufacturer advises avoid
Fluorouracil	Discontinue breastfeeding
Fluphenazine	Amount excreted in milk probably too small to be harmful; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Furosemide	Amount too small to be harmful
Glibenclamide	Theoretical possibility of hypoglycaemia in infant
Haloperidol	Amount excreted in milk probably too small to be harmful; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Halothane	Excreted in milk
Hydralazine	Present in milk but not known to be harmful; monitor infant
Hydrochlorothiazide	Use alternative drug; may inhibit lactation
Hydrocortisone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Ibuprofen	Amount too small to be harmful; short courses safe in usual doses
Imipenem + Cilastatin	Present in milk—manufacturer advises avoid
Indinavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Insulin	Amount too small to be harmful
Iodine	Stop breastfeeding; danger of neonatal hypothyroidism or goitre; appears to be concentrated in milk
Isoniazid	Monitor infant for possible toxicity; theoretical risk of convulsions and neuropathy; prophylactic pyridoxine advisable in mother and infant
Ivermectin	Avoid treating mother until infant is 1week old
Lamivudine	Present in milk; breastfeeding recommended during first 6 months if no safe alternative to breast milk
Levamisole	Breastfeeding contraindicated
Levodopa + Carbidopa	No information available

Drug	*Comment*
Levonorgestrel	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (preferably start 6 weeks after birth or later)
Levothyroxine	Amount too small to affect tests for neonatal hypothyroidism
Lidocaine	Amount too small to be harmful
Lithium	Present in milk and risk of toxicity in infant; continue breastfeeding; monitor infant carefully, particularly if risk of dehydration
Lopinavir + Ritonavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Lumefantrine	*see* Artemether + Lumefantrine
Mebendazole	No information available
Medroxyprogesterone	Present in milk—no adverse effects reported (preferably start injectable contraceptive 6 weeks after birth or later)
Mefloquine	Present in milk but risk to infant minimal
Mercaptopurine	Breastfeeding contraindicated
Metformin	Present in milk but safe in usual doses; monitor infant
Methotrexate	Breastfeeding contraindicated
Methyldopa	Amount too small to be harmful
Metoclopramide	Present in milk; adverse effects possible; monitor infant for adverse effects
Metronidazole	Significant amount in milk; continue breastfeeding; avoid large doses; use alternative drug if possible
Morphine	Short courses safe in usual doses; monitor infant
Nalidixic acid	Continue breastfeeding; use alternative drug if possible; one case of haemolytic anaemia reported
Naloxone	No information available
Nelfinavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Neostigmine	Amount probably too small to be harmful; monitor infant
Nevirapine	Present in milk; breastfeeding recommended during first 6 months if no safe alternative to breast milk
Nifedipine	Small amount in milk; continue breastfeeding; monitor infant
Nitrofurantoin	Only small amounts in milk but could be enough to produce haemolysis in G6PD-deficient infants
Norethisterone	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (preferably start injectable contraceptive 6 weeks after birth or later)
Nystatin	No information available, but absorption from gastrointestinal tract negligible
Ofloxacin	Continue breastfeeding; use alternative drug if possible
Oxamniquine	No information available, but considered preferable to avoid
Paracetamol	Small amount present in milk: short courses safe in usual dosage; monitor infant
Pentamidine isetionate	Manufacturer advises avoid unless essential
Pentavalent antimony compounds	Avoid
Phenobarbital	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness; *see also* section 1.7.1
Phenoxymethylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Phenytoin	Small amount present in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness; *see also* section 1.7.1
Polyvidone–iodine	Avoid; iodine absorbed from vaginal preparations is concentrated in milk
Potassium iodide	Stop breastfeeding; danger of neonatal hypothyroidism or goitre; appears to be concentrated in milk

Drug	*Comment*
Praziquantel	Avoid breastfeeding during and for 72 hours after treatment; considered safe to continue breastfeeding in treatment of schistosomiasis
Prednisolone	Systemic effects in infant unlikely with maternal dose of *less than* prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Primaquine	Avoid; risk of haemolysis in G6PD-deficient infants
Procainamide	Present in milk; continue breastfeeding; monitor infant
Procarbazine	Breastfeeding contraindicated
Proguanil	Amount probably too small to be harmful; inadequate for reliable protection against malaria, *see* section 9.3.1
Promethazine	Safe in usual dosage; monitor infant for drowsiness
Propranolol	Present in milk; safe in usual dosage; monitor infant
Propylthiouracil	Monitor infant's thyroid status but amounts in milk probably too small to affect infant; high doses might affect neonatal thyroid function
Pyrazinamide	Amount too small to be harmful
Pyridostigmine	Amount probably too small to be harmful
Pyrimethamine	Significant amount—avoid administration of other folate antagonists to infant
Quinidine	Significant amount but not known to be harmful
Ranitidine	Significant amount present in milk, but not known to be harmful
Retinol	Theoretical risk of toxicity in infants of mothers taking large doses
Rifampicin	Amount too small to be harmful
Ritonavir	*See* Lopinavir with Ritonavir
Salbutamol	Safe in usual dosage; monitor infant
Saquinavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Senna	Avoid; large doses may cause increased gastric motility and diarrhoea
Silver sulfadiazine	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants particularly with long-acting sulphonamides, and of haemolysis in G6PD-deficient infants
Sodium cromoglicate	Unlikely to be present in milk
Sodium valproate	*see* Valproic acid
Stavudine	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Sulfadiazine	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants particularly with long-acting sulphonamides, and of haemolysis in G6PD-deficient infants
Sulfadoxine + Pyrimethamine	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to sulfadoxine)
Sulfamethoxazole + Trimethoprim	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to sulfamethoxazole)
Sulfasalazine	Continue breastfeeding; monitor infant for jaundice—small amounts in milk (1 report of bloody diarrhoea and rashes); theoretical risk of neonatal haemolysis especially in G6PD-deficient infants
Tamoxifen	Suppresses lactation; avoid unless potential benefit outweighs risk
Testosterone	Avoid; may cause masculinization in the female infant or precocious development in the male infant; high doses suppress lactation
Tetracaine	No information available
Tetracycline	Continue breastfeeding; use alternative drug if possible (absorption and therefore discoloration of teeth in infant probably usually prevented by chelation with calcium in milk)
Theophylline	Present in milk—irritability in infant reported; modified-release preparations preferable

RETURN

Drug	*Comment*
Thiamine	Severely thiamine-deficient mothers should avoid breastfeeding as toxic methyl-glyoxal excreted in milk
Trimethoprim	Present in milk; safe in usual dosage; monitor infant
Valproic acid	Small amount present in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness; *see also* section 1.7.1 (sodium valproate)
Vancomycin	Present in milk—significant absorption following oral administration unlikely
Vecuronium	No information available
Verapamil	Amount too small to be harmful
Vinblastine	Breastfeeding contraindicated
Vincristine	Breastfeeding contraindicated
Warfarin	Risk of haemorrhage; increased by vitamin-K deficiency; warfarin appears safe
Zidovudine	Breastfeeding recommended during first 6 months if no safe alternative to breast milk

Appendix 4: Renal impairment

RETURN

Reduced renal function may cause problems with drug therapy for the following reasons:

1. The failure to excrete a drug or its metabolites may produce toxicity.
2. The sensitivity to some drugs is increased even if the renal elimination is unimpaired.
3. The tolerance to adverse effects may be impaired.
4. The efficacy of some drugs may diminish.

The dosage of many drugs must be adjusted in patients with renal impairment to avoid adverse reactions and to ensure efficacy. The level of renal function below which the dose of a drug must be reduced depends on how toxic it is and whether it is eliminated entirely by renal excretion or is partly metabolized to inactive metabolites.

In general, all patients with renal impairment are given a *loading dose* which is the same as the usual dose for a patient with normal renal function. *Maintenance doses* are adjusted to the clinical situation. The maintenance dose of a drug can be reduced either by reducing the individual dose leaving the normal interval between doses unchanged or by increasing the interval between doses without changing the dose. The interval extension method may provide the benefits of convenience and decreased cost, while the dose reduction method provides more constant plasma concentration.

In the following table drugs are listed in alphabetical order. The table includes only drugs for which specific information is available. Many drugs should be used with caution in renal impairment but no specific advice on dose adjustment is available; it is therefore important to also refer to the individual drug entries. The recommendations are given for various levels of renal function as estimated by the glomerular filtration rate (GFR), usually measured by the creatinine clearance. The serum-creatinine concentration can be used instead as a measure of renal function but it is only a rough guide unless corrected for age, sex and weight by special nomograms.

Renal impairment is usually divided into three grades:

mild —GFR 20–50 ml/minute or approximate serum creatinine 150–300 micromol/litre
moderate —GFR 10–20 ml/minute or serum creatinine 300–700 micromol/litre
severe —GFR or serum creatinine >700 micromol/litre

When using the dosage guidelines the following must be considered:

- Drug prescribing should be kept to a minimum.
- Nephrotoxic drugs should, if possible, be avoided in all patients with renal disease because the nephrotoxicity is more likely to be serious.
- It is advisable to determine renal function not only before but also during the period of treatment and adjust the maintenance dose as necessary.
- Renal function (GFR, creatinine clearance) declines with age so that by the age of 80 it is half that in healthy young subjects. When prescribing for the elderly, assume at least a mild degree of renal impairment.
- Uraemic patients should be observed carefully for unexpected drug toxicity. In these patients the complexity of clinical status as well as other variables for example altered absorption, protein binding or metabolism, or liver function, and other drug therapy precludes use of fixed drug dosage and an individualized approach is required.

Table of drugs to be avoided or used with caution in renal impairment

Drug	*Degree of Impairment*	*Comment*
Abacavir	Severe	Avoid
Acetazolamide	Mild	Avoid; metabolic acidosis
Acetylsalicylic acid	Severe	Avoid; sodium and water retention; deterioration in renal function; increased risk of gastrointestinal bleeding
Aciclovir	Mild	Reduce intravenous dose
	Moderate to severe	Reduce dose
Alcuronium	Severe	Prolonged duration of block
Allopurinol	Moderate	100–200 mg daily; increased toxicity; rashes

Drug	Degree of Impairment	Comment
	Severe	100 mg on alternate days (maximum 100 mg daily)
Aluminium hydroxide	Severe	Aluminium is absorbed and may accumulate NOTE: Absorption of aluminium from aluminium salts is increased by citrates which are contained in many effervescent preparations (such as effervescent analgesics)
Amidotrizoates	Mild	Reduce dose and avoid dehydration; nephrotoxic
Amiloride	Mild	Monitor plasma potassium; high risk of hyperkalaemia in renal impairment; amiloride excreted by kidney unchanged
	Moderate	Avoid
Amoxicillin	Severe	Reduce dose; rashes more common
Amoxicillin + Clavulanic acid	Moderate to severe	Reduce dose
Amphotericin B	Mild	Use only if no alternative; nephrotoxicity may be reduced with use of complexes
Ampicillin	Severe	Reduce dose; rashes more common
Artemether + Lumefantrine	Severe	Caution; monitor ECG and plasma potassium
Atenolol	Moderate	Reduce dose (excreted unchanged)
	Severe	Start with small dose; higher plasma concentrations after oral administration; may reduce renal blood flow and adversely affect renal function
Azathioprine	Severe	Reduce dose
Azithromycin	Moderate to severe	Use with caution —no information available
Benzathine benzylpenicillin	Severe	Neurotoxicity—high doses may cause convulsions
Benzylpenicillin	Severe	Maximum 6 g daily; neurotoxicity—high doses may cause convulsions
Bleomycin	Moderate	Reduce dose
Carbamazepine		Manufacturer advises caution
Ceftazidime	Mild	Reduce dose
Ceftriaxone	Severe	Maximum 2 g daily; also monitor plasma concentration if both severe renal impairment and hepatic impairment
Chlorambucil	Moderate	Use with caution and monitor response; increased risk of myelosuppression
Chloramphenicol	Severe	Avoid unless no alternative; dose-related depression of haematopoiesis
Chloroquine	Mild to moderate	Reduce dose in rheumatic disease
	Severe	Reduce dose for malaria prophylaxis; avoid in rheumatic disease
Chlorphenamine	Severe	Dose reduction may be required
Chlorpromazine	Severe	Start with small doses; increased cerebral sensitivity
Ciclosporin		Monitor kidney function—dose dependent increase in serum creatinine and urea during first few weeks may necessitate dose reduction (exclude rejection if kidney transplant)
Ciprofloxacin	Moderate	Use half normal dose
Cisplatin	Mild	Avoid if possible; nephrotoxic and neurotoxic
Clindamycin		Plasma half-life prolonged—may need dose reduction
Clonazepam	Severe	Start with small doses; increased cerebral sensitivity
Cloxacillin	Severe	Reduce dose
Codeine	Moderate to severe	Reduce dose or avoid; increased and prolonged effect; increased cerebral sensitivity
Colchicine	Moderate	Reduce dose
	Severe	Avoid or reduce dose if no alternative
Cyclophosphamide		Reduce dose

Drug	Degree of Impairment	Comment
Dacarbazine	Mild to moderate	Dose reduction may be required
	Severe	Avoid
Daunorubicin	Mild to moderate	Reduce dose
Deferoxamine		Metal complexes excreted by kidneys (in severe renal impairment dialysis increases rate of elimination)
Diazepam	Severe	Start with small doses; increased cerebral sensitivity
Didanosine	Mild	Reduce dose; consult manufacturer's literature
Diethylcarbamazine	Moderate to severe	Reduce dose; plasma half life prolonged and urinary excretion considerably reduced
Digoxin	Mild	Reduce dose; toxicity increased by electrolyte disturbances
Dimercaprol		Discontinue or use with extreme caution if impairment develops during treatment
Doxycycline	Mild	Use with caution; avoid excessive doses
Efavirenz	Severe	No information available—caution advised
Eflornithine		Reduce dose
Enalapril	Mild to moderate	Use with caution and monitor response; initial dose 2.5 mg once daily. Hyperkalaemia and other adverse effects more common
Ephedrine	Severe	Avoid; increased CNS toxicity
Ergometrine	Severe	Manufacturer advises avoid
Ergotamine	Moderate	Avoid; nausea and vomiting; risk of renal vasoconstriction
Erythromycin	Severe	Maximum 1.5 g daily (ototoxicity)
Ethambutol	Mild	Reduce dose; if creatinine clearance less than 30 ml/minute monitor plasma-ethambutol concentration; optic nerve damage
Fluconazole	Mild to moderate	Usual initial dose then halve subsequent doses
Flucytosine		Reduce dose and monitor plasma-flucytosine concentration—consult manufacturer's literature
Fluphenazine	Severe	Start with small doses; increased cerebral sensitivity
Furosemide	Moderate	May need high doses; deafness may follow rapid i/v injection
Gentamicin	Mild	Reduce dose; monitor plasma concentrations; *see also* section 9.1.2.5
Glibenclamide	Severe	Avoid
Haloperidol	Severe	Start with small doses; increased cerebral sensitivity
Heparin	Severe	Risk of bleeding increased
Hydralazine	Mild	Reduce dose if creatinine clearance less than 30 ml/minute
Hydrochlorothiazide	Moderate	Avoid; ineffective
Ibuprofen	Mild	Use lowest effective dose and monitor renal function; sodium and water retention; deterioration in renal function possibly leading to renal failure
	Moderate to severe	Avoid
Imipenem + Cilastatin	Mild	Reduce dose
Insulin	Severe	May need dose reduction; insulin requirements fall; compensatory response to hypoglycaemia is impaired
Iohexol	Moderate to severe	Increased risk of nephrotoxicity; avoid dehydration
Iopanoic acid	Mild to moderate	Maximum 3 g
	Severe	Avoid
Isoniazid	Severe	Maximum 200 mg daily; peripheral neuropathy
Lamivudine	Mild	Reduce dose; consult manufacturer's literature
Lithium	Mild	Avoid if possible or reduce dose and monitor plasma concentration carefully

Drug	Degree of Impairment	Comment
	Moderate	Avoid
Lopinavir + Ritonavir		Avoid oral solution due to propylene glycol content; use capsules with caution in severe impairment
Magnesium hydroxide	Moderate	Avoid or reduce dose; increased risk of toxicity
Magnesium sulfate	Moderate	Avoid or reduce dose; increased risk of toxicity
Mannitol		Avoid unless test dose produces diuretic response
Meglumine antimoniate	*see* Pentavalent antimony compounds	
Meglumine iotroxate	Moderate to severe	Increased risk of nephrotoxicity; avoid dehydration
Mercaptopurine	Moderate	Reduce dose
Metformin	Mild	Avoid; increased risk of lactic acidosis
Methotrexate	Mild	Reduce dose; accumulates; nephrotoxic
	Moderate	Avoid
Methyldopa	Moderate	Start with small dose; increased sensitivity to hypotensive and sedative effect
Metoclopramide	Severe	Avoid or use small dose; increased risk of extrapyramidal reactions
Morphine	Moderate to severe	Reduce dose or avoid; increased and prolonged effect; increased cerebral sensitivity
Nalidixic acid	Moderate to severe	Use half normal dose; ineffective in renal failure because concentration in urine is inadequate
Nelfinavir		No information available—manufacturer advises caution
Neostigmine	Moderate	May need dose reduction
Nitrofurantoin	Mild	Avoid; peripheral neuropathy; ineffective because of inadequate urine concentrations
Penicillamine	Mild	Avoid if possible or reduce dose; nephrotoxic
Pentamidine isetionate	Mild	Reduce dose; consult manufacturer's literature
Pentavalent antimony compounds	Moderate	Increased adverse effects
	Severe	Avoid
Phenobarbital	Severe	Avoid large doses
Polyvidone–iodine	Severe	Avoid regular application to inflamed or broken mucosa
Potassium chloride	Moderate	Avoid routine use; high risk of hyperkalaemia
Procainamide	Mild	Avoid or reduce dose
Procaine benzylpenicillin	Severe	Neurotoxicity—high doses may cause convulsions
Procarbazine	Severe	Avoid
Proguanil	Mild	100 mg once daily
	Moderate	50 mg on alternate days
	Severe	50 mg once weekly; increased risk of haematological toxicity
Propranolol	Severe	Start with small dose; higher plasma concentrations after oral administration; may reduce renal blood flow and adversely affect renal function
Propylthiouracil	Mild to moderate	Use three-quarters normal dose
	Severe	Use half normal dose
Pyridostigmine	Moderate	Reduce dose; excreted by kidney
Quinine		Reduce parenteral maintenance dose for malaria treatment
Ranitidine	Severe	Use half normal dose; occasional risk of confusion
Ritonavir	See Lopinavir with Ritonavir	
Saquinavir	Severe	Dose adjustment possibly required
Sodium chloride	Severe	Avoid

Drug	Degree of Impairment	Comment
Sodium hydrogen carbonate	Severe	Avoid; specialized role in some forms of renal disease
Sodium nitroprusside	Moderate	Avoid prolonged use
Sodium valproate	see Valproic acid	
Spironolactone	Mild	Monitor plasma K+ ; high risk of hyperkalaemia in renal impairment
	Moderate	Avoid
Stavudine	Mild	20 mg twice daily (15 mg if body weight less than 60 kg)
	Moderate to severe	20 mg once daily (15 mg if body weight less than 60 kg)
Streptomycin	Mild	Reduce dose; monitor plasma concentrations
Sulfadiazine	Severe	Avoid; high risk of crystalluria
Sulfamethoxazole + Trimethoprim	Mild	Use half normal dose if creatinine clearance 15–30 ml/minute; avoid if creatinine clearance less than 15 ml/minute and if plasma-sulfamethoxazole concentration cannot be monitored
Sulfasalazine	Moderate	Risk of toxicity including crystalluria—ensure high fluid intake
	Severe	Avoid
Trimethoprim	Mild	Use half normal dose after 3 days if creatinine clearance 15–30 ml/minute
	Moderate to severe	Use half normal dose if creatinine clearance less than 15 ml/minute; avoid if creatinine clearance less than 10 ml/minute (unless plasma-trimethoprim concentration monitored)
Valproic acid	Mild to moderate	Reduce dose
	Severe	Alter dosage according to free serum valproic acid concentration
Vancomycin	Mild	Reduce dose—monitor plasma-vancomycin concentration and renal function regularly
Vecuronium	Severe	Reduce dose; duration of block possibly prolonged
Warfarin	Severe	Avoid
Zidovudine	Severe	Reduce dose; manufacturer advises oral dose of 300–400 mg daily in divided doses or intravenous dose of 1 mg/kg 3–4 times daily

Appendix 5: Hepatic impairment

RETURN

Liver disease may alter the response to drugs. However, the hepatic reserve appears to be large and liver disease has to be severe before important changes in drug metabolism take place. The ability to eliminate a specific drug may or may not correlate with liver's synthetic capacity for substances such as albumin or clotting factors, which tends to decrease as hepatic function declines. Unlike renal disease, where estimates of renal function based on creatinine clearance correlate with parameters of drug elimination such as clearance and half-life, routine liver function tests do not reflect actual liver function but are rather markers of liver cellular damage.

The altered response to drugs in liver disease can include all or some of the following changes:

- Impaired intrinsic hepatic eliminating (metabolizing) capacity due to lack of or impaired function of hepatocytes.
- Impaired biliary elimination due to biliary obstruction or transport abnormalities (for example rifampicin is excreted in the bile unchanged and may accumulate in patients with intrahepatic or extrahepatic obstructive jaundice).
- Impaired hepatic blood flow due to surgical shunting, collateral circulation or poor perfusion with cirrhosis and portal hypertension.
- Altered volume of distribution of drugs due to increased extracellular fluid (ascites, oedema) and decreased muscle mass.
- Decreased protein binding and increased toxicity of drugs highly bound to proteins (for example phenytoin) due to impaired albumin production.
- Increased bioavailability through decreased first-pass metabolism.
- Decreased bioavailability due to malabsorption of fats in cholestatic liver disease.

In severe liver disease increased sensitivity to the effects of some drugs can further impair cerebral function and may precipitate *hepatic encephalopathy* (for example morphine). *Oedema* and *ascites* in chronic liver disease may be exacerbated by drugs that cause fluid retention (for example acetylsalicylic acid, ibuprofen, prednisolone, dexamethasone).

Usually drugs are metabolized without injury to the liver. A few drugs cause dose-related hepatotoxicity. However, most hepatotoxic reactions to drugs occur only in rare persons and are unpredictable. In patients with impaired liver function the dose-related hepatotoxic reaction may occur at lower doses whereas unpredictable reactions seem to occur more frequently. Both should be avoided.

Information to help prescribing in hepatic impairment is included in the following table. The table contains only those drugs that need dose adjustment. However, absence from the table does not automatically imply safety as for many drugs data about safety are absent; it is therefore important to also refer to the individual drug entries.

Table of drugs to be avoided or used with caution in liver disease

Drug	Comment
Abacavir	Avoid in moderate hepatic impairment unless essential; avoid in severe hepatic impairment
Acetylsalicylic acid	Avoid—increased risk of gastrointestinal bleeding
Alcuronium	Possibly slower onset, higher dose requirement and prolonged recovery time
Allopurinol	Reduce dose
Aluminium hydroxide	In patients with fluid retention, avoid antacids containing large amounts of sodium; also avoid those causing constipation (can precipitate coma)
Aminophylline	Reduce dose
Amitriptyline	Sedative effects increased (avoid in severe liver disease)
Amodiaquine	Avoid
Amoxicillin + Clavulanic acid	Monitor liver function in liver disease. Cholestatic jaundice reported either during or shortly after treatment; more common in patients over the age of 65 years and in males; duration of treatment should not usually exceed 14 days

Drug	Comment
Artemether + Lumefantrine	Caution in severe impairment; monitor ECG and plasma potassium
Azathioprine	May need dose reduction
Azithromycin	Avoid; jaundice reported
Bupivacaine	Avoid (or reduce dose) in severe liver disease
Carbamazepine	Metabolism impaired in advanced liver disease
Ceftriaxone	Reduce dose and monitor plasma concentration if both hepatic and severe renal impairment
Chloramphenicol	Avoid if possible—increased risk of bone-marrow depression; reduce dose and monitor plasma-chloramphenicol concentration
Chlorphenamine	Sedation inappropriate in severe liver disease—avoid
Chlorpromazine	Can precipitate coma; hepatotoxic
Ciclosporin	May need dose adjustment
Ciprofloxacin	Hepatic dysfunction reported
Clindamycin	Reduce dose
Clomifene	Avoid in severe liver disease
Clomipramine	Sedative effects increased (avoid in severe liver disease)
Clonazepam	Can precipitate coma
Cloxacillin	Cholestatic jaundice may occur up to several weeks after treatment has been stopped; administration for more than 2 weeks and increasing age are risk factors
Codeine	Avoid or reduce dose—may precipitate coma
Contraceptives, oral	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Cyclophosphamide	Reduce dose
Cytarabine	Reduce dose
Dacarbazine	Dose reduction may be required in mild to moderate liver disease; avoid if severe
Daunorubicin	Reduce dose
Diazepam	Can precipitate coma
Didanosine	Insufficient information but consider dose reduction
Doxorubicin	Reduce dose according to bilirubin concentration
Doxycycline	Avoid (or use with caution)
Efavirenz	In mild to moderate liver disease, monitor liver function; avoid in severe hepatic impairment
Enalapril	Closely monitor patients with impaired liver function
Ergometrine	Avoid in severe liver disease
Ergotamine	Avoid in severe liver disease—risk of toxicity increased
Erythromycin	May cause idiosyncratic hepatotoxicity
Ether, anaesthetic	Avoid
Ethinylestradiol	Avoid; *see also* Contraceptives, oral
Etoposide	Avoid in severe hepatic impairment
Fluconazole	Toxicity with related drugs
Fluorouracil	Caution advised
Fluphenazine	Can precipitate coma; hepatotoxic
Furosemide	Hypokalaemia may precipitate coma (use potassium-sparing diuretic to prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis
Glibenclamide	Increased risk of hypoglycaemia in severe liver disease; avoid or use small dose; can produce jaundice
Griseofulvin	Avoid in severe liver disease
Haloperidol	Can precipitate coma
Halothane	Avoid if history of unexplained pyrexia or jaundice following previous exposure to halothane
Heparin	Reduce dose in severe liver disease
Hydralazine	Reduce dose
Hydrochlorothiazide	Avoid in severe liver disease; hypokalaemia may precipitate coma (potassium-sparing diuretic can prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis

Drug	Comment
Ibuprofen	Increased risk of gastrointestinal bleeding and can cause fluid retention; avoid in severe liver disease
Indinavir	Reduce dose to 600 mg every 8 hours in mild to moderate hepatic impairment; not studied in severe impairment
Iopanoic acid	Avoid in severe hepatic disease
Isoniazid	Use with caution; monitor liver function regularly and particularly frequently in the first 2 months
Levonorgestrel	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Lidocaine	Avoid (or reduce dose) in severe liver disease
Lopinavir + Ritonavir	Avoid oral solution because of propylene glycol content; use capsules with caution in mild to moderate hepatic impairment and avoid in severe impairment
Magnesium hydroxide	Avoid in hepatic coma if risk of renal failure
Magnesium sulfate	Avoid in hepatic coma if risk of renal failure
Medroxyprogesterone	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Mefloquine	Avoid for prophylaxis in severe liver disease
Meglumine antimoniate	*see* Pentavalent antimony compounds
Mercaptopurine	May need dose reduction
Metformin	Withdraw if tissue hypoxia likely
Methotrexate	Dose-related toxicity—avoid in non-malignant conditions (for example, rheumatic disorders)
Methyldopa	Manufacturer advises caution in history of liver disease; avoid in active liver disease
Metoclopramide	Reduce dose
Metronidazole	In severe liver disease, reduce total daily dose to one-third and give once daily
Morphine	Avoid or reduce dose—may precipitate coma
Nalidixic acid	Hepatic dysfunction reported; partially conjugated in liver
Nelfinavir	No information available—manufacturer advises caution
Nevirapine	Caution in moderate hepatic impairment; avoid in severe hepatic impairment, *see also* section 9.5.2.2
Nifedipine	Reduce dose
Nitrofurantoin	Cholestatic jaundice and chronic active hepatitis reported
Norethisterone	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Ofloxacin	Hepatic dysfunction reported; reduce dose in severe liver disease
Paracetamol	Dose-related toxicity—avoid large doses
Pentavalent antimony compounds	Increased risk of liver damage and hepatic failure in pre-existing liver disease
Phenobarbital	May precipitate coma
Phenytoin	Reduce dose to avoid toxicity
Prednisolone	Adverse effects more common
Procainamide	Avoid or reduce dose
Procarbazine	Avoid in severe hepatic impairment
Promethazine	Avoid—may precipitate coma in severe liver disease; hepatotoxic
Propranolol	Reduce oral dose
Propylthiouracil	Reduce dose; *see also* section 10.2
Pyrazinamide	Avoid—idiosyncratic hepatotoxicity more common
Ranitidine	Increased risk of confusion; reduce dose
Rifampicin	Impaired elimination; may be increased risk of hepatotoxicity; avoid or do not exceed 8 mg/kg daily
Ritonavir	*See* Lopinavir + Ritonavir
Saquinavir	Plasma concentration possibly increased; manufacturer of gel-filled capsules advises caution in moderate hepatic impairment and avoid in severe impairment; manufacturer of capsules containing saquinavir mesilate advises caution in severe impairment
Sodium nitroprusside	Avoid in severe liver disease

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Drug	Comment
Sodium valproate	*see* Valproic acid
Sulfadiazine	Avoid if severe
Sulfamethoxazole + Trimethoprim	Manufacturer advises avoid in severe liver disease
Suxamethonium	Prolonged apnoea may occur in severe liver disease due to reduced hepatic synthesis of plasma cholinesterase
Testosterone	Preferably avoid—possibility of dose-related toxicity and fluid retention
Theophylline	Reduce dose
Thiopental	Reduce dose for induction in severe liver disease
Valproic acid	Avoid if possible—hepatotoxicity and hepatic failure may occasionally occur (usually in first 6 months)
Verapamil	Reduce oral dose
Vinblastine	Dose reduction may be necessary
Vincristine	Dose reduction may be necessary
Warfarin	Avoid in severe liver disease, especially if prothrombin time already prolonged
Zidovudine	Accumulation may occur

Appendix 6: Caution and advice to patients on the use of dispensed medicines

RETURN

S/No.	Recommended Label Wordings	Explanation
1.	**May cause drowsiness**	To be used on children's preparation containing antihistamines, e.g. paediatric elixirs and linctuses, or other preparations given to children where the warnings of label 2 on driving or alcohol would not be appropriate.
2.	**Warning. May cause drowsiness, if affected do not drive or operate machinery. Avoid alcoholic drink.**	To be used on preparations that can cause drowsiness, thereby affecting the ability to drive and operate hazardous machinery. The main preparations are most antihistamines; Central nervous system depressants such as anxiolytics, antipsychotics, and tricyclic antidepressants; some antihypertensives; some analgesics; some antiepileptics; some anti–emetics; and some relaxants.
3.	**Warning. May cause drowsiness if affected, do not drive or operate machinery**.	To be used on monoamine–oxidase inhibitors (because alcohol is covered by label 10 and MAOI treatment card).
4.	**Warning. Avoid alcoholic drink.**	To be used on preparations where a reaction such as flushing may occur if alcohol is taken, e.g. metronidazole and chlorpropamide.
5.	**Do not take indigestion remedies at the same time of the day as this medicine.**	To be used in conjunction with label 25 on preparations coated to resist gastric acid, such as enteric–coated tablets, capsules, and granules. The coating may be ruptured prematurely in the presence of alkalis present in antacids. Labels 5 also applies to drugs such as ciproflaxcin and ketoconazole where the absorption is significantly affected by antacids; the usual period of avoidance recommended is two to four hours.
6.	**Do not take iron preprations or indigestion remedies at the same time of day as this medicine.**	To be used on preparations of doxycycline, minocycline and penicillamine. These drugs chelate iron and calcium ions and are less well absorbed when given with iron or calcium–containing antacids. If necessary these incompatible preparations may be given about two hours apart.
7.	**Do not take milk, Iron preparation or indigestion remedies at the same time of day as this medicine**.	To be used on preparations of tetracycline, minocycline and penicillamine. These drugs chelate iron and calcium and magnesium ions and are then less well absorbed. If necessary these incompatible preparations may be given about 2 hours apart.

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8.	**Do not stop taking this medicine except on your doctor's advice.**	To be used on preparations of beta–adrenoceptor blocking drugs, certain antihypertensive drugs, drugs used in the treatment and prophylaxis of asthma, antituberculous drugs, and allopurinol. This label is used to encourage compliance where the drug is to be taken over long periods without the patient necessarily perceiving any benefit. Patient should however be encouraged to consult the prescriber if side–effects occurs.
9.	**Take at regular intervals. Complete the prescribed course unless otherwise directed.**	To be used on preparations where a course of treatment should be completed to reduce the incidence of relapse, the development of resistance, or failure of treatment. The preparations are antimicrobial drugs by mouth. The patient may need to be advised to stop the treatment quickly and report to the doctor if severe side effects occur. For example, the development of diarrhoea with clindamycin or lincomycin, or sensitivity reaction with the penicillins.
10.	**Warning. Follow the printed instructions you have been given with this medicine.**	To be used particularly on anticoagulant, MAOIs, and oral corticosteroids. The appropriate treatment card should be given to the patient and any necessary explanation given.
11.	**Avoid exposure of skin to direct sunlight or sun lamps**.	To be used on preparation that may cause phototoxic or photoallergic reactions if the patient is exposed to ultraviolet radiation. The drugs involved are amiodarone, azapropazone, demeclocycline, nalidixic acid and protriptyline.
12.	**Do not take remedies containing aspirin while taking this medicine**.	To be used on preparations containing salicylate derivatives, where it may not be known to the patient that the medicine has a similar action to aspirin, and on preparations containing the uricosuric drugs probenecid and sulphinpyrazone whose activity is reduced by aspirin.
13.	**Dissolve or mix with water before taking.**	To be used on preparations that are intended to be dissolved in water (e.g. soluble tablet) or mixed with water (e.g. powders, granules) before use.
14.	**This medicine may colour the urine or stools.**	To be used on preparation that may cause the patients urine to turn unusual colours. These include anthraquinones (alkaline urine red), phenolphthalein (alkaline urine pink), triamterene (blue), levodopa (dark reddish), phenazopyridine (reddish orange), and rifampicin (red). Iron preparations may colour the urine and stools black.
15.	**Caution flammable: Keep away from fire or flames.**	To be applied to preparations containing sufficient alcohol, acetone, ether, or other flammable solvent to render them flammable if exposed to a naked flame.
16.	**Allow to dissolve under the tongue. Do not transfer from**	To be used on glyceryl trinitrate tablets to remind the patient not to transfer the tablets to plastic or less

	this container. Keep tightly closed. Discard eight weeks after opening.	suitable containers.
17.	**Do not take more than ...in 24 hours**.	To be used on preparations for the treatment of acute migraine except those containing ergotamine, for which label 18 is used.
18.	**Do not take more than ... in 24 hours or ... in any one week**.	To be used on preparations of ergotamine tartrate. The number of tablets should correspond to 6 to 8mg in day and 10 to 12mg in a week.
19.	**Warning. Causes drowsiness which may persist the next day. If affected, do not drive or operate machinery. Avoid alcoholic drinking**.	To be used on hypnotics (e.g. nitrazepam) and anxiolytics (e.g diazepam) when prescribed to be taken at night. It is hoped that this wording will convey adequately the problem of residual morning sedation after taking sleeping tablets.
20.	**The omission of this label, according to BNF, is to accommodate any furture requirement within the series.**	
21.	**... with or after food**.	To be used on preparations that are liable to cause gastric irritation with nausea and vomitting or those that are better absorbed with food. Iron salts and their preparations are usually best absorbed when given on an empty stomach but may then cause irritation. They are therefore often taken with a meal.
22.	**... half to one hour before food**.	To be used on drugs whose absorption or local effect is improved when so taken, e.g. anticholinergic or antacid preparations; some pancreatin and other enzyme preparations, most appetite suppresants; etc.
23.	**... an hour before food or on an empty stomach**	To be used on some oral antibiotics, e.g. ampicillin whose absorption may be reduced by the presence of food and acid in the stomach.
24.	**... sucked or chewed**.	Certain preparations must be chewed before swallowing to impove their absorption or because of their size; others have been specially formulated to be chewed. All pastiles and lozenges should be sucked slowly to aid their local effect on the oropharynx.
25.	**... swallowed whole, not chewed**.	To be used on preparations designed for modified release; on certain preparations that are very unpleasant or may damage the mouth or oesophagus if not swallowed whole; and with label 5 for enteric coated preparations. Most sustained–release preparations rely on the coating of pellets, granules, tablets or capsules or compression in a matrix material to achieve their effect. Chewing can cause premature release of active ingredient.
26.	**... dissolved under the tongue**.	To be used on preparations intended for sublingual use. Several drugs are absorbed into the circulation more effectively from the mucosa of the mouth,

		thereby avoiding the portal circulation into the liver. Patients should be advised to hold the tablet still under the tongue and avoid swallowing until the tablet is dissolved. The buccal mucosa between the gum and cheek is occassionally recommended.
27.	**... with plenty of water.**	To be used on preparations that should be well diluted (e.g. chloral hydrate), where a high fluid intake is required (e.g. Sulphonamides), or where water is required to aid the action of the preparation (e.g. methylcellulose). The patient should be advised that plenty means at least 150ml (about a tumblerful). In most cases a beverage such as fruit juice, tea, or coffee could be used. There have been reports of solid–dose preparations sticking in the oesophagus, particularly in the elderly, and all patients should be reminded of the necessity of taking capsules and tablets with water or other liquid. As much as 100ml may be required and the patient should stand or sit while taking the dose.
28.	**To be applied sparingly...**	To be used with external corticosteroid preparations and dithranol preparations. The application of excessive quantities to the skin can increase the incidence of local side–effects and give rise to undesirable systemic effects.
29.	**Do not take more than 2 at any one time. Do not take more than 8 in 24 hours.**	To be used on containers of dispensed solid dose preparations containing paracetamol for adults. This label has been introduced because of the serious consequences of overdosage with paracetamol.

(Adapted from British National Formulary (BNF) with written permission from the Joint Formulary Committee)

Appendix 7: Abbreviations

RETURN

a	Arterial blood
a	before
aa	of each
AB	abortion
abd	Abdomen
ABGs	Arterial blood gases
ABO	Three main blood types
AC	Air conduction
ac	Before meal (ante cibum)
ACE	Angiotensin-converting enzyme
Accom	Accommodation
ACh	Acetylcholine
AchE	Acethylcholin esterase
ACTH	Adrenocorticotrpic hormone
ACVD	Arteriosclerotic cardiovascular disease
AD	Right ear (auris dextra)
ad lib	As desired
ADH	Antidiuretic hormone
ADP	Adenosine diphosphate
AF	Arterial Fibrillation
AFB	Acid–fast bacillus
AHF	Antihaemophic factor
AI	Aortic insufficiency
AKA	Above–knee amputation
ALL	Acute lymphocytic leukemia
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase (liver and heart enzyme); formerly SGPT
a.m.	Morning (ante meridien)
AMA	against medical advice
amb	ambulation
AML	Acute myelocytic (myelogenous leukemia
AMP	Adenosine monophosphate
amp	Ampule, ampere
ANA	antinuclear antibodies
ant	anterior
AP	Anteroposterior and percussion
A&P	Auscultation and percussion
APTT	activated partial thromboplastin time
Aq	Water (aqua)
AR	Assisted respiration
ara–C	Cytosine arabinoside
ARDS	Acute respiratory distress syndrome
AROM	active range of motion
AS	Left ear (auris sinistra); aortic stenosis
ASA	acetylsalicylic acid (aspirin)
ASAP	as soon as possible
ASD	Atrial Septal Defect
ASH	Asymmetrical septal hypertrophy
ASHD	Arteriosclerotic heart disease
AST	Asparate aminotransferase (liver and heart enzyme); formerly SGOT
Astigm	Astigmatism
ASV	Anti-snake venom
ATP	Adenosine triphosphate
Au	Gold
Ausc	Auscultation
A–V	Arteriovenous, atrioventricular
AVR	Aortic Valve replacement
Ba	Barium
BaE	Barium eneme
BAL	blood alcohol level
b.b.a	Born before arrival
BBB	Blood brain barrier
BC	Bone conduction
B–Cells	Lymphocytes produced in the bone marrow
BCG	Bacille Calmette–Guerin
BCNU	Bischloroethylnitrosourea
b.d	Twice a day (bis in die)
BE	Barium enema
b.i.d	Twice a day (bis in die)
BM	bowel movement
BMR	Basal metabolic rate
BNF	British National Formulary
BO	Blood pressure
B/P	blood pressure
BPH	Benign prostatic hypertrophy
bpm	beats per minute
BS	blood sugar
BSP	Bromsulphalein (dye used in liver function test; its retention is indicative of liver damage or disease).
BT	Bleeding time
BUN	Blood Urea Nitrogen
BZO	Benzodiazepine
Bx	Biopsy
c	With (cum)
C	Celsius (centigrade)
C–1,C–2	First, second cervical vertebra
C.A.	Chronological age
Ca	Calcium; cancer
CAD	Coronary artery disease

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cap	capsule
Ca	cancer
cath	catheterization or catheterize
CBC,c.b.c	Complete blood count
cc	Cubic centimeter (1/100 litre)
CC	chief complaint
CD	Controlled drug
Chem	Chemotherapy
CHF	Congestive heart failure
chr	Chronic
Ci	Microcurie
Cigl	Correction with glasses
CK	Creatine kinase
Cl	Chlorine
CLL	Chronic lymphocytic leukemia
cm	centimeter
CMF	Cytoxan, methotrexate, and 5-fluorouracil
CML	Chronic myelocytic (myelogenous) leukemia
CMV	Cytomegalovirus
CNS	Central nervous system
Co	Cobalt
CO_2	carbon dioxide
c/o	complains of
CONT	continuous
COP	Cytoxan, Oncovin, and prednisone (antineoplastic drug given in combination chemotherapy)
COPD	Chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPC	Clinicopathological conference
CPK	Creatinine phosphokinase (enzyme released into blood following injury to heart or skeletal muscles)
CPR	Cardiopulmonary resuscitation
CPZ	Chlorpromazine
CrCl	creatinine clearance
CRF	Chronic renal failure
CS	Ceasarean section
C&S	culture and sensitivity
C–Section	Ceasarean section
CSF	Cerebrospinal fluid
ct.	Count
CV	cardiovascular
CVA	Cerebrovascular accident
CVP	central venous pressure
CVP	Cytoxan, vincristine and prednisone (antineoplastic drugs given in combination chemotherapy)
CVS	Cardiovascular system
C/W	Compare with
CXR	Chest x–ray
cyl.	Cylindrical lens
cysto	Cystoscopy
D & C	Dilatation and curettage
DD	Discharge diagnosis
decub	Lying down
DES	Diethylstilboestrol
DI	Diabetes insipidus; diagnostic imaging
diff	Differential count (white blood cells)
DIR INF	direct infusion
DLE	Discoid lupus erythematosus
DM	Diabetes mellitus
DNA	Deoxyribonucleic acid
DOA	dead on arrival
DOB	Date of birth
DOE	Dyspnea on exertion
dr	dram
dsg	dressing
DT's	Delirium tremens
DTR	Deep tendon reflexes
D_5W	5% glucose in distilled water
Dx	Diagnosis
e	Without
EBV	Epstein–Barr virus
e–c	Enteric–coated
ECF	Extended–care facility
ECG (EKG)	Electrocardiogram
EDC	Expected date of confinement
EDD	Expected date of delivery
EDL	Essential drug list
EDTA	ethylenediamine tetraacetic acid
EEG	Electroencephalogram
EENT	ear, eye, nose, and throat
EM	Electron microscope
Em	Emmethropia
EMDEX	Index of Essential Medicines
EMG	Electromyogram
ENT.	Ear, nose, and throat
eos	Eosinophils
EPS	extrapyrimidal symptoms
ER	Emergency room; estrogen receptor
ESR	Erythrocyte Sedimentation Rate
et	and
ETF	Eustachian tube function
EUA	Examination under anaesthesia
exc.	Excision
F	Fahrenheit

Fb	Fingerbreadth
FBC	full blood count
FBS	Fasting blood sugar
f–c	Film coated
FDA	Food and Drug Administration
Fe	Iron
FH	Family history
FHT	Fetal heart tones
Flo_2	inspired oxygen concentration
FSH	Follicle–stimulating hormone
FTA–ABS	Fluorescent treponemal antibody absorption test
F/u	Follow–up
5–Fu	5–Fluorouracil
FUO	Fever of undetermined origin
fx	fracture
g	gram
Ga	Gallium
GABA	γ–amino butyric acid
gal	gallon
GB	Gall blader
GC	Gonorrhoea
GFR	Glomerular filtration rate
GH	Growth hormone
GI	Gastrointestinal
Gm,gm	Gram
gr	Grain(s)
Grav, 123	First, second, third pregnancy
GTT	Glucose tolerance test
gtt	Drops (Guttae)
GU	Genitourinary
Gyn	Gyneacology
H	Hydrogen; hypodormically
Hb (Hgb)	Haemoglobin
H & H	hematocrit and hemoglobin
HbIG	Hepatitis B Immuno globulin
HCG(hCG)	Human choronic gonadotropin
HCT(Hct)	Haematocrit
HD	Hearing distance
HD	Hodgkin s disease
h.d	At bedtime (hora decubitus)
HDCV	human diploid cell rabies vaccine
HDL	High density lipoproteins
He	Helium
Hg	Mercury
Hgb	hemoglobin
hGH	Human growth hormone
5-HIAA	5-hydroxyindoleacetic acid
h/o	History of
H_2O	water
HOB	head of bed
HR	heart rate
h.p.f	High power field (microscope)
HR	heart rate
hr	hour
hs	At bedtime (hora somni)
HSG	Hysterosalpingography
h–s megaly	Hepatosplenomegaly
HVD	Hypertensive vascular disease
HVS	High Vaginal Swab
hx	History
I	Iodine
IADH	Inappropriate antidiuretic hormone
ICP	Intracranial pressure
ICU	Intensive care unit
IgA, IgD, IgG	Immunoglobulins
IM	Intramuscular (injection)
inf.	Infusion; inferior
INH	inhalation
INH	Isoniazid (drug used to treat tuberculosis)
Inj.	Injection
I&O	intake and output
INT	intermittent
I.O.P	Intra–Ocular Pressure
IPPB	Intermittent postive–pressure breathing
I.Q	Intelligence quotient
ITP	idiopathic thrombocytopenic purpura
I.U.	International Unit
I.U.C.D	Intrauterine Contraceptive Device
IUD	Intrauterine device; intrauterine death
IV (i.v)	Intravenous (injection)
IVAC	intravenous controller
IVP	Intravenous pyelogram
IVPB	intravenous piggyback
k	Potassium
Kg	kilogram
KUD	Kidney, ureter, and bladder (Abdominal x–ray)
L	Liter, left, lower
L–1,L–2	First, second lumber vertebra
LA	Left Atrium
lap	Laparotomy
LAT (lat)	Lateral
LB	Large bowel
Ib	pound
LBW	Low birth weight
LCM	Left costal margin
LD (LDH)	Lactic dehydrogenase
LDL	Low density lipoproteins
LE	Lupus erythematosus
LFT	Liver function test
LH	Luteinizing hormone
liq	liquid
LLL	Left lower lobe

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LLQ	Left lower quadrant (abdomen)
LMP	Last menstrual period
LN, ln	Lymph node
LOC	loss of consciousness
LP	Lumbar puncture
l.p.f	Lower power field
LR	lactated Ringer's solution
LSD	Lysergic acid diethylamide
LSK	Livert, spleen, and kidneys
LTH	Prolactin
LUL	Left upper lobe (lungs)
LUQ	Left upper quadrant (abdomen)
LV	Left ventricle
L&W	Living and well
lymph	Lymphocyte
m	minim
M	Monocytes; meter
m_2	square meter
MAC	monitored anaesthesia care
M.A	Mental age
MAOI	Monoamine Oxidase inhibitor
MAP	Mean arterial pressure
mc	Millcure (dose of radiation)
MCA	motorcycle accident
MCH	Mean corpuscular haemoglobin (amount of haemoglobin per unit of blood
mCi	Millicure
MCL	Midclavicular line
MCV	Mean corpuscular volume (measurement of size on individual red cell)
M/C/S	Microscopy, culture and sensitivity
mEq/L	Milliequivalent per liter (measurement of the concentration of a solution)
mets	Metastases
mg	milligram
mcg	microgram
MH	Marital history
MI	Myocardial infraction; mitral insufficiency
min	minute
mixt	mixture
ml	milliliter
mm	millimeter
mm Hg	Millimeters of mercury
mo	month
6–MP	6–mercaptopurine (antineoplastic drug)
MPD	Maximum permiseable dose
mRNA	Messenger RNA
MS	Mitral stenosis; multiple sclerosis; morphine sulfate
MSL	Midsternal line
MTX	Methotrexate
MVA	motorvehicle accident
MVP	Mitral valve prolapse
MVR	Mitral valve replacement
Myop	Myopia
N	Nitrogen; Node; Normal
Na	Sodium
NANB	Non–A, Non–B hepatits
NB	Newborn
NBS	Normal bowel or breath sounds
NC	nasal cannula
NED	No evidence of disease
neg	negative
NERD	No evidence of recurrent disease
N.F	National Formulary
NG	Nasogastric tube
NKA	no known allergies
noc	night
NOS	Not otherwise specified
NPDL	Nodular, poorly differentiated lymphocytes
NPI	National programme on immunisation
NPO	Nothing by mouth (nulla per os)
NS	normal saline
NTP	Normal temperature and pressure
NV	neurovascular
O_2	Oxygen
OB	Obstetrics
OBS	organic brain syndrome
OCG	Oral Cholecystogram
OD	Right eye (oculus dexter)
17–OH	17–Hydroxycorticosteroids
OOB	out of bed
OR	Operating room
ORIF	open reduction, internal fixation
os	mouth
OS	Left eye (oculus sinister)
OT	Old tuberculin; occupational therapy
OTC	Over the counter
Oto	Otology
OU	Each eye (oculus uterque)
OV	Office visit
oz	Ounce
P	Phosphorus; pulse
p	after
P56	plasma-lyte 56
PA	Posteroanterior
P&A	Percussion and ausculation
PAC	Premature atrial contractions
$PaCO_2$	arterial carbon dioxide

	tension (pressure)
palp	Palpable; palpation
PaO_2	arterial oxygen tension (pressure)
Pap smear	Papanicolaou smear
para 1,2,3	Unipara, bipara, tripara (number of viable births)
PAT	Paroxysmal atrial tachycardia
Path	Pathology
PA view	Posteroanterior view (x–ray position)
PBI	Protein–bound iodine
pc	After meals (post cibum)
PCN	penicillin
PCO_2	Carbon dioxide pressure
PCV	Packed cell volume
PCWP	Pulmonary capillary wedge
pressure	
PDA	Patent ductus arteriosus
PDR	Physicians' Desk Reference
PE	Physical Examination
PEEP	positive end expiratory pressure
PE tube	Ventilating tube for eardrum
PEG	Pneumoencephalography
PERRLA	pupils equal, round, react to light and accommodation
PFT	Pulmonary function test
PG	Prostaglandin
pH	Hydrogen ion concentration (alkalinity and acidity measurement)
PID	Pelvic inflammatory disease
PKU	Phenylketonuria
plts	Platelets
PM	Post mortem; petit mal; after noon (post meridian)
PMI	point of maximum impulse
PMN	Polymorphonu clear leukocytes
PMT	Premenstrual tension
PND	Paroxysmal nocturnal dyspnoea
PO	by mouth
p/o	Postoperative
postop	Postoperative
po	Orally (per os)
PO_2	Oxygen pressure
polys	Polymorphonuclear leukocytes
POM	Prescription only Medicine
POMP	Prednisone, Oncovin, methotrexate, and 6–mercaptopurine (combination chemotherapy)
pos	Positive
postop	postoperatively
PP	Postprandia (after meals)
PPD	Purified protein derivative (test for tuberculosis)
pre–op	Preoperative
prep	preparation
PRL	Prolactin
p.r.n	As required (pro re nata)
Pro-time	Prothrombin time (test of blood clotting)
PSP	Phenylsulfonaphthalein (dye test for kidney impairment)
PT	Prothrombin time, physical
therapy	
pt	Patient
PTA	Prior to admision
PTH	Parathyroid hormone
PTT	Partial thromboplastin time
PU	Pregnancy urine
PUD	Peptic ulcer disease
PUO	Pyrexia of undetermined origin
PVC	Premature ventricular contractions
pwd	powder
q	every
qAM	every morning
qod	every other day
qPM	every night
q.d	Every day (quaque die)
q.h	Every hour (quaque hora)
q.i.d	Four times daily (quater in die)
q.n.s	Quantity not sufficient
q.s	Sufficient quantity (quantum sufficiat)
qt	quart
q2h	every 2 hours
q3h	every 3 hours
q4h	every 4 hours
q6h	every 6 hours
q12h	every 12 hours
R	respirations, rectal
r	right
RA	Rheumatoid arthritis;right atrium
Ra	Radium
rad	Radiation absorbed dose
RAI	Radioactive iodine
RAIU	Radioactive iodine uptake
Ratx	Radiation therapy
RBC	Red blood cell (corpuscle); red blood count
RCM	Right costal margin
RECT	rectal
REM	rapid eye movement
RF	Rheumatoid factor
Rh	Rhesus (monkey) factor in

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	blood
RIA	Radioimmunoassay
RLL	Right lower lobe (lung)
RLQ	Right lower quadrant (abdomen)
RNA	Ribonucleic acid
R/O	Rule out
ROM	range of motion
ROS	Review of Systems
RP	Retrograde pyelogram
RT	Radiation therapy
RUQ	Right upper quadrant (abdomen)
RV	Right ventricle
Rx	Treatment; therapy; prescription.
s.	Without (sine)
S–1,S–2	First, second sacral vertebra
S–A	Sinoatrial
SAN	sinoatrial node
SBE	Subacute bacterila
endocarditis	
SBFT	Small bowel follow-through (x-ray study)
SC	subcutaneous
S–C	Sugar coated
Sed–rate	Sedimentation rate (rate of blood sedimentation)
s,gl	Without correction (glasses)
SGOT	Serum glutamic oxaloacetic transminase
SH	Serum hapatitis
sig	label
SIMV	synchronous intermittent mandatory ventilation
SL	sublingual
SLE	Systematic lupus erythematous
SOB	Shorthess of breath
sol.	Solution
S.O.S	When necessary (su opus sit)
S/P	Status post (refers to previous disease condition)
sp.gr.	Specific gravity
SPE	Serum protein Electrophoresis
SR	Sedimentation rate
Sr	Strontium
s/r	Sustained release
ss	one half
st	Stage (of disease)
Staph.	Staphylococcus
stat.	Immediately (statim)
STH,	Somatotropin (growth) hormone
Strep.	Streptococcus
S.T.S	Serological test for syphilis
Subcu.	Subcutaneous
surg	surgical
supp	suppository
SV–40	Simian vacuolating virus
SVC	Superior vena cava
Sx	Symptoms
syr	syrup
T	Temperature
T–1,T–2	First, second thoracic vertebra
T3	Triodothyronine
T4	Thyroxine
T&A	Tonsillectomy and adenoidectomy
tab	Tablet
TAH	Total abdominal hysterectomy
TAT	Thematic Apperception Test
TB; tbc	Tuberculosis
TBI	Total–body irradiation
tbsp	tablespoon
Tc	Technetium
T–cell	Lymphocytes produced in the thymus gland
temp	temperature
TIA	Transient ischemic attack
t.i.d	Three times daily (ter in die)
tinc	tincture
TNI	total nodal irradiation
TNM	Turmor, nodes and metastases
tomos	Tomograms
TOP	Termination of Pregnancy
top	topical
TPI	Treponema pallipidum immobilisation (test of syphilis)
TPN	total parenteral nutrition
TPR	Temperature, pulse, and respiration
TRH	Thyrotropin-releasing hormone
TSH	Thyroid-stimulating hormone
tsp	teaspoon
TT	thrombin time
TUR	Transurethral resection (for
prostatectomy)	
Tx	Treatment
U	Unit
UA	Urinalysis
UC	Uterine contractions
UGI	Upper gastrointestinal series
umb	Navel (umbilicus)
ung	Ointment
Ur	Urine
URI	Upper respiratory infection
Urol	Urology
u/s	Ultrasound
U.S.P	United States Pharmacopeia
UTI	Urinary tract infection

UV	ultraviolet
VA	Visual acuity
vag	vaginal
VCU	Voiding cystourethogram
VD	Veneral disease
VDRL	Veneral Disease Research Laboratory (an antibody test for syphilis)
VF	Visual field
VLDL	Very low density lipoproteins
VMA	vanillylmandelic acid
VO	verbal order
vol	volume
VS	vital signs
WBC	White blood cell; white blood count
W–E	Wide excision
wk	week
w/n	Well nourished
WMF	WHO Model Formulary
WNL	within normal limits
wt	weight
y/o	Year old
yr	year
>	greater than
<	less than
=	equal
≠	not equal
↑	increase
↓	decrease
2°	secondary
°	degree
%	percent
@	at
α	alpha
β	beta
γ	gamma

Appendix 8: Guide to drug administration

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1. Introduction
2. Guidelines for safe and effective administration of medications
3. The seven "Rights" of drug administration
4. Documentation of drug administration
5. Calculation of dosages
6. Understanding the various routes of drug administration
7. Other routes of drug administration

1. Introduction

Safe and effective administration of drugs to patients require that caregivers, particularly the nurses, should know the right procedures, precautions and techniques. This is because a potentially dangerous error can occur with each route of administration.

The following Appendix 8 offers step-by-step instructions and practical guidelines on safe and effective drug administration. All major routes of administration are covered namely gastrointestinal, dermatomucosal, respiratory, ophthalmic, otic, nasal, laryngeal and parenteral.

Guide to Drug Administration for Nurses is intended as a dictionary of sorts on drug administration for nurses and other caregivers in all clinical settings.

Understanding drugs and how they work

Definitions:

A **drug substance** is the active ingredient or component that produces pharmacologic activity.

A **drug product** is the finished dosage form (e.g., tablet, capsule, ointment) that contains the active drug substance, generally in association with non-drug (usually inactive) ingredients (excipents) that make up the vehicle, or formulation matrix.

Biopharmaceutics is the study of the relation of the physical and chemical properties of a drug to its bioavailability, pharmacokinetics, and pharmacodynamic and toxicologic effects.

Bioavailability is the fraction of an administered dose that reaches the systemic circulation. It is a measure of the Rate and Extent of absorption.

Volume of distribution is the amount of drug in the body relative to the concentration of drug in the blood (or plasma).

$$V_D = D/C_P$$

where V_D is the apparent volume of distribution, D is the drug dose, and C_P is the plasma concentration of the drug.

Half-life is the time required for the drug concentration in the plasma to be reduced by 50%, provided no drug absorption occurs during the decline. Half-life is also a measure of the time required for the drug concentration in the plasma to reach a steady-state concentration with a new dosing regimen.

Steady-state concentration is the drug concentration at which body is in equilibrium (i.e., the rates of drug absorption and elimination are equal).

Loading dose is the amount of drug that must be administered to bring concentration in the blood (or plasma) into the therapeutic range rapidly when initiating therapy or when increasing the dosing rate after a subtherapeutic dosing.

Maintenance dose is the amount of drug that must be regularly administered to maintain a steady-state concentration.

Dosing interval is the amount of time between consecutive doses of a regularly administered drug. This is usually a multiple of 24 hours or a number that is easily divided into 24 hours.

Pharmacokinetics is the study of the time course of drug movement in the body during absorption, distribution, and elimination (excretion and biotransformation).

Pharmacodynamics is the study of the relation of the drug concentration or amount at the site of action (receptor) and its pharmacologic response.

How drugs work:

On administration to the body, a drug undergoes through the processes of absorption, distribution, metabolism and excretion.

RETURN

Absorption is the transport of drug molecules across cell membranes from the site of administration into the bloodstream. Common sites of drug administration include the mucosa, the GI tract, parenteral administration sites, the respiratory and the skin.

Distribution occurs when a drug binds to plasma protein in the blood and is transported via the circulation to all parts of the body, crossing cell membranes and entering body tissues.

Drugs distribute rapidly to tissues with high blood flow and more slowly to tissues with low blood flow.

Drugs cross capillary membranes into tissues in varying degrees. Drugs easily cross the capillaries of the glomerulus of the kidney and the sinusoids of the liver. The capillaries of the brain are surrounded by glial cells that create a blood- brain barrier (BBB) that acts as a thick lipid membrane. Polar and ionic hydrophilic drugs cross this barrier slowly.

Drugs may accumulate in tissues as a result of their physicochemical characteristics or special affinity of the tissue for the drug. Lipid-soluble drugs may accumulate in adipose (fat) tissue because of partitioning of the drug. Tetracycline may accumulate in bone because complexes are formed with calcium.

Plasma protein binding of drugs affects drug distribution. A drug bound to a protein forms a complex that is too large to cross cell membranes. Albumin is the major plasma protein involved in drug protein binding. Potent drugs, such as phenytoin, that are highly bound (more than 90%) to plasma proteins, may be displaced by other highly bound drugs. The displacement of the bound drug results in more free (nonbound) drug, which rapidly reaches the drug receptors and causes a more intense pharmacologic response.

Drug **metabolism** (also called **biotransformation**) refers to the biochemical changes that drugs and other foreign chemicals (xenobiotics) undergo in the body, leading to the formation of different metabolites with different effects. Major site of metabolism is in the liver. Metabolites may be **inactive** e.g. oxidation of 6-mercaptopurine to 6-mercaptopuric acid which has no anticancer activity; **active** e.g. imipramine is demethylated to the essentially equiactive antidepressant, desipramine. Some pharmacologically inactive parent compounds (also known as **prodrugs**) are converted to active species (bioactivated metabolites) within the body. For example, the prodrug enalapril is hydrolyzed to enalaprilat, a potent antihypertensive; sulindac, a sulfoxide, is reduced to the active sulfide; antiparkinsonian levodopa is decarboxylated in the neuron to active dopamine.

Extrahepatic metabolism refers to drug biotransformation that takes place in tissues other than the liver. The most common sites include the portals of entry (e.g., GI mucosa, nasal passages, and the lungs) and the portals of excretion (e.g., kidneys). However, metabolism can occur throughout the body.

Urinary excretion: Most drugs are removed by the kidneys, either as unchanged drug or as metabolites; therefore, renal function greatly influences drug concentration.

Biliary and faecal excretion: Some drugs undergo biliary excretion and enterohepatic recycling. These drugs may be eliminated in the faeces, even though they were administered intravenously. Several **other minor routes** of drug elimination exist. Some volatile anaesthetics (e.g., halothane) are eliminated primarily on exhalation. A few drugs are eliminated through perspiration, saliva, tears, and breast milk.

Factors that influence drug action include age, body size and sex. Hepatic and renal functions are altered by age extremes (immature function in neonates, and diminished function in the elderly). Such patients usually require reduced dosages. Patients who are above or below average size require dosage adjustments based on the body weight. Women of childbearing age must avoid taking drugs that would be harmful to a foetus because most foetal damages occur before pregnancy is identified.

2. Guidelines for safe and effective administration of medications

- Be sure that you have a clear, written order for each drug administered; question orders you consider incorrect. The physician's order should include the name of the medication, the dosage, and the method and frequency of administration. The order may include additional directions, e.g. "withhold dosage if the pulse is below 60". In an emergency, you can use a correctly documented verbal order.
- Nurses must concentrate on the task to avoid errors while preparing and administering medications.
- To prevent an error when preparing medications, you should read the label on the container three times: before taking it off the shelf, while pouring the medication and after placing it back on the shelf.
- Do not administer medication taken from an unlabeled or illegibly labeled container.
- The medicine cupboard or shelf must be properly arranged. Look-alike medications must be

separated and toxic chemicals must be separated from the rest of the medications. Store medications out of reach of patients. Discard all outdated drugs.

- Medications that are cloudy or discoloured, that have unusual smell or contain any precipitate (for liquids) should be returned to the pharmacy. Write the reason for such return on their label.
- Nurses should always use the seven "rights" system to check the dispensed medication against the patient's medication card: right drug, right dose, right patient, right time, right route and the patient's right to know about his medication as well as his right to refuse his medication or I.V. therapy.
  Medications that are refused must be discarded after reporting to the physician, and reason for refusal should be recorded.
- Read and follow all the necessary precautions for administering the medication. Nursing units should have Drug Reference books.
- Before administering a medication, identify the patient correctly and carefully using the appropriate means of identification. Don't just rely on calling the patient's name because a patient who is not fully alert may answer yes without realizing what he is saying.
- Do not administer medication prepared by someone else (except for unit dose forms prepared by a pharmacist). If the medication were prepared incorrectly, you would be equally responsible for the error.
- For parenteral medications, use only accepted injection sites; aspirate before giving an I.M. injection; choose and use the right length of needle.
- Never return an unused portion of medication to a stock bottle to avoid returning a drug to the wrong container or contaminating the drug in the stock bottle.
- Provide the correct adjunctive nursing measures with the medication, e.g. provide safety measures (i.e., side rails, night light and call button) and supervise ambulation for patients on sedatives and hypnotics.
- Always watch patient swallow a medication rather than leave it at the bedside for him to take later. Some patients may forget; some may discard it because of the unpleasant taste; others may save it in an attempt to commit suicide. If a patient is not on the bed, do not leave medication on his bedside; return the medication to the cupboard with proper labeling so that other caregivers can identify the owner easily.
- Medications should not be left at the bedside, with the exception of antacids, non-narcotic cough syrups, lotions or ointment and inhalants. This depends on the hospital; make sure you check the hospital policy. When medications are left at the bedside, determine from the patient when he takes or applies them.
- Give medications within 30 minutes of the time ordered, except for preoperative medications, which must be given hourly or every 2 hours (e.g., eye medications prior to surgery).
- If a patient vomits after taking an oral medication, report the incidence to the responsible nurse and state the names of all medications given. Withhold further medications. Often, the physician reorders the same drug by a different route, e.g. intramuscularly.
- Special precautions must be observed for certain drugs. In most hospitals, two qualified nurses must double-check the dosages of controlled drugs or schedule IV drugs, insulin, digitalis and anticoagulants
- Document all drug administration as soon as you have completed it to prevent accidental repetition of the dose by another caregiver. The record should include the name of the drug, the dosage, the time and method of administration and any related data.
- Evaluate the effectiveness of the medication at a suitable time after its administration, e.g. the effectiveness of an I.M. analgesic can be evaluated 10-20 minutes after administration.
- When medications are intentionally omitted, e.g. before surgery or a diagnostic test, record the omission and the reason on the patient's chart. Notify the physician.
- Medication errors sometimes occur. When an error is made, report it immediately to the responsible nurse so that corrective measures can be implemented promptly. Errors are usually documented in an "Unusual Incident Form" that becomes a part of the hospital file.

3. The seven "Rights" of drug administration

Traditionally, the basic rules for safe medication administration include five "rights" namely the right drug, the right dose, the right route of administration, the right time, and the right patient. The sixth "right" is that the patient should know the reason why he is receiving medication and what effects to expect. The seventh "right" is the refusal of medication or I.V. therapy by patient.

* **The right drug**: Always check the name of the medication against the doctor's prescription. If the physician's order is unclear, clarify it to avoid error. Read the label of the medication three times:
  a) When you select the drug,
  b) When you pour the drug or remove the tablet from the container and
  c) When you return the bottle to the shelf or medicine cupboard.
* **The right dose**: Make sure the dispensed dose is the same as the ordered dose. Some medications are so strong that they may be toxic if given in even slightly wrong dosage. It is better to double-check the dosage with another nurse before administration.
* **The right route**: Ensure that the correct route is used by looking one more time at the prescription. There are various forms of medications for different routes and they are not interchangeable.
* **The right time**: Recheck the prescription to make sure you have the correct time and frequency of administration. You should read and follow the

various cautions and advice to patients on the use of dispensed medications (e.g., some medications should be given with or after food). You should be able to differentiate between orders such as q4h and q.i.d., the former means every 4 hours while the later means 4 times daily or every 6 hours. Medications must be given on time so that a therapeutic blood level is maintained. If given too early, an excessive drug level may be reached and when given too late, effects may be inadequate. Medications should be given within 30 minutes of the specified time (e.g., a 2:00 pm medication should be given between 1:30 pm and 2:30 pm).

* **The right name**: Always check the name of the patient on the prescription. Do not use the name tag on a bed or on the door. A patient may be sitting on the wrong bed or may have been transferred without your knowledge. Don't rely on asking patient, for instance, " Are you Mr. Jones?" He may answer incorrectly under strain or stress. You can verify with another nurse. Be extremely careful when two patients in a nursing unit have the same name.
* **The patient's right to know**: Patient should be informed about what drugs he is receiving and what effects to expect. Such knowledge can enhance his compliance and cooperation with the treatment schedule. When administering drugs, educate the patient on their purpose by a statement such as "This is an expectorant, it will make you cough more effectively".
* **The patient's right to refuse medication or I.V. therapy**: Never force a patient to take medication. If a patient refuses his medication, try to find out why. In most cases, it may be due to lack of information about the drug's purpose. After you have explained what the medication is and its purpose, the patient will usually take the dose. Some patients do refuse their medication because a tablet or capsule is difficult to swallow or a liquid that tastes bitter; crushing the tablet or opening the capsule and taking it with milk or juice can solve the problem. Never crush or open coated tablets or capsules or hard capsules.
* The patient may still refuse his medications after all your explanation; report this to the responsible nurse and the physician, and record the reason for refusal. Discard the medication accordingly.

4. Documentation of drug administration

All data pertaining to drug administration must be recorded. All drugs, their doses, route of administration and the exact time of administration must be recorded in the chart. This serves three purposes:

a) The chart is a legal document.
b) It helps in establishing the relationship between drug and symptoms of adverse reactions.
c) Time of drug administration influences its effect. For best results the right drug must be given in right dosage by the correct route at the right time.

A medication card should contain the following basic information:

a) The patient's name and room number.
b) The date.
c) The name of the medication.
d) Dosage.
e) Route, frequency, and time of administration.
f) Name of the nurse and title.
g) Name of the physician in charge of the patient.

When administering a drug by the parenteral route, always record the injection site for ease of site rotation.

Avoid writing abbreviations or numbers in a way that might be confusing, for instance, abbreviating "unit" to "U", which may be misread as a poorly written zero. Always write doses with fractions clearly, for instance, **0.20 mg** digoxin should not be written as **.20 mg**, which may be misread as **20 mg** digoxin.

After giving a medication, document it as soon as possible. If a drug was ordered but not given, record it in the medication card and state the reason.

5. Calculation of dosages

It is an important aspect of drug administration in the sense that there might be need to calculate dosages because drugs may be dispensed from pharmacy in grams when the order specifies milligrams, or they are dispensed in milligrams but ordered in micrograms. There are two systems of measurement currently in use: **Metric** and **Apothecary**. To calculate dosages, you must be familiar with both. At home, people make measurements with household equipments such as the spoons. Nurses should therefore be familiar with household equipments so as to be able to instruct clients. In all situations, it is the duty of a nurse to convert units of measure or weight and thus nurses must be aware of approximate equivalents within each system of measurement and among systems.

Converting weights within the metric systems

It is relatively simple to arrive at equivalent units of weight within the metric system, since the system is based on units of ten. Only three metric units of weight are used for drug dosages: the gram (g), milligram (mg) and microgram (mcg). 1000 mg or 1,000,000 mcg equals 1 g. Equivalents are computed by dividing or multiplying, e.g. to change milligrams to grams, milligrams are divided by 1000. The simplest way to divide by 1000 is to move the decimal point three places to the left.

1000 mg = 1 g
500 mg = 0.5 g

To convert grams to milligrams, the grams are multiplied by 1000, or the decimal point is moved 3 places to the right.

0.006 g = 6 mg

Metric	Apothecaries	Household
1 ml =	15 minims	15 drops (gtt)
15 ml =	4 fluidrams (fz)	1 tablespoon
30 ml =	1 fluidounce (foz)	-
500 ml =	1 pint (pt)	-
1000 ml =	1 litre (Lt)	-
4000 ml =	4 litres (1 gallon)	-

Weight is a unit measure of kilogramme containing 1000 gm

1 kg = 1000 gm
1 gm = 1000 mg
1 mg = 1000 mcg
1 kg = 2.2 lb

Dose computations for liquid drugs

The traditional formula to calculate the correct drug dose for an oral or parenteral drug is the quantity you want to

$$\frac{\text{administer (strenght desired)}}{\text{the strenght on the bottle label (strenght you have)}} \times \frac{\text{quantity desired}}{\text{quantity you have}} = \text{Answer.}$$

The abbreviation is $\frac{D}{H} \times \frac{QD}{QH}$ = Answer.

A newer, quicker method to compute doses by Peery (1983) is:

Amount ordered X dose on hand = answer.

Suppose you have a prescription for Gentamicin 50 mg intramuscularly. Ampoule available on hand is 80 mg in 2 ml. Calculate how much you would administer by the traditional formula.

$$\frac{\text{50 mg (strenght you desired to give)}}{\text{80 mg (strenght you have)}} \times \frac{\text{X is unknown or what you are asking in ml}}{\text{2 ml or the quantity in which 80 mg comes}}$$

To solve this equation, you must cross multiply the top right number by the lower left, and the lower right number by the top left number

80 X =100 (i.e., 2 x 50)

The next step is to divide the value of X into the opposite half of the equation (100 divided by 80). The answer is 1.25 ml; therefore, you should administer 1.25 ml to provide 50 mg of Gentamicin injection.

To use the shorter formula, place the figures you have in the appropriate place:

Amount ordered =50 mg

Dose on hand = 80 mg in 2 ml

$$\frac{50\text{ mg}}{1} \times \frac{2\text{ ml}}{80\text{ mg}} = \text{answer}$$

Solve the equation by canceling units and reducing to the lowest denominator:

$$\frac{50}{1} \times \frac{2}{80} = \frac{5}{4} = 1.25\text{ ml}$$

A nurse needs to be proficient in simple calculations as correct measurement of dosages for drugs is quite essential in nursing practice to avoid over dosage, which may be dangerous, and under dosage which may be ineffective. Developing ability to solve mathematical problems like these may take practice.

Dosages for children

Although, the dosage is stated in the medication order, nurses must understand something about safe dosages for children. Unlike adult dosages, children's dosages are not always standard. There are several formulas for determining paediatric dosages using body surface area method, body weight method, Clarke's rule, Young's rule and Fried's rule.

(a) **Body surface area method**:

This is used for all children except neonates. The formula is:

$$\frac{\text{Surface area of child in square metres}}{1.7} \times \text{Adult dose}$$

(1.7 is the average square metre surface of adult). Suppose you have a prescription for a child with a surface area of 0.4 square metre, and the adult dose of the drug is 20 mg.

$$\frac{0.4}{1.7} \times \frac{20}{1} = \frac{4}{17} \times \frac{20}{1} = \frac{80}{17} = 4.2\text{ mg}$$

(b) **Body weight method**:

Most paediatric drug dosages are based on weight. The formula is:

$$\frac{\text{Body weight X Recommended dose per kg}}{\text{Frequency of administration}} = \text{Single dose.}$$

If a child is weighing 15 kg and is placed on intramuscular Ampicillin 60 mg/kg body weight 6 hourly daily. Calculate the amount for single dose.

$$\frac{15 \times 60}{4\text{ (6 hourly daily)}} = \frac{900}{4} = 225\text{ mg/dose.}$$

The amount for single dose = 225 mg.

(c) **Clarke's Rule**:

This formula is meant for infants and young children. The formula is:

$$\frac{\text{Weight in kg}}{70\text{ kg}} \times \text{Adult dose}$$

70 kg is the weight for an average adult.

What will be the recommended dose for a child weighing 12 kg, if the adult dosage of the drug is 500 mg?

$$\frac{17}{70} \times \frac{500}{1} = \frac{12}{1} \times \frac{50}{1} = \frac{600}{7}$$

= 85.7 mg ~ 86 mg.

(d) **Young's rule**:
The formula is used for children of two years and above. The formula is:

$$\frac{\text{Age in years}}{\text{Age in years + 12}} \times \text{Adult dose}$$

Supposing a child is 4 years and he is to have Cloxacillin and the adult dose is 250 mg.

$$\frac{4}{4 + 12} \times \frac{250}{1} = \frac{1}{4} \times \frac{250}{1}$$

= 62.5 mg

(e) **Fried's rule**:
This formula is used for infants under 1 year. The formula is:

$$\frac{\text{Age of child in month}}{150} \times \text{Adult dose}$$

150 is a constant.

If adult dose for a drug is 75 mg, what will be the dose for a child of 8 months?

$$\frac{8}{150} \times \frac{75}{1} = 4 \text{ mg}$$

Dilution of lotion

This is used in case there might be need to dilute a lotion to a required strength to facilitate treatment. The formula is:

$$\frac{\text{Strength required}}{\text{Strength of stock solution}} \times \text{Volume required}$$

i.e., $\frac{\text{Want}}{\text{Have}} \times \text{Amount}$

To prepare 1000 ml of 1 in 100 from a stock solution of 1 in 20

$$\frac{1:100}{1:20} \times 1000 \text{ ml}$$

$$\frac{1}{100} \times \frac{20}{1} \times \frac{1000}{1}$$ = 200 ml, i.e. you will dilute 200 ml of the 1 in 20 stock solution to get 1000 ml of 1 in 100.

Infusion rate

There is need to calculate the rate of flow of an infusion in order to avoid over hydration which can lead to overloading of the heart, and consequently pulmonary oedema which may eventually lead to the client's death.
Infusion passes from the bag into a barrel. It has a fixed drop size, which can be adjusted. For adult, there are two types: the "macro" which has a drop factor of 15 drops per milliliter while the second one has 20 drops per milliliter; the "micro" is used for paediatrics with 60 drops per milliliter.
The number of drops in 1 milliliter is called "Drop Factor". To calculate the number of drops per minute or the "Drip Rate", the formula is:

$$\frac{\text{Total volume of infusion X Drop Factor}}{\text{Total Time of infusion in minutes}} = \text{Drip rate.}$$

Supposing a patient is to have 500 ml of 5% D/W for 6 hours, calculate the drip rate.

$$\frac{500 \times 15}{6 \times 60} = \frac{250}{9}$$ = 27.7 drops per minute ~ 28 drops per min.

For paediatrics, they have a special barrel called "Bureto 1" which emits 60 drops per ml.
A year old boy is to have 200 ml of Hartman's solution for 6 hours. Calculate the rate in drops per minute.

$$\frac{200 \times 60}{6 \times 60} = \frac{200}{6}$$ = 33.33 drops per minute ~ 33 drops per min.

6. Understanding the various routes of drug administration

GASTROINTESTINAL ROUTE

(a) **Peroral (Oral) Drug Administration**
The drug is administered orally, is swallowed, and undergoes absorption from the GI tract through the mesenteric circulation to the hepatic portal vein into the liver and then to the systemic circulation (bioavailability $\leq$ 100%). The oral route is the most common route of administration.

- **Entry of the drug** into the circulation is slower than with IV administration and limited by many factors:
- **First-pass effect**. Orally administered drugs must pass through the portal circulation and the liver before entering the systemic circulation. Bioavailability of many drugs is reduced because they are significantly metabolized before reaching the blood stream. Some drugs must be administered in much larger doses orally than intravenously (e.g., propranolol requires an oral dose 20-40 times larger than its IV dose).
- **Metabolic activation**. Some drugs are activated as they pass through the liver before entering the systemic circulation. Drugs administered in an inactive form (e.g., sulindac, enalapril) must be metabolically altered to a pharmacologically active and available form. Prodrugs, as they are also known, will have much smaller effect if administered intravenously because only a small fraction of the systemic circulation passes through the liver. This is in contrast with gastrointestinal absorption in which virtually all of the portal circulation passes through the liver.
- **Gastric emptying and peristaltic rate**. Drugs molecules are absorbed throughout the GIT, but the duodenum is the primary absorption site

because of its large surface area with the villi and microvilli. Altered gastric emptying affects the arrival of the drug in the duodenum for systemic absorption. Factors that affect gastric emptying include meal content, emotional factors, and drugs that affect GIT motility (e.g., anticholinergics). Body position can also affect gastric emptying. Positioning the patient upright or on the right side can enhance gastric emptying. Conversely, positioning the patient on the left side will slow gastric emptying and keep the medication in the stomach longer (e.g., to prolong the effect of an antacid in the stomach).

Advantages

- The oral route is the most convenient, least expensive and the safest route.
- Administration is simple and usually, the patient can self-administer the drug.
- In case of overdose, gastric lavage or induced vomiting may dilute or retrieve the drug before it can cause toxic effects.
- There are different oral dosage forms, which can be used interchangeably. Only the dosage will be different.

Disadvantages

- The drug may not be absorbed from the GI tract consistently or completely.
- Presence of food may inhibit absorption.
- Relatively slow absorption rate makes the oral route unsuitable for most emergencies.
- The drug may be digested by GI enzymes or decomposed by the acid pH of the stomach.
- Some drugs may be incompletely absorbed because of first-pass effects or presystemic elimination (e.g., the drug is metabolized by the liver before systemic absorption occurs).
- The drug may irritate the mucosal epithelial cells or complex with the contents of the GI tract. Some drugs can discolour the teeth.
- The absorption rate may be erratic because of delayed gastric emptying or changes in intestinal motility.
- Unsuitable for unconscious patient, vomiting patient or patient with oral pathology.

Solid oral forms include tablets, capsules, extended release tablets or capsules, and enteric (coated) tablets or capsules.
Liquid forms include syrups, elixirs, emulsions, and suspensions.

How to administer oral medications (tablets and capsules)

Follow the guidelines for safe administration of medications by comparing the name of the medication on the label with that in the doctor's prescription three times: as you select the medication, just before you open the container, and as you dispose of the container or return it to the shelf or trolley.

- Administration of oral medications requires clean technique throughout the procedure. Wash your hands thoroughly, gather, wash and wipe dry all the equipments namely trolley, tray, saucer, two spoons, jug of drinking water, tumbler, tea cloth, 2 large bowls (one containing detergent for washing and the other containing warm water for rinsing). Collect the medication bottle from the medicine cupboard or from the pharmacy and then wheel the trolley to the patient's bedside.
- Identify the patient accordingly and establish rapport.
- Take the treatment sheet and read the prescription thoroughly noting the date, name of drug, dose, frequency and duration, route of administration.
- Assess the patient's condition, e.g. measure the patient's apical pulse rate before giving digitalis preparation and other drugs that slow the heart rate. You may have to withhold the medication and notify the physician if pulse rate is below 60 beats/minute.
- Pour the required number of tablets or capsules into the bottle lid or the container cover. You can return the excess, if any, to the container. Do not pour the medication directly into the spoon because returning the excess from such spoon may contaminate the stock bottle. For similar reason, do not touch the excess medication nor return the unused portion of a divided tablet to the bottle; discard it. Never pour medication into your hand.
- Transfer the medication to the spoon and recap the bottle. Give the spoon to the patient or tap the medication into his hand making sure the spoon does not touch the patient's hand. Provide him with water and make sure he has swallowed the medication before leaving the bedside. If he has difficulty swallowing the tablets or capsules, let him drink some water before taking the medication.
- Advise the patient to place the tablets or capsules well back on the tongue either one at a time or all at once, whichever is more convenient. H e should tip his head slightly forward before swallowing a mouthful of water. Patient should not throw his head back as he swallows as this may prevent the airway from closing and thereby increasing the risk of aspiration.
- Document drugs given on the medication chart.
- Put back the tray of drugs in the medicine cupboard and discard the other contents of the trolley appropriately. Clean the trolley.

How to administer oral liquid medications

The procedure is the same as for tablets and capsules except that you will use a medicine cup to measure the liquid medication. Carry out the three identification checks to be certain that you are administering the right medication.

- Wash your hands. Read the prescription thoroughly. Identify and assess the patient.
- Gather together all the requirements including the medication container. Always choose a medicine cup or glass that has the correct marking you need. Never try to estimate measurements between markings to avoid giving inaccurate dosage.
- Suspensions should be shaken before opening the bottle. Always remove the cap, and place it upside down on the trolley to avoid contaminating it. The medicine cup should be rinsed with water to

prevent medication from sticking to its sides.

- Hold the measuring glass at eye level with your thumb placed at the correct marking and pour the medication to the desired level. Always hold the medication bottle with the label pointed up against the palm of your hand so you pour away from the label thereby preventing the medication from running down the label and soiling it and making it illegible. Never use a medication if the label has been soiled by medicine, which previously dripped on it. Never relabel such a bottle, always return it to the pharmacy for relabelling.
- After pouring the medication, wipe the bottle lip clean and recap the bottle. Recheck the label against the medication card to confirm that you are giving the right drug.
- Position the patient well and serve him the medication making sure that he has taken it before you leave the bedside. Document the procedure accordingly.
- If you do not have a medicine glass with small markings to measure a very small dose accurately, use a syringe marked in minims to draw up and measure the dose.
- For infants, the medicine can be administered using the syringe or dropper. You need to be familiar with them to be able to administer drugs to them; otherwise, their mothers can be used.

Nursing considerations (Oral administration)

- Clarify the prescription whenever in doubt with the senior nurse or physician before administering any medication to the patient.
- Inform patient adequately about his medication so as to enhance his compliance and cooperation.
- Administer oral medications one hour before meals or two hours after meals unless otherwise instructed.
- Patients must be served with their medications within 30 minutes before or 30 minutes after the stipulated time.
- Monitor vital signs especially when indicated before administering drugs to patients.
- Shake the bottle well, holding first finger over the cap, when administering mixtures, suspensions, etc.
- Drugs must not be left with the patients, if they are not ready to take them. Always ensure drugs are taken before leaving the bedside.
- To facilitate the swallowing of tablets or capsules, you may crush uncoated tablets or open soft capsules and then mix the medication in a small amount of beverage or fluid. Confirm that such mixture won't affect the drug's action.
- Never crush or open coated tablets or capsules or hard capsules as such may affect absorption of the medication.
- Coated tablets and capsules should be administered with plenty of water in an empty stomach to ensure their quick passage into the small intestine. Such tablets or capsules should be swallowed whole and not chewed.
- Document all drugs administered to avoid duplication.
- Observe patient for any reaction and if any, document it and report to the most senior nurse who will inform the physician.
- Oral medications are contraindicated in a patient who is vomiting or unconscious.
- Medication with unpleasant taste can be served with juice (except if incompatible). Alternatively, patient can be given iced cube to suck if her condition permits; this will deaden the taste buds and he will not feel the taste.
- Protect tablets and capsules from light, humidity, and air. Signs of deterioration include discoloration, unusual odour and change in consistency. Return any medication that looks or smells strange to the Pharmacy.
- Warn patient to expect certain common side effects with some medications, e.g. dizziness with sedatives, which can affect driving, or operation of machinery.
- Always check and discard any expired medication.

(b) **Nasogastric (NG) Tube Administration**

This is passing a Ryle's tube through the nose to the stomach for the purpose of administering medication or food in a patient that is unconscious or paralyzed, and in children who cannot eat well. Drug action is the same as with oral administration; however, the drug must be in liquid form or crushed and well dissolved just before administration.

How to give medication through an NG Tube

- Ensure that the tube is neither too flexible nor too stiff for easy insertion. If too flexible, use ice or cold water to give it the right rigidity; if too stiff, dip in warm water for several minutes to achieve the right flexibility.
- Check both nostrils for possible obstruction. Select the more patent of the two nostrils for the insertion by alternately pressing each of them and asking the patient to inhale through the open nostril.
- Avoid lubricating an NG tube with petroleum jelly as the patient may aspirate and develop lipoid pneumonia.
- To make insertion easier, direct the tube toward the patient's ear on that side, not her other nostril. As the tubing enters the patient's nasopharynx, she may gag. To prevent vomiting, stop advancing the tube and tell the patient to take several deep breaths or ask her to swallow water through a straw. Either action will relax the pharynx and calm the gag reflex. The water will also lubricate the tube.
- Watch out for the signs of the tube wrongly entering the patient's trachea instead of the oesophagus:
  - inability to insert the tube full length
  - vapour in the tubing
  - respiratory distress.

  The tube should be withdrawn immediately if such signs are observed.
- To confirm placement of the tube in the stomach, aspirate gastric fluid using a bulb or piston syringe
- Prepare the medication to be administered and let

it warm to room temperature.

- Pour the medication into the syringe. Unclamp or release the tubing, and let the medication flow through it by gravity. Never force liquids down an NG tube. To control the flow of liquid, raise or lower the syringe height, or pinch and release the tube. Before the syringe empties completely, begin flushing the tube with 30 to 50ml water for an adult and 20 to 25 ml water for a child. The flushing will clear any medication on the sides of the tube and the openings at the end of the tube thereby preventing clogging.
- After administering the medication and water, remove the syringe or funnel and clamp the tube (leave the tube open for the patient having nausea until the feeling stops). The patient should sit up in bed for about 30 minutes or, if uncomfortable, lie on his right side with the head of the bed partially elevated. Either position will aid stomach emptying and prevent regurgitation.
- For medications that are needed to act longer in the stomach, you can delay gastric emptying by positioning the patient on her left side with the head of the bed slightly elevated, and the NG tube clamped for about 30 minutes.
- To withdraw the tube, ensure that it moves freely otherwise flush with 30 ml normal saline. The patient should sit upright and then slowly withdraw the tube. The tube should be clamped or folded with the non-dominant hand before withdrawal. This is to prevent any fluid in the tube from running down the patient's throat and getting into her lungs during withdrawal.

(c) **Rectal Administration**

The drug in solution (enema) or suppository form is placed in the rectum. Drug diffusion from the solution or release from the suppository leads to absorption across the mucosal surface of the rectum (bioavailability = 100%). Absorption is slow, erratic, and often incomplete. Bioavailability may be greater than with oral administration because only one (the superior haemorrhoidal vein) of the three rectal veins empties into the portal circulation. Drug absorbed in the lower two-thirds of the rectum enters the systemic circulation directly, by-passing the liver and any first-pass effects. Rectal ointment may be applied to a sore or inflamed rectum for its soothing, local effect.

Advantages

- A safe route for the patient who is vomiting, unconscious, or unable to swallow.
- An effective route to treat vomiting.
- It doesn't irritate the patient's upper GI tract, as some oral medications do.
- It avoids destruction of medication by digestive enzymes in the stomach and small intestine.
- It avoids biotransformation in the liver because drugs absorbed from the lower rectum by-pass the portal system.

Disadvantages

- It may be uncomfortable and embarrassing for the patient.
- Rectal absorption may be irregular or incomplete, depending on the patient's ability to retain the medication and on the presence of faeces in the rectum. Rectal dosages of some medications may be larger than oral doses due to the incomplete absorption.
- It should be used with caution in cardiac patients because it may stimulate the patient's vagal nerve by stretching his anal sphincters.

How to administer rectal medication

Drugs are administered rectally as rectal ointments, suppositories or enemas for local or systemic effects.

Suppository is a solid medication in a firm base, such as cocoa butter, that melts at body temperature. It should be stored in a refrigerator before use to maintain firmness. It has both local and systemic uses, e.g. analgesic, astringent or antiemetic, laxative.

Ointment is a semisolid medication that may be applied externally to the anus or internally to the rectum using an applicator. It is used mainly for the local effect, e.g. as antipruritic or anti-inflammatory agent.

Enema is a liquid given as either a retention enema (retained by the patient for at least 30 minutes or until absorbed) or a non-retention enema (retained by the patient for at least 10 minutes and then expelled). Enemas given to clean the lower bowel are not medicated. Enemas are given for both local (e.g. astringent or laxative) and systemic (e.g. sedative or nutritive) effects.

- Assemble all the requirements together, which may include the medication, the applicator, water-soluble lubricant, linen saver pad, paper towels, hand gloves or finger cots. For the enema, include the enema solution and tubing, funnel or a bulb syringe (without the bulb), gauze swabs, receiver, enema soap/toilet soap, etc.
- Assist the patient to lie on her left side with her upper leg flexed so the anus is visible. Provide privacy for the patient. Place the linen saver pad under the patient's buttocks. Put on gloves or finger cot as appropriate.
- Remove the suppository from the wrapper and if it is too soft, place it under a cold running water until it is firm or in a refrigerator for several minutes. Lubricate the suppository as well as the gloved index finger to prevent anal friction and tissue damage during insertion.
- Ask patient to breath through the mouth to relax the anal sphincter.
- Gently insert the suppository tapered end first and use your gloved index finger to direct it along the rectal wall toward the umbilicus and away from the faecal mass. To avoid expelling the suppository, for adult, insert as far as 10cm (4") and in children or infants, 5 cm (2") or less. Then withdraw your finger, and remove the glove by turning it inside out and place it on a paper towel.

- To prevent the patient from expelling the suppository, press the patient's buttocks together until her urge to defecate subsides.
- Advise the patient to retain the suppository for at least 20 minutes. In case of laxative suppository, ask the patient to defecate as soon as she feels an urge.
- If inserting an ointment, attach the ointment tube to the applicator and lubricate the applicator before insertion. Follow the same precautions as above.
- For the enema, the solution should be warmed to between 37.8º and 40.6ºC to avoid stimulating peristalsis during administration. Lubricate the tip of the tube and gently insert it about 4" (10.3 cm) into the rectum directing it toward the patient's umbilicus as described above. Pour the warmed solution slowly into the enema container or syringe and remove the clamp on the tube. Allow the solution to flow into the patient by gravity. Rushing it by either pouring the solution faster or raising the syringe height will increase the fluid pressure in the rectum thereby stimulating the urge to defecate. After administering all of the enema solution, clamp the tubing and ask the patient to take a deep breath before withdrawing the tube gently but quickly. Do not allow the enema container to be completely empty before you clamp the tube or you may introduce air into the rectum. As for suppository, hold the patient's buttocks together until the urge to defecate subsides.
- Document the procedure and your findings.

Nursing considerations (Rectal administration)

- Educate the patient on the procedure so as to gain his co-operation.
- Because intake of food and fluid stimulates peristalsis, insert a laxative suppository about 30 minutes before mealtime to help soften the feaces in the rectum and facilitate defecation.
- Enema solution should not be too hot as it can cause burns and it should not be too cold as it can cause shock.
- Do not use antiseptic soap so as not to cause rash.
- Monitor the amount of fluid instilled and expelled to assess for retention of enema fluid particularly in patients with fluid and electrolyte disturbance.
- Retention enema should be given before meals as food can stimulate peristalsis and make retention difficult.
- Avoid giving enema to a patient while sitting as the catheter can injure the rectal wall and also, the enema solution will not flow high enough into the colon thereby distending the rectum and causing rapid expulsion of the solution.

DERMATOLOGICAL ROUTE

(a) **Transdermal and Topical Administration**

Transdermal (percutaneous) drug administration is the placement of the drug (in a lotion, ointment, cream, paste, or patch) on the skin surface for systemic absorption. An occlusive dressing or film improves systemic drug absorption from the skin. Small lipid-soluble molecules, such as nitroglycerine, nicotine, scopolamine, clonidine, fentanyl, and steroids are readily absorbed from the skin.

Drugs are applied topically to the skin for a local effect. Topical route can be used for any of the following purposes:

- To relieve itching (pruritus).
- To lubricate and soften the skin.
- To cause local vasoconstriction or vasodilatation.
- To increase or decrease secretions from the skin.
- To provide a protective coating for the skin.
- To apply an antibiotic or antiseptic to treat or prevent infection.

Inunction is topical administration of drugs by rubbing to create friction. Such drugs are not readily absorbed through the epidermis but they can be absorbed into the lining of the sebaceous glands and sweat pores. Washing the area well before the application enhances absorption. Topical dosage forms include powder, lotion, cream, ointment, liniment, and paste.

Advantages of topical drug administration include a long duration of action and the ability to remove the dosage form when it is no longer needed.

Lotion is a suspension of insoluble powder in water or an emulsion without powder, e.g. Calamine lotion. It has soothing, cooling and protective effect on the skin. It also gives feeling of dryness. It may be poured on the sterile gauze and patted onto the affected area.

Nursing considerations

- Shake the container well before using.
- Remove residue from the previous applications, if ordered.
- To increase absorption in certain skin conditions, warm the patient's skin with heat packs or a bath before applying.
- Apply medication to clean, dry skin.
- Thoroughly massage into the skin.
- After application, observe the patient's skin for local irritation.

Ointment is a semisolid preparation characterized by its oleaginous nature. It is used as emollient and protective barrier. It provides prolonged medication contact.

Nursing considerations

- As for lotion, but ointment does not require shaking before application.
- Apply thin layer of ointment to patient's skin, and rub it in well.
- Wear hand gloves when treating open wounds or if large area is affected.

Cream is generally oil-in-water or water-in-

oil emulsion. It lubricates as a barrier.

Nursing considerations

As for lotion, but cream does not require shaking before application.

Paste is a semisolid preparation characterized by high content of solids. It reduces and repels moisture, e.g. Zinc Oxide Paste, which is used to protect excoriated skin areas from urine and faeces.

Nursing considerations

- Apply medication to clean, dry skin.
- Cover medication to increase absorption and to protect the patient's clothing and bed linen.

Topical powders are intimate mixtures of dry, finely divided drugs and /or chemicals intended for external use. They are usually applied to protect the skin, promote skin drying, and reduce moisture, maceration, and friction. Examples are talcum powders, antiseptic powders, and mentholated powders. The disadvantages of powders are that they do not adhere to dry skin surfaces and tend to cake on most surfaces. It is generally sprinkled on the skin surface, usually after cleaning and drying. The area may be covered with a dressing. To prevent inhalation of powder particles, instruct patient to turn his head to one side during application.

Liniment is a liquid that usually contains an anodyne or a rubefacient. It is applied to stimulate circulation to an area by vasodilatation of the capillaries. Pour the liniment on the affected area and rub the skin with long, firm smooth strokes. The liniment should be at room temperature as a cold one can cause vasoconstriction of the area.

(b) **Buccal and sublingual administration (Oral mucosa)**

A tablet or lozenge is placed under the tongue (sublingual) or in contact with the mucosal (buccal) surface of the cheek (between the cheek and the gums). This type of administration allows a nonpolar, lipid-soluble drug to be absorbed across the epithelial lining of the mouth. After buccal or sublingual administration, the drug is absorbed directly into the systemic circulation, by-passing the liver and any first-pass effects.

Advantages

- The drug is absorbed directly into the bloodstream and takes effect quickly.
- It bypasses both the lower GI tract and portal system, thereby protecting the drug from transformation in the stomach, small intestine, or liver.
- The mucosal route is convenient and safe to use.

How to give medication by the sublingual or buccal routes

The procedure is the same as for oral route. The only difference is that the drugs in oral route are swallowed while the drugs in these two routes are left to dissolve on their own under the patient's tongue (sublingual) and between the patient's cheek and teeth (buccal). In either case, caution the patient not to swallow the tablet.

(c) **Vaginal administration**

Drugs are applied to the vagina with the aid of an applicator in form of suppository, cream, ointment, tablet or pessary, gel or foam. Drug effects are usually local, but systemic absorption does occur through the vaginal mucosa. Systemic effects are usually side effects rather than the desired therapeutic goal

How to administer vaginal medication

- Assemble all the requirements together namely the prescribed medication (suppository, tablet or pessary, cream, ointment, jelly or foam), applicator, gloves, cotton balls, water-soluble lubricant, perineal pads, drape, linen saver pad, paper towel, receiver, soap and water.
- Inform the patient about the procedure and ask her to urinate since a full bladder can make the treatment uncomfortable. Privacy is essential for the procedure.
- Fill the applicator with the prescribed amount of medication and cover the tip of the applicator with water or water-soluble lubricant to make insertion easier.
- Assist the patient to lie on her back, with knees flexed and legs spread apart. Place a linen saver pad under the patient and a drape over her legs leaving only her perineum exposed. Ensure adequate lighting to be able to identify the vagina orifice.
- Put on gloves. With the gloved nondominant hand, part the labia and examine the perineum. If you see any discharge, clean it using the cotton balls soaked in soapy warm water. Then, gently inert the applicator about 2" (5cm) into the vagina and push the plunger to instill the medication. Remove the applicator and place it on a paper towel or a receiver for used instrument. Remove the gloves by turning them inside out and place them on the paper towel or receiver. Wash your hands.
- Tell patient to remain supine for 10-15 minutes after the instillation; the hips may be elevated on a pillow. The position will allow the melted medication to flow into the posterior fornix. Failure to remain in this position, the medication will run out because the vagina has no sphincter. Finally, apply a clean perineal pad and a T binder if there is excessive

drainage. A pant can be used to put it in place.

(d) **Urethral administration (Bladder irrigation)**

Bladder irrigation is carried out on a physician's order, usually to wash out the bladder and /or apply an antiseptic solution to the bladder lining. This is done after bladder or prostate surgery with retention catheters. Continuous bladder irrigation may be prescribed to reduce the possibility of clot formation or urinary tract infection.

It can also be used to maintain bladder tone intermittently.

A special catheter with three lumina is used. One lumen is used to inflate the balloon, one allows fluid into the bladder and one allows fluid to flow out of the bladder.

How to administer continuous bladder irrigation

It is a sterile procedure, so aseptic technique should be used. In this procedure, a specified solution mostly normal saline is allowed to drip into the catheter from a bag attached to a tube that is similar to that of I.V. infusion. This fluid mixed with collecting urine will continuously flow out of the bladder through the catheter into the collection bag through the third lumen.

If intermittent irrigation is to be done, then a clamp will be needed on the tube from the solution container, which will be released and specified amount of fluid is allowed to enter the bladder. Drainage tubing is then clamped to cause the solution to remain in the bladder for a specified time, after which the clamp will be released to let urine and solution drain out from the bladder. This is to be repeated until a desired result is gotten. In order to measure urine output with these systems, the amount of fluid infused (in flow volume) is subtracted from the total amount collected to be able to get the amount of urine.

Always make sure that the drainage collection bag is emptied at regular intervals (as often as a very 4 hours or as needed) in order to prevent backflow of solution into the bladder, which can cause infection.

Document the time, date and appearance of drainage, and any complaints by the patient.

OPHTHALMIC, OTIC, NASAL, AND LARYNGEAL ROUTES

(a) **Ophthalmic administration**

The drug in form ointment or drops is administered onto the conjunctiva using sterile technique to avoid irritation or infection. The effect is usually local with systemic side effects occasionally occurring. Absorption into the CNS may be a problem at times because of the proximity of the eyes to the brain and the lipophilic nature of ophthalmically active medications. Hand gloves may be worn if there is visible drainage from the eyes. Eye medication is usually instilled into the eye's lower conjunctival sac with resultant distribution throughout the tear film.

How to instill eye drops

Medication is applied to the eye either in form of drops or ointment. All medications for use in the eye must be labeled "ophthalmic preparation " (safe for use in contact with the eye). They must be kept sterile and applied aseptically to prevent eye infection.

The patient assumes a back lying position with the head slightly hyper extended or can be in a sitting up position with the head tilted backwards and holds a tissue to soak up the excess medication that leaves the eye.

The nurse wipes the lids and lashes gently from inner to the outer canthus with a cotton ball dampened with normal saline solution.

The nurse instructs the patient to look at the ceiling, and then exposes the lower conjunctival sac by placing several fingers on the patient's cheek just below the affected eye and drawing the skin downward. Using a side approach, the nurse brings a dropper filled with the eye medication over the conjunctival sac and instills the ordered number of drops in the center or outer part of the lower conjunctival sac. The dropper should be 1 or 2cm above the sac. The dropper should touch neither the cornea nor the mucous membrane of the conjunctiva sac. The skin is permitted to return to its normal position, and the patient asked to close the eye gently, not squeeze it shut. Closing the eye spreads the medication over the eyeball. With a cotton ball or gauze swab, the nurse presses firmly on the nasolacrimal duct for several seconds before the eye is closed, to prevent medication from running out of the eye down the duct.

Finally she wipes the eyelids gently from the inner to the outer canthus to remove excess medication and if necessary, applies an eye pad and secures it with tape.

Instillation of eye ointment

The patient assumes the same position as for eye drops and the nurse draws down the lower lid as described under the eye drop instillation. Holding the ointment tube in the other hand, the nurse approaches the eye from below, and

squeezes about 2 cm of ointment from the tube onto the conjunctival sac, moving from the inner aspect to the lateral aspect. The patient closes the eye and moves it to spread the ointment unless this is contraindicated.

Nursing considerations

- Caution patient against driving or operating machinery if blurred vision, dizziness or drowsiness occurs.
- Carefully check dosage of drugs as many are quite small and over dosage is easily possible.
- Apply ointment as a thin ribbon onto the lower conjuctival surface. Instruct patient to close eye gently and massage area lightly.
- Keep ointment tube tightly closed to prevent moisture absorption and loss of potency.
- Do not allow tip of dropper or ointment tube to touch eyelid or any moist surface.
- Do not use more often than directed because overdose resulting in systemic toxicity can occur.
- Apply ointment at bedtime if possible to avoid daytime blurring of vision.

(b) **Otic administration**

Solutions are applied to the ear in form of eardrops or irrigation for local therapeutic activity (such as an anti-inflammatory or anti-infective effect). The ear is irrigated to clear blockage of the auditory canal.

How to instill eardrops

Some ear instillations are used to treat diseases of bacterial or fungal origin, or to relieve pain or to soften cerumen (wax). Eardrops should be at room temperature when administered. A cold substance placed in the ear can affect the equilibrium of the body so drastically that the person may vomit from the sudden spinning sensation he experiences. It can cause acute pain from the membrane contraction. All ear medications are marked "Otic Solution". Remember to include three safety checks for medicine identification.

Gather all the requirements needed: the prescribed medication, the medicine dropper, gauze swab or cotton wool. The patient assumes a side-lying position with the ear being treated uppermost. The nurse wipes the external meatus with a cotton tipped applicator and straightens the ear canal as follows: for adult, gently pull the pinna up and back; for a child under 3 years, gently pull the pinna downward and backward. Following the instillation, the tragus of the ear is pressed two or three times to move the drops inward, unless contraindicated. The patient remains in the side lying position for about 5 minutes. This position prevents the drops from escaping and allows medication to reach all sides of the ear canal. A small piece of cotton fluff may be inserted loosely into the meatus of the auditory canal for 15 to 20 minutes to keep the medicine in place unless otherwise instructed.

How to irrigate the ear

Irrigating the ear involves washing the external auditory canal with a stream of solution to clean the canal of discharges, to soften and remove impacted cerumen, or dislodge a foreign body. Sometimes, irrigation aims at relieving localized inflammation and discomfort. The procedure must be performed carefully to avoid causing the patient discomfort or vertigo, to prevent maceration of tissue that lines the canal, and to avoid increasing the risk of otitis externa. Because irrigation may contaminate the middle ear if the tympanic membrane is ruptured, an otoscopic examination always precedes ear irrigation.

This procedure is contraindicated when a vegetable foreign body such as a pea, a bean, or a corn obstructs the auditory canal. These foreign bodies are hygroscopic, that is, they attract and absorb moisture. In contact with an irrigant or other solution, they swell, causing intense pain and complicating removal of the object by irrigation. The procedure is contraindicated also if the patient has a cold, fever, ear infection, or an injured or ruptured tympanic membrane.

- Assemble all the equipment including ear irrigation syringe, otoscope, prescribed irrigant, large bowl, linen saver pad and bath towel, emesis bowl or big receiver, cotton balls or cotton tipped applicators, 4 x 4 gauze swab, angle poised lamp, container for irrigant. Wear gloves if you expect contact with infected matter.
- Select the appropriate syringe and obtain the prescribed irrigant. Put the container of irrigant into the large bowl filled with hot water to warm the solution to body temperature (37ºC). Avoid extreme temperature changes because they can affect inner ear fluids causing nausea and dizziness.
- Test the temperature of the solution by sprinkling a few drops on your inner wrist. Inspect equipment, e.g. syringe for breaks or cracks; inspect all metal tips for roughness.
- Explain the procedure to the patient; provide privacy. Wash your hands and put on gloves (if necessary).
- If you haven't already done so, use otoscope to inspect the auditory canal to be irrigated.
- Help the patient to a sitting position. To prevent the solution from running down his neck, tilt his head slightly forward and toward the affected side. If he can't sit, have him be on his back and tilt his head slightly forward and toward the affected ear.
- Make sure that you have adequate lighting.
- If the patient is sitting, place the linen saver pad, covered with bath towel on his shoulder and upper

arm, under the affected ear. If he's lying down, cover his pillow and the area under the affected ear.

- Have the patient hold the receiver or emesis basin close to his head under the affected ear.
- To avoid getting foreign matter into the ear canal, clean the auricle and the meatus of the auditory canal with a cotton ball moistened with normal saline or the prescribed irrigating solution.
- Draw the irrigant into the syringe and expel any air.
- Straighten the auditory canal; then insert the syringe tip and start the flow.
- During the irrigation, observe the patient for signs of pain or dizziness. If he reports either, stop the procedure immediately.
- When the syringe is empty, remove it and inspect the return flow. Then refill the syringe and continue the irrigation until the return flow is clear. Never use more than 500ml of irrigant during the procedure.
- Remove the syringe and inspect the ear canal for cleanliness with the otoscope.
- Dry the patient's auricle and neck. Remove the bath towel and linen saver pad. Help the seated patient lie on the affected side with the 4"x 4" gauze pad under his ear to promote drainage of residual debris and solution.
- Discard all the disposables, put away all equipment, and remove the gloves and record the date, time of irrigation. Also note the volume and the solution used, the appearance of the canal before and after irrigation, the appearance of the return flow, the patient's tolerance of the procedure, and any comments he made about his condition, especially regarding his hearing acuity.

(c) **Nasal administration**

The drug contained in a solution or suspension is administered to the nasal mucosa, either as spray or as drops. Onset is generally rapid, but bioavailability can be variable and depends on the condition of nasal membranes. The medication may be used for local (e.g., nasal decongestants, intranasal steroids) or systemic effects. The duration of action may be from minutes to hours, depending on the drug.

How to administer nasal drugs

Nose drops and sprays should be at room temperature when administered, for greatest comfort. Be certain to maintain three identification safety checks with both types. They are instilled for their astringent effect (to shrink swollen mucous membranes) or to treat infections of the nasal cavity or sinuses. The equipment required is the medication solution, which usually comes in a bottle with an attached dropper, disposable tissues, and a tray. Prior to the instillation, the patient blows the nose to clear the nasal passages.

The patient assumes a back-lying position. For treating the opening of the Eustachian (auditory) tube, the patient can assume a dorsal recumbent position. The drops flow into the pharynx, where the Eustachian tube opens. To treat the ethmoid and sphenoid sinuses, the nurse has the patient assume a back-lying position with the head over the edge of the bed or a pillow under the shoulders so that the head is tipped backward. This is known as PROETZ position. To treat the maxillary and frontal sinuses, the nurse has the patient assume the same back-lying position with the head turned toward the side to be treated. This is called PARKINSON position. She makes sure that the patient is positioned so that the correct side is accessible if only one side is to be treated. If the patient's head is over the edge of the bed, it must be supported by the nurse's hand so that the neck muscles are not strained.

Once the patient has assumed the correct position, the nurse administers the drops. The dropper is held just above the nostril, and the drops are directed toward the midline of the superior concha of the ethmoid bone as the patient breathes through his mouth. If the drops are directed toward the base o f the nasal cavity, they will run down the Eustachian tube. The mucous membranes of the nostrils should not be touched to avoid injury to tissue and contamination of the dropper. The patient will remain in the position earlier mentioned for 5 to 10 minutes so that the solution will flow into the desired area. After the drops are instilled, ask him to "sniff" or attempt to move the medication back into the deep recesses of his nasal cavity.

The nurse will discard the medication remaining in the dropper before returning the dropper to the bottle.

How to give nose drop to an infant

To administer nose drops to an infant, the nurse places a pillow under the infant's shoulders and allow the child's head to fall back slightly over the edge of pillow onto the nurse's arm; this arm can also be used to restrain the infant's arm. The other hand can be used to administer the nose drops.

How to use a nasal aerosol device

This is also known as nebulization. Nebulization therapy is also referred to as inhalation therapy or aerosol therapy. It is used in the nose mainly to treat inflamed nasal passages. Nasal aerosol devices are available in different designs and materials.

Ask the patient to gently blow her nose to remove excess mucous and clear the nostrils. Shake the aerosol device well and remove the

protective cap from the adapter tip. Get the patient to place the tip in her nostril, hold her breath and then firmly press down once on the cartridge, and release it. Encourage her to continue to hold her breath for several seconds afterwards to avoid inhaling the mist. After removing the device from her nostril, let her exhale through the mouth and then repeat the procedure for the other nostril, if ordered. Instruct the patient not to blow her nose for at least 2 minutes after each spray.

Administration of aerosol medication carries the same responsibility, as does the administration of other forms of medication. Check the drug label three times as with other preparations to be certain that you are giving the right medication. The patient should be instructed carefully on the use of the aerosol device and should be cautioned that she should use only as prescribed.

(d) **Laryngeal administration**

The drug in form of solution is applied as mouthwash or gargle. Mouthwash provides clean oral feeling. It can be used by patients who cannot clean their mouths by themselves. It may be used after the normal brushing of the teeth to prevent halitosis. It is also used for patients with throat problems.

How to administer a mouthwash or gargle

Gather all the requirements namely the solution, drinking cup, emesis basin, mackintosh and a towel preferably patient's, etc. For unconscious patient, mouth gag is needed or padded spatula with an angle poised lamp or torchlight

It is a clean procedure. Inform patient about the procedure in order to gain his consent.

Prepare the required lotion as ordered.

Preferably the patient should sit upright if the state of health permits.

Place the mackintosh and the towel around the neck. Position the receiver under the angle of chin. Assist him to rinse out mouth but if the patient is unconscious, it is a little bit difficult to clean behind of the teeth; there may be need for mouth gag, and somebody to hold the pen torch for you. Artery forceps or mounted swabs may be used. They are dipped in the solution and used until the mouth is clean. After this, the prepared solution can be given to rinse the mouth. Patient should not swallow the solution but should spit it into the emesis basin. Note that this cannot replace toothbrush.

In case a patient needs a gargle, e.g. a patient with tonsillitis or who has just done tonsillectomy, seat him upright with his head erect or tilted back slightly. Then pour the lotion and ask the patient to gargle with it, making sure the essential parts are touched before spitting the lotion out. This is done more than once before stoppage. The solution should be warm.

Nursing Considerations

- This cannot replace good tooth brushing as routine oral care; does not clean plaque from teeth.
- It should be done for patient thrice a day especially unconscious patient and patient with milk diet.
- Educate patient on the importance of oral care.
- Observe the rules of oral medication e.g. do not give more than required.

RESPIRATORY ROUTE

(a) **Pulmonary inhalation**

The drug, as liquid or solid particles, is inhaled into the lungs, where the site of action may be local (e.g., beclomethasone) or systemic (e.g., inhalation anaesthetics).

Absorption is generally rapid, because of the vascular nature of the pulmonary capillary system, but it depends on drug lipophilicity, droplet or particle size, pulmonary function, and respiratory status.

Most systemic inhaled drugs are generally short acting (minutes to hours) and may be eliminated by the lungs. Locally acting inhaled drug generally have longer duration of action and may last from 2 to 12 hours or more.

The drug is inhaled perorally with a nebulizer or metered-dose inhaler. Factors such as the rate and depth of inhalation, length of time that the breath is held after inhalation and placement of the inhaler mouthpiece into the mouth can affect the bronchial concentration of inhaled medications.

How to use a metered-dose inhaler

For the proper use of the pressurized metered–dose aerosol inhalers, use the following procedure:

- Shake the aerosol canister before each use and remove the cap.
- Hold the inhaler about 2 inches from an open mouth or inhale the medication through a four–inch paper tube spacer placed on the end of the actuator in order to enhance the amount of medication reaching the bronchial receptors.
- Tilt your head back slightly to form as straight a channel as possible to maximize the dept of airway penetration by the drug.
- Breathe out fully but normally. The dose of the drug will be more uniformly distributed in the lungs when inhaled after a normal exhalation.
- Breathe in deeply and slowly over 4-5 seconds while simultaneously depressing fully the top of the metal canister. A fourteen-fold higher

concentration of the drug will be deposited in the lung after a slow 4-5 second inhalation (0.5 L/sec) as compared to a fast 1-2 second inhalation (2.0 L/sec) because more drug reaches the airways instead of impacting on the large airways. The dept of inhalation also enhances the amount of drug retained by the lung.

- Hold your breath for about 5-10 seconds after inhalation to prevent exhaling particles of drug, which would normally deposit in the lung due to gravitational effects.
- Allow 5-10 minutes for the first inhaled dose to take effect and repeat the above procedure if a second inhalation is prescribed.
- Clean the inhaler thoroughly; remove the metal canister and rinse the plastic case and cap thoroughly under running water at least once a day.
- Dry the plastic case and cap; and put the metal canister back into the case with a twisting motion, and then put the cap back on.
- Do not store the inhaler near heat or an open flame because its contents are under pressure.

(b) **Endotracheal (ET) tube administration**
In an emergency, if I.V. access isn't available, certain drugs can be administered through an ET tube. It allows uninterrupted resuscitation and avoids such complications as coronary artery laceration, cardiac tamponade, or pneumothorax, which can occur with intracardial administration of emergency medication. The effect of a drug after ET administration is more prolonged than after I.V. administration because absorption is sustained in the alveoli (depot effect). Repeat doses and continuous infusions should therefore be adjusted to prevent adverse reactions.

PARENTERAL ADMINISTRATION ROUTES

(a) **General guide to parenteral route**
Parenteral routes commonly used by nurses to administer medications are intradermal, subcutaneous and intramuscular. In some settings, nurses also give intravenous medications, although the type of medication a nurse can administer by this route may be restricted by the hospital policy. Parenteral medications are absorbed more quickly than oral medications and are irretrievable once injected. Therefore, it is important that they be prepared and administered carefully and accurately. Preparing and administering parenteral medications often involve mixing drugs, preparing powdered drug (reconstitution) and employing sterile techniques.

Equipment

Syringes are devices for injecting, withdrawing, or instilling fluids. There are several kinds of syringes used for injections. Three commonly used types are:

1. The standard hypodermic syringe
2. The insulin syringe
3. The tuberculin syringe

Most syringes used today are made of plastic, and are individually packaged for sterility, and can be disposed of together with the needles after use.

Hypodermic syringes come in 2 ml/cc, 2.5 ml/cc, 5 ml/cc, 10 ml/cc, 20 ml/cc and 50 ml/cc. These syringes usually have two scales marked upon them, the minim and the milliliter scale. The milliliter scale is normally used; the minim scale is used for very small dosages.

Insulin syringes are similar to hypodermic syringes except that they have a specially designed scale for insulin. They have unit graduations (100 units/ml) rather than volume graduations. They are available in disposable and non-disposable types.

Tuberculin syringe was designed to administer tuberculin. It is narrow and calibrated in tenths and hundredths of a milliliter (up to 1 ml) on one scale and in sixteenths of a minim (up to 1 minim) on the other scale. This syringe can also be used to administer other drugs, particularly when small or precise measurement is indicated, e.g. infant dosage.

Prefilled syringes contain premeasured, ready-to-dispense doses enclosed in plastic cartridges that need only the attachment of a needle to be ready for use.

Prefilled cartridges are ready-to-use parenteral packages, which consist of a plastic cartridge holder and a prefilled medication cartridge with a needle attached. The medication is premixed and premeasured.

All syringes have three parts:

- the TIP of the syringe, which connects with the needle;
- the BARREL or outside part, on which the scales are printed;
- and the PLUNGER or PISTON, the part that fits inside the barrel.

Needles are stainless steel or aluminium devices that penetrate the skin for the purpose of administering or transferring a parenteral product. They are usually disposable. A needle has three parts: the HUB, which fits onto the syringe; the CANNULA or SHAFT, which connects to the hub; and the BEVEL which is the slanted part at the tip of the needle. A long bevel provides a sharp needle, used for subcutaneous and intramuscular injections.

Short bevels are used for intravenous injections; a long bevel is not used because it might become occluded if it rests against the side of a blood vessel.

Needles have three variables: the slant of the bevel; the length of the shaft, which varies from ¼ to 5 inches and the gauge or diameter of the shaft, which varies from 14 (largest diameter) to 27 gauge. The larger the gauge, the smaller the diameter of the cannula.

For subcutaneous injections, it is usual to use a 24 to 26-gauge needle, 3/8 to 5/8 inch long. Obese patients require 1-inch needle.

For intramuscular injections, a longer needle with a larger gauge is used, for example, 20 to 22 gauge and 1 to 1½ inches long.

Selection of needles depends on the viscosity of the medicine that will be given. Blood is thick, so 18 and 19 gauge needles are generally used to withdraw blood; antibiotics are fairly thick and so are usually injected through a 20-gauge needle; water based medications are injected through a 22 or 25 gauge needle. Always try and use the smallest gauge and the shortest length possible in order to reduce client's discomfort and increase the ease of administration. At times, the infants may need a fairly large gauge in case you want to administer antibiotics but a fairly short needle (1 inch).

Intradermal injections are very shallow and thus require a very short needle (½ or 5/8 inch) if the solutions are water-based, and a gauge of 25 or even 27 can be chosen.

Ampoules are frequently used to package parenteral medications. An ampoule is a glass container that usually holds a single dose of a drug. It is made of glass and has a constricted neck. Some ampoules have coloured marks around their necks and some are scored. If the neck is not prescored, it is scored with a razor blade before opening. Often the drug is in the upper stem of the ampoule above the neck and as well as in the main portion of the ampoule; the upper part is flicked several times with fingernail to bring the medication to the main portion of the ampoule. To open it, you place sterile gauze on top of the ampoule and break the neck off by bending it outward. The sterile gauze protects the nurse's fingers from the glass. A hypodermic needle is inserted to remove the medication from the bottom of the ampoule, and might need to tilt the ampoule to obtain all the medication incase of a single dose ampoule.

Vial is a small glass bottle sealed with a rubber cap. It may contain a single dose but most often contain multidoses, e.g., 50ml of a drug. Vials usually have a metal cap that protects the rubber seal; the cap is readily removed. Before withdrawing the medication from a vial, the nurse swabs the rubber cap with an alcohol, or methylated spirit. Then the nurse draws into the syringe the volume of air equals to the amount of medication to be withdrawn; inserts the needle into the vial through the rubber cap and injects the air into the vial. The air prevents a negative vacuum and allows the medication to be withdrawn easily. The bevel is kept above the medication to avoid creating bubbles. The prescribed amount of drug is then withdrawn into the syringe by inverting the vial, holding it upward at eye level, and pulling back the plunger.

(b) **Preparing medication for injection**

Parenteral medication may be in form of a liquid or powder. Liquid medications are available in glass ampules or vials and are ready to draw into a syringe. Solutions of drugs for parenteral administration may also be further diluted before administration.

Dry powders of parenteral drugs for reconstitution are used for drug products that are unstable as solutions. Correct diluents must be used for such reconstitution.

Reconstitution of a dry powder from vial

- Assemble the required equipment. Select the appropriate needle size and syringe; the syringe should be slightly larger than the volume required for reconstitution.
- Remove the protective cap from the diluent vial and wipe the stopper with alcohol; allow the alcohol to evaporate.
- Inject an amount of air equal to the recommended amount of diluent into the diluent vial; then draw the recommended amount of diluent into the needle and syringe.
- Wipe the surface of the medication vial with alcohol, allow to dry and then inject the diluent into the vial.
- Roll the vial or shake it gently to allow the powder to dissolve.
- After the powder has dissolved, the vial is inverted and the desired volume is withdrawn.

Removing liquid medication from an ampoule

- Hold the ampoule upright, and tap the top to remove any solution trapped there.
- Score the neck of the ampoule with a razor blade if it is not prescored. Then, swab the neck of the ampoule with an alcohol swab.
- Grasp the ampoule on each side of the neck with thumb and index finger of each hand and quickly snap open.
- Place a filter needle in the open ampoule and

withdraw the prescribed dose.

Removing drug solution from a vial

- Remove the protective cap around the rubber stopper on the vial and clean the stopper with alcohol; allow to dry.
- Ensure that appropriate needle size and syringe are used.
- Pull back the plunger until the amount of air in the barrel equals the amount o f medication ordered.
- Insert the needle into the vial stopper, inject the air, and withdraw the medication.
- The air is injected into the vial to prevent a negative vacuum from being created and to allow the drug to be removed.

(c) **Precautions for safe parenteral injection**

Wrong injection of a drug may damage nerves, tissues, or blood vessels, or introduce bacteria into the bloodstream. To avoid such complications:

- Be sure you are injecting the right patient. Injection into a wrong patient can have immediate and fatal consequences. Also follow the three safety checks to be certain that you are injecting the right drug.
- Select the site carefully to avoid damaging nerves and vessels.
- Avoid areas that are inflamed or have lesions, hair or birthmarks.
- Use only sterile needles and syringes and avoid contamination.
- Select the right needle and syringe sizes for the medication and the patient's size.
- Check for blood backflow to ensure placement in a vein before I.V. injection. For S.C., I.M., and intradermal injections, remove the needle if you see blood in the syringe barrel. Select another site and try again with a new needle.
- Rotate injection sites for frequent injections and record such sites in the patient's medication chart.
- All materials used should be discarded properly.

(d) **Parenteral routes**

The various routes of administration of parenteral medications include:

1. INTRADERMAL ADMINISTRATION

An intradermal (intracutaneous) injection is the administration of drugs into the dermal layer of the skin just beneath the epidermis. Usually only a small amount of liquid is used, e.g. 0.1 ml. The maximum injection volume is approximately 1 ml. This method of administration is frequently indicated for allergy and tuberculin test and for vaccinations. Common sites for intradermal injections are the inner lower arm, the upper chest, and the back beneath the scapulae.

Procedure for intradermal injection

- The equipment normally used is a 1 ml syringe calibrated into hundreds of a milliliter. The needle is short and fine, frequently a 25, 26 or 27 gauge, ¼ inch to 5/8 inch long.
- Inform patient about the procedure; gather all you will need. Maintain privacy if necessary.
- Prepare the injection and take it to the patient's bedside.
- Arrange patient in a position that will suit the procedure. Clean the site with an alcohol pad and allow to dry. Injection while the skin is still wet can introduce antiseptic into the dermis, which can cause skin irritation and affect test results.
- Hold the patient's forearm and stretch the skin with your thumb. With your other hand, hold the syringe between your thumb and forefinger and expel any air in the needle.
- Position the needle at about 15° angle to the skin with the bevel of the needle upward. The bevel is thrust through the epidermis into the dermis, and then the fluid is slowly and gently injected. The needle is correctly placed if you feel some resistance while injecting the medication. But if the plunger moves too freely, you have inserted the needle too deeply; withdraw slightly and try again.
- After injecting the medication, leave the needle momentarily in place and observe for a small blister or wheal to form. The needle is then withdrawn quickly, and the site is very lightly wiped with an antiseptic swab. The area is not massaged because the medication may disperse into the tissue or out through the needle insertion site. Massaging may also interfere with the test result. Intradermal injections are absorbed slowly through blood capillaries in the area.
- Document the name of the medication and the amount administered. Observe the patient for allergic reaction and notify the physician accordingly.

2. SUBCUTANEOUS ADMINISTRATION

It is the injection of drug into the subcutaneous tissue beneath the skin layers, usually of the arm or thigh (bioavailability ≤100%). It is also referred to as hypodermic injection. This method of administration has a number of advantages. The drug is almost completely absorbed from the tissues, provided that blood circulation is normal. Thus, the amount of drug absorbed is predictable. The patient's state of consciousness or ability to swallow does not affect subcutaneous injection. The drug administered in this route generally acts within 30 minutes. The chief disadvantage of this method, as is true of all methods of parenteral administration is that the skin is broken by the insertion of a needle. Any break in the skin poses the risk of infection, particularly if aseptic technique is not adopted.

The common **sites** used for a subcutaneous injection are usually the outer upper arms or the anterior thighs. These are convenient sites for injections and they normally offer adequate area and have satisfactory circulation. Patients

who administer their own injections, e.g. those with diabetes mellitus, usually use the subcutaneous tissue of the anterior thighs and abdomen. Sites on the upper back below the scapulae are also used when administering subcutaneous injections. It is advisable to alternate sites if a patient is taking or receiving a number of injections; a site rotation plan should be devised.

S.C. injection should be avoided if:

1)The patient is in shock or has occlusive vascular disease with poor perfusion.
2)The patient's skin tissue is grossly adipose, oedematous, hardened, or swollen at all the common injection sites.
3)The patient's skin is diseased, or damaged by previous injections

Adverse effects:

1)Injection of concentrated or irritating solutions can cause sterile abscesses to form as a result of natural immune response.
2)Repeated injections into the same site can cause lipodystrophy, atrophy of the S.C. tissue. Diabetic patients who require daily injections of insulin should have planned rotation of injection sites to minimize tissue damage.

Procedure for subcutaneous injection

- Wash hand using a surgical hand wash before assembling the supplies to avoid transmitting microorganisms to the patient or to the sterile equipment.
- Gather the following requirements:
  - The patient's medication card or list
  - The injection pack containing a galipot for lotion with cotton swabs
  - A vial or ampoule of the correct sterile medication
  - A sterile syringe and needle. Generally a 2ml syringe and a 25-gauge needle are used for subcutaneous injections. The length of the needle depends on the amount of adipose tissue and the angle used to administer the injection. Generally, a 5/8 inch needle is used for adults when the injection is administered at a 45º angle; a ½ inch needle is used at a 90º angle. Shorter needles, e.g. 3/8 inch, may be used for children and longer ones, e.g. 1 inch, may be necessary for very obese adults. To determine the appropriate length of the needle for a 90º-angle injection, pinch a fold of skin between your thumb and forefinger at the injection site, and then measure the width of the skin fold by placing a needle that will not be used for injection against the skin surface. The appropriate needle length is one half the width of the skin fold (Pitel, 1971). When this method of measuring is used, the needle is inserted without pinching the skin.
  - Disinfectant to clean the top of the medication vial and the injection site.
- After withdrawing the required dosage, cover the needle to maintain sterility. Place the syringe in the receiver. Dispose the ampoule and any unused solution.
- Identify the patient and explain the procedure. Select a site free of tenderness, hardness, swelling, scarring, itching, burning or localized inflammation. Select a site that has not been used frequently. These conditions could hinder the absorption of the medication. These signs could also increase the likelihood of an infection at the injection site. Provide privacy.
- Clean the site with an antiseptic swab. Start at the center of the site and clean in a widening circle. Allow the area to dry thoroughly. Place the swab between the third and fourth fingers of the non-dominant hand for later use.
- Remove the needle cap while waiting for the antiseptic to dry. Pull the cap straight off to avoid contaminating the needle.
- Expel any air bubbles from the syringe by inverting the syringe and gently pushing on the plunger until a drop of solution can be seen in the needle bevel. If air bubbles still remain, flick the side of the syringe barrel. Alternatively, when it is important that the entire amount of medication be administered, leave 0.2 ml of air in the syringe (Wong, 1982).
- Take the syringe in your dominant hand by holding it between your thumb and fingers with your palm facing upward for a 45ºangle insertion or with the palm downward for a 90ºangle insertion.
- Using a non-dominant hand, pinch or spread the skin at the site, and pierce it with the bevel upward for 45º angle using a firm steady push. When the needle is inserted, move your non-dominant hand to the barrel of the syringe and your dominant hand to the end of the plunger.
- Aspirate by pulling back on the plunger. If blood appears in the syringe, withdraw the needle, discard the syringe, and prepare a new injection. If blood does not appear, inject the medication by holding the syringe steady and depressing the plunger with a slow even pressure.
- Remove the needle quickly, pulling along the line of insertion and supporting the tissue with your non-dominant hand.
- Massage the site lightly with a sterile disinfectant soaked swab or apply slight pressure.If bleeding occurs, apply pressure to the site until it stops. Bleeding rarely occurs after subcutaneous injection.
- Dispose the used needles and syringe. Needle covers should be re-applied
- Assist patient to a comfortable position
- Wash hands
- Record the medication given, dosage, time, route, and any complaints by the patient, and your signature.
- Assess the effectiveness of the medication 15 to 30 minutes after the injection or as appropriate, depending on the medication.

Guidelines for Heparin Administration

The subcutaneous administration of heparin requires special precautions because of its anticoagulant properties.

- The preferred site is the lower abdominal fat pad,

2" (5.1 cm) beneath the umbilicus between the iliac crests. This site is away from major muscles and is not involved in muscular activity, as the arms and legs are; thus, the possibility of haematoma is reduced.

- Do not administer any injections within 2" of a scar, a bruise, or the umbilicus.
- Use a ½ inch, 25 or 26-gauge needle with air, which prevents any leakage of heparin into the intradermal layers when the needle is inserted and when the needle is withdrawn, thus minimizing the possibility of a haematoma.
- Do not aspirate to check for blood return when giving heparin because it may cause bleeding into tissue at the site.
- Do not massage the site after the injection to avoid haemorrhages or bruises.
- Alternate sites for subsequent injections.

Guidelines for insulin administration

- To establish more consistent blood levels, rotate insulin injection sites within anatomic regions. Absorption varies from one region to another. Preferred insulin injection sites are the arms, abdomen, thighs and buttocks. Make sure the type of insulin, dose, and syringe are correct.
- When combining insulin in a syringe, make sure they are compatible. Regular insulin can be mixed with other insulins. Protamine insulin zinc suspension (Semilente insulin) cannot be mixed with isophane insulin suspension (NPH). Follow hospital policy regarding which insulin to draw up first.
- Do not mix insulins of different purities or origins.
- Before drawing up insulin suspension, gently roll and invert the bottle to ensure even drug particle distribution. Don't shake the bottle because this can cause foam or bubbles to develop in the syringe.
- Do not aspirate for blood return; it is not necessary.

3. INTRAMUSCULAR ADMINISTRATION

The drug is injected into muscle tissue, usually deep muscle, such as the gluteus or deltoid (bioavailability ≤100%).

The rate of absorption depends on the vascularity of the muscle site, the lipid solubility of the drug, and the formulation matrix. Intramuscular absorption is similar to but more rapid than subcutaneous absorption because of increased blood flow to the muscles. Entry of the drug into the circulation is slower than with I.V. administration.

Like the S.C. route, the peak effect is generally much less than with I.V. administration but the duration of action is generally longer because of the slower release into the circulation.

The maximum injection volume is approximately 2-5 ml.

Advantages of I.M. administration

1)It is commonly and frequently ordered for medications that irritate subcutaneous tissue e.g. penicillin and paraldehyde.
2)The speed of absorption is faster than with oral and subcutaneous routes because of the greater blood supply to the muscles.
3)This route can take a larger volume of fluid without discomfort than subcutaneous tissues, although the amount varies among people, chiefly with muscle size and condition.
4)The sites for intramuscular routes are many, so different sites can be chosen depending on the amount of drug to be given.
5)This route is recommended for patients who are uncooperative or can't take medication orally; and for drugs that are altered by digestive juices.
6)It allows less painful administration of irritating drugs because muscular tissue has fewer sensory nerve endings.
7)It is convenient for both the patient and the nurse.

Disadvantages

1) Not all drugs are used for this route; oral and intravenous routes are preferred for administration of drugs that are poorly absorbed by muscle tissue such as phenytoin, digoxin, chlordiazepoxide, diazepam and haloperidol.
2) The needle may enter blood vessel accidentally while the drug is being injected causing the drug to go into blood circulation and forming an embolus.
3) It is contraindicated in patients with impaired coagulation mechanisms and in patients with occlusive peripheral vascular disease, oedema and shock, because these conditions impair peripheral absorption.

Intramuscular injection sites

Selecting the appropriate site for an intramuscular injection is critical. Not only should a large, healthy muscle be used, but also the site should have no large nerves or blood vessels and be free of infection and abrasions. When a person is to receive several injections, it is essential to alternate sites to avoid overusing and irritating one muscle. For babies and very young children, the quadriceps muscles on the anterior and lateral aspects of the thighs are the sites of choice. The gluteal muscles of babies and children who cannot yet walk are not sufficiently well developed to receive injections. The proximity of the large sciatic nerve and the danger of damaging it usually militate against placing injections in the gluteal muscles of children younger than 3 years.

The site for an I.M injection must be chosen carefully, taking into account the patient's general physical status and the purpose of the injection. I.M. injection should not be administered at inflamed, oedematous or irritated sites or at those containing moles, birthmarks, scar tissue or other lesions.

The most common site is **dorsogluteal**, which

is the thick muscle of the buttock. Commonly used for adult. Not recommended for children below the age of 3 because the muscle is not developed enough to prevent injury to the sciatic nerve. Position the patient flat on the stomach, with toes pointed inward and arms apart and flexed toward the head. The injection site must be carefully chosen to avoid striking the sciatic nerve, major blood vessels or bone. *To give an injection in this site, divide the buttocks into imaginary quadrants. The vertical line extends from the crest of the ilium to the gluteal fold. The horizontal line extends from the medial fold to the lateral aspect of the buttock. Locate the upper outer aspect of the upper outer quadrant. It is important to palpate the crest of the ilium so that the site chosen is high enough. Visual calculations alone can result in an injection that is too low and that can injure the patient.*

Other sites are:

Ventrogluteal (Gluteus minimus) - Suitable for all patients because it is relatively free from large nerves and fatty tissue. Position the patient on his back or side.

Vastus lateralis is situated at the anterior lateral aspect of the thigh. Suitable for all patients especially the children because it is well developed and has few major blood vessels and nerves. Position the patient in bed sitting up or lying flat

Rectus femoris is on the anterior aspect of the thigh. Mainly used for self-injection because of its accessibility. Position the patient in bed sitting up or lying flat.

Deltoid and **triceps** are on the lateral aspect of the upper arm. Seldom used because the muscle is small and can take only small volumes of medication; also dangerously near the radial nerve. Position the patient in bed sitting upright or lying flat.

Procedure for intramuscular administration

- Wash hands using a surgical hand wash before gathering the necessary equipment to avoid transmitting microorganisms to the patient.
- Assemble the following items: the medication card or the patient's chart; the sterile medication either in ampoule or vial; sterile disposable syringe and needle (Use appropriate size of syringe, which is usually 2-5ml. A large muscle such as gluteus medius requires 20-23-gauge needle, 1½ 3 inches long whereas deltoid muscle requires smaller 23- to 25-gauge needle,5/8 to 1 inch long); alcohol pads, gloves, etc.
- Check the medication orders. Prepare the correct dosage of the drug from a vial or ampoule.
- Identify the patient and explain the procedure
- Select the site with adequate muscle mass. The skin surface over the site should be free of bruises, abrasions and infections. Determine if the size of muscle is appropriate to the amount of medication to be injected. An average adult's deltoid muscle can usually absorb 0.5 to 2 ml of drug whereas gluteus medius can absorb 1 to 5 ml. If injection is to be frequent, sites should be alternated.
- Provide privacy if patient will be exposed.
- Clean the site with an antiseptic swab using a circular motion, start at the center and move outward about 5 cm
- Remove the needle cover and withdraw the prescribed amount of medication. Invert the syringe and expel any air that has accidentally entered the syringe
- Use the non-dominant hand to spread the skin at the site. Holding the syringe between the thumb and forefinger, pierce the skin quickly at a 90º angle and insert the needle into the muscle.
- *Aspirate by pulling back on the plunger, if blood appears in the syringe, withdraw the needle, discard the syringe, and prepare a new injection.*
- If blood does not appear, inject the medication steadily and slowly, holding the syringe steady.
- After the injection, withdraw the needle quickly. Massage the site lightly while applying slight pressure with alcohol pad to spread the medication over a greater area. Avoid massaging the site when you want to slow absorption or when you are injecting an extremely irritating medication.
- Dispose the used needles and syringe. Needle covers should be re-applied
- Assist patient to a comfortable position
- Wash hands
- Record the medication given, dosage, time, route, site and any complaints by the patient, and your signature.
- Assess the effectiveness of the medication up to 30 minutes after the injection or as appropriate, depending on the medication.

Giving I.M. Injection to infants

Infants and children up to about 5 years of age must be restrained for parenteral injections. They require extra hands to help in restraining them so that they will not injure themselves, because quick movement once the needle has been inserted could break the needle shaft.

Injections are contraindicated in certain sites like dorsogluteal and ventrogluteal muscles and the only acceptable site for I.M. injection is the anterior thigh (Vastus lateralis) and for subcutaneous route is anterior thigh and the deltoid area.

In preparing for an infant injection, put into consideration the size of the syringe and the gauge of the needle, and then calculate the dosages using any formula that is appropriate to the age and weight of the child.

Clean the anterior thigh with methylated spirit and allow to dry. Restrain the knee of the selected leg with your non-dominant hand; lean

your body weight over the child's body to prevent his torso-from moving. Use your dominant hand to administer the injection. Ask for assistance to restrain them, do not under estimate their strength. With older children, you must ask for help. When assisting, always ask for their permission; this will ensure cooperation, e.g., "Let me help you hold still". This will elicit more cooperation than forcing them to do something unwillingly. Praise and comfort them afterward. Do not ask parents to restrain their children because some pain is associated with injection, and their role in this case will be contrary to what role they are expected to play, i.e. protecting them rather than causing pain, Hand the child to the parents immediately after the injection to be comforted.

How to use the Z-track method

A Z-track intramuscular injection is a special technique used to administer intramuscular medications that are highly irritating to subcutaneous and skin tissues. The technique is the same as the technique for an intamuscular injection except that the skin and subcutaneous tissue at the site of injection are pulled about 2.5 to 3.5 cm to one side of the site before the needle is inserted at 90º angle. This will ensure that the medication enters the muscle tissue. Aspirate for blood return and if none appears, inject the drug slowly. Wait for 10 seconds before removing the needle; this is to ensure dispersion of medication as the muscle tissues relax. The needle is withdrawn slowly; then release the displaced skin and subcutaneous tissue. When the skin returns to its normal position, the needle track is sealed off by pulling the patient's skin to minimize subcutaneous irritation or discolouration. The site is not massaged and do not allow the patient to wear a tight fitting garment over the site because it might cause seepage into the delicate tissue and cause irritation.

Reducing the pain of intramuscular injection

This can be achieved by holding a syringe for injection in the same manner as you would hold a dart. Use a quick thrust, with the needle at a steep angle (90º) to guarantee that it pierces deeply. Do not be concerned that the needle will pierce too deeply. If the site and length of needle are appropriate, this will not occur. Never use a blunt needle when there is usually a skin resistance to even a sharp needle. A greater concern is that with too soft a thrust, the needle will not pierce the skin and you will have to attempt the procedure again after changing the needle. Insert the needle through the skin as rapidly as possible. A needle passing rapidly through tissue does not cause pain whereas a needle pushed slowly does.

Pain can be relieved also by putting ice to a site for a few minutes prior to an injection or by massaging the area for few seconds immediately after injection. *Note that massaging is contraindicated in certain injection procedures like heparin, insulin, z-track injection, etc.* Counter irritation will help decrease the pain because nerve endings at the site will then transmit the feeling of rubbing or cold rather than the stretched or painful sensation.

Also if the patient is relaxed, there is less tension on the tissue. Relaxation can be achieved by proper positioning, or diverting the patient's attention by communicating with the patient. Most importantly is the confidence of the nurse handling the procedure. This will allay patient's fear and anxiety.

4. INTRAVENOUS ADMINISTRATION

This is administration of medicine or fluid through the vein. It is the most rapid way to achieve a drug's effect because it bypasses absorption. 100% of the drug is delivered directly into the circulation thereby producing immediate therapeutic effect (bioavailability = **100%**). Any adverse effects such as anaphylaxis also occur rapidly. With I.V. route, it is impossible to recall an inadvertent overdose.

Bolus: The entire dose is administered rapidly, producing a high plasma concentration and usually, the most rapid effect. Injection volume is limited only by the patient's size (i.e., plasma volume) and the properties (i.e., toxicities) of the drug or fluid administered.

Infusion: The drug is given at a constant rate. Constant rate I.V. infusion maintains a relatively constant plasma drug concentration. Injection volume is unlimited.

IV route is indicated in the following conditions:

- For immediate treatment of life-threatening conditions such as shock;
- To deliver drugs that can't be given by any other route, such as dopamine;
- To deliver large doses of medication;
- When other routes are not possible, e.g. in unconscious patient;
- When using potentially harmful drugs which can damage subcutaneous or intramuscular layer.

IV route should be avoided if the patient can swallow and an oral form is available. Patients with blood coagulation disorders should not receive IV therapy unless for the treatment of

the coagulation disorder.

In I.V. administration, medication is injected by piercing the skin and sliding the needle of the syringe into an evident available vein. Before piercing the skin, a tourniquet must have been tied round the limb, which will have to be removed immediately a vein is got. It requires a new puncture of the vein with each administration. When veins are entered too many times at the same site, inflammation and some oozing of blood into the subcutaneous tissue may occur leading to haematoma and blocking of the site.

There are other potential hazards in giving I.V. medications. Infection and rapid, severe reactions to the medication. To prevent infection, sterile technique is used during all aspects of I.V. administration procedures. To safeguard the patient against severe reaction, the nurse must administer the drug slowly, taking several minutes and following the manufacturer's recommendations. The patient is assessed closely during the administration, and the medication is discontinued immediately if an untoward reaction occurs. Common signs of an adverse reaction are: Noisy respirations, changes in pulse rate, chills, nausea and headache. If any adverse signs occur, the nurse notifies the most senior nurse in the ward or charge nurse who will in turn report to the physician.

The patient is also assessed for signs of problems associated with I.V. therapy, such as an infection at the I.V. site or fluid infiltration.

Various intravenous administration methods

Selection of an I.V. delivery method depends upon the therapy's purpose and duration; the patient's diagnosis, age and health history; and the condition of his veins.

Intravenous drug administration can be done in five ways in case of an existing intravenous line:

1) Directly into a bottle or bag of intravenous fluid;
2) Into a volume-controlled chamber in the tubing;
3) Directly into the lower tubing at a bolus injection site;
4) Directly into a heparin lock;
5) By a separate bag of solution (a piggyback).

(1) **Directly into a bottle or bag of intravenous fluid:**

Medications are put directly into a bottle or bag of intravenous fluid. It then means the medication will flow along with the fluid, and will last as long as the fluid lasts i.e. if the fluid is supposed to run for six hours, the medication will run for that period of time e.g. vitamin B complex, syntocinon. It's quite advantageous because it is gradual in onset, and it can quickly be put off and the effect of the medication stopped.

(2) **Into a volume-controlled chamber in the tubing**:

Medications in this case are injected into the volume-controlled chamber in the tubing. There are different volume controlled sets and they are designed to deliver a variety of different-sized drops (10, 15, 20, 50 or 60 drops). This is a calibrated chamber (e.g., Buretrol, Metriset, and Soluset), 100 to 250 ml in size that is filled with intravenous fluid from the solution bag ahead. The clamp above the volume-control chamber is closed after a set amount of fluid has filled the chamber so that no more fluid can enter it. It serves as a safety device in case the lower regulating clamp is released accidentally or deliberately by a child, the patient will receive no more fluid than that contained in the chamber. I.V. therapy is not done for children under 2 years of age without using such a safety feature to eliminate the danger of circulatory overload. They are also useful if the solution contains a medication such as potassium or heparin to ensure that a large volume of a potentially dangerous medication is not accidentally administered too rapidly.

(3) **Directly into the lower tubing at a bolus injection site**:

For this method, the medication is injected into the lower tubing at bolus injection site; the infusion is clamped in order to inject the medication after which the infusion will be unclamped to allow the flow. The drug is put directly in the bloodstream and the infusion will help to expedite the action. It can be used in emergency and when a drug is to be administered at frequent intervals.

(4) **Directly into the heparin lock**:

This is also called an intermittent infusion device. A heparin lock consists of either a steel winged tip needle with tubing that ends in a resealable rubber injection port or a catheter with injection cap attached. Filled with dilute heparin to prevent blood clot formation, the device maintains venous access in patients receiving I.V. medication regularly and intermittently, but not requiring continuous infusion of fluids.

A heparin lock proves superior to a keep-vein-open line because it minimizes the risk of fluid overload and electrolyte imbalance. It also cuts costs and reduces the risk of contamination by eliminating I.V. solution containers and administration sets; increases patient's comfort

and mobility; reduces patient's anxiety; and if inserted in a large vein, allows collection of multiple blood samples without repeated venipuncture.

(5) **By a separate bag of solution (a piggyback)**:

This is drug infusion through a secondary I.V. line. A piggyback set includes a small I.V. container, short tubing, and a macro drip system. This set connects to the primary line's upper Y port, also known as a piggyback port. A piggyback set is used solely for intermittent drug administration. Antibiotics are most commonly administered by intermittent (piggyback) infusion. To make this set work, the primary I.V. container must be positioned below the piggyback container (provision is made by the manufacturer for an extension hook for that purpose).

The greater hydrostatic pressure in the piggyback container due to the raised position will cause the fluid to infuse.

A secondary set may be used in place of the piggyback set as an additive set. A secondary set includes an I.V. container of any size, long tubing, and either a micro drip or a macro drip system. The set connects into the primary line's lower Y port, which is also called the secondary port. A secondary set is used to administer drugs intermittently or simultaneously with a primary solution.

Do not allow an infusion bag to be completely empty so that air will not enter into the vein.

Choosing the venipuncture site

Venipuncture involves piercing a vein with a needle and inserting the venipuncture device for the purpose of an I.V. therapy or collection of blood samples.

In both adults and children, it may be done at the antecubital space in the basilic, median cubital, or cephalic vein, or from one of the veins on the back of the hand (dorsal, metacarpal, basilic, or cephalic). Even for newborns, these sites are available and easy to use for a skilled person. If the veins in the hands or arms cannot be used, either because they are collapsed due to hypotension or damaged due to burns, the femoral vein can be used although infection and phlebitis are common with this site.

Assess the point where blood will be drawn for skin lesions or erythema (red and tender areas that suggest infection). Do not penetrate such areas to reach veins; doing so might push microorganisms from the surface lesion into the blood stream, causing blood infection (septicaemia). Determine whether the person is on any medication that interferes with blood clotting e.g. heparin. If so more careful compression is necessary to stop blood flow after the procedure.

How to perform venipuncture

- Wash your hand, identify client and explain procedure to him.
- Assess client's status and analyze plan according to the client's needs.
- Gather all the requirements including injection pack, tourniquet, appropriate size needle and syringe, adhesive plaster, gloves, etc.
- Locate the best puncture site, which may be the back of the hand (antecubital space) by observation and palpation. Choose as distal a site as possible to preserve remainder of vein. Select a vein large enough to accommodate needle.
- Apply tourniquet in a way that it can be removed with one hand after procedure and proximal to venipuncture site. If adult ask client to make a fist. Tap vein and stroke vein toward heart to enhance distension.
- Put on your gloves; clean the site with methylated spirit using circular motion. Place thumb distal to puncture site and pull skin taut over site.
- Insert needle, bevel side up, at 30º angle about ½ inch distal to point at which needle will enter vein; decrease angle slightly and push the needle into the vein, following the course of the vein until when blood appears in syringe. Slowly and steadily aspirate desired amount of blood or inject the medication if giving bolus injection.
- Remove tourniquet, place dry compress on needle tip; apply gentle pressure and withdraw needle, holding it flat to skin surface.
- Put specimen into the suitable container, allowing blood to run gently down the side of the tube. Label appropriately and send to the laboratory for analysis. Dispose of needles, syringes and anything contaminated with blood into the sluice room. Do not bend or break the needles before disposal.
- Be certain that there is no oozing of blood at the puncture site. Apply adhesive plaster snugly to maintain faint pressure.
- Evaluate the effectiveness, efficiency, safety, cost and comfort of procedure. Document the entire procedure.

Avoiding common I.V problems

It involves the following:

- Careful preparation of the medication. nUsing aseptic procedure to administer I.V therapy.
- Using correct size of needle.
- Choosing an appropriate site for the therapy.
- Proper monitoring and calculation of rate of flow so as not to overload the heart.
- Stop the I.V. therapy immediately if swelling occurs at the site of administration.
- Never use a device for more than stipulated time.
- Assess the site properly for any signs of tenderness, swelling, scar, etc.

Paediatric I.V therapy

Paediatric I.V. therapy is almost the same as adult except that children are extremely frightened; explain the procedure to the child. There is need for splint to restrain the movement of the hand especially at the elbow or the wrist. If older child, evaluate whether the child can hold still or not. If not ask for help.

I.V. therapy is not administered to children less than 2 years of age without using safety measures such as volume control sets, to eliminate the danger of circulatory overload. For these children, fill the volume-control chamber with no more fluid than they are to receive in an hour. This calibrated chamber is known as Buretrol or Soluset; often used in paediatric wards. It is a minidrip chamber. It supplies 60 drops per milliliter.

Risks of peripheral I.V. therapy

There are local and systemic complications.

Local complications such as:

Phlebitis, which may be caused by poor blood flow around venipuncture device or friction from catheter movement in vein or venipuncture device left in vein for too long. The patient will manifest with puffy area over the vein, and elevated temperature.

Extravasation, which is as a result of device dislodging from vein or perforated vein. Patient will manifest with swelling at and above I.V. site (may extend along entire limb); pain, discomfort or burning at the site (may be painless at times).

Occlusion, which is caused by interrupted I.V. flow or I.V. line clamped for too long. Patient will complain of discomfort at insertion site.

Haematoma as a result of inadequate pressure applied when catheter is discontinued. It also occurs when vein is punctured through opposite wall at time of insertion. Patient will manifest with tenderness at the site and bruised area around the site.

Thrombosis, which is caused by injury to endothelial cells of vein wall, allowing platelets to adhere and thrombus to form. It results in painful, reddened and swollen vein, or sluggish or stopped I.V. flow.

Thrombophlebitis, which results from thrombosis and inflammation. There is severe discomfort or hardened, swollen and reddened vein.

Nerve tendon or ligament damage, which is caused by improper venipuncture technique resulting in injury to surrounding nerves, tendons or ligaments or tight taping or improper splinting with arm board. Patient will complain of extreme pain similar to electrical shock when nerve is punctured, numbness and muscle contraction.

Systemic complications

Circulatory overload, which could be as a result of flow rate too rapid, or miscalculation of fluid requirement. Patient will manifest with discomfort, neck vein engorgement, respiratory distress, increased blood pressure, increased difference between fluid intake and output.

Systemic infections (Septicaemia or Bacteraemia), which may be due to failure to maintain aseptic technique during insertion or site care, prolonged indwelling time of device, weak immune system. Patient will show signs and symptoms of fever, chills and malaise for no apparent reason

Air embolism can be caused by an empty solution container resulting in the added container pushing air down the I.V. line. The patient will manifest with respiratory distress, unequal breath sounds, weak pulse, increased central venous pressure, and loss of consciousness, decreased blood pressure.

Allergic reactions, which can be caused by allergens such as medications and patient will react by having itching, watery eyes and nose, bronchospasm, wheezing, urticarial rash; anaphylactic reaction may occur within minutes or up to 1 hour after exposure (flushing, chills, anxiety, agitation, palpitations, cardiac arrest).

Central venous infusion

Pros and cons of central venous infusion

Pros

- It allows monitoring of C.V. pressure, which is an indication of circulatory function.
- It permits aspiration of blood samples for diagnostic tests
- It also allows administration of I.V. fluids in large amounts, if necessary in emergencies or when decreased peripheral circulation causes peripheral veins to collapse
- Used when prolonged I.V. therapy reduces the number of accessible peripheral veins
- Also utilized when solutions must be diluted
- Used for irritating or hypertonic fluids such as total parenteral nutrition (TPN) solutions
- Can be employed when a patient requires long term venous access because repeated blood samples can be drawn through it; the C.V. line decreases the patient's anxiety and preserves or restores peripheral veins.

Cons

- It increases the risk of complications, such as pneumothorax, sepsis, thrombus formation, and perforation of adjacent organ
- It is more expensive than peripheral I.V. catheter.
- It may decrease patient's mobility.

- It requires more time and skill to insert than a peripheral I.V. device.

Central venous infusion sites

A central venous (C.V.) line is a sterile catheter made of polyurethane, poly vinyl chloride (PVC) or silicone rubber (silastic). It is inserted through a major vein such as subclavian vein or less common jugular. The catheter may terminate in the superior vena cava or in the right atrium.

How to perform central line insertion

- Gather the Equipments: shave preparation kit, sterile gloves and gowns, linen saver pad, blanket, sterile towel and drape, masks, cotton swabs, iodine, methylated spirit, hydrogen peroxide, antibiotic ointment, syringes and needle, injectable lignocaine, 5% dextrose in water, suture material, two 14G or 16G C.V catheters, I.V solution with administration set prepared for use, infusion pump or controller, sterile scissors, sterile gauze, heparin or normal saline flushes, adhesive tape, X-ray machine (portable)
- Before insertion of a C.V. line, confirm catheter type and size with the doctor. Set up the I.V. solution and prime the administration set, using strict aseptic technique. Attach the line to the infusion pump or controller if ordered. Recheck all connections to make sure they're tight. Notify radiology department for a portable X-ray machine.
- Wash your hand thoroughly to prevent the spread of microorganisms.
- Reinforce the doctor's explanation of the procedure and its related complications in terms the patient can understand; and answer the patient's questions.
- Ensure that the patient has signed a consent form, if necessary, and check his history for hypersensitivity to iodine or the local anaesthetic.
- Place the patient in Trendelenburg's position to dilate the veins and reduce the risk of air embolism.
- For subclavian insertion, place a rolled blanket length-wise between the shoulders to increase venous distention.
- For jugular insertion, place a rolled blanket under the opposite shoulder to extend the neck, making anatomic landmarks more visible. Place a mackintosh under the appropriate area to prevent soiling the bed.
- Turn the patient's head away from the site to prevent possible contamination from airborne pathogens and to make the site more accessible.
- Prepare the insertion site. Make sure the skin is free of hair because hair can harbour microorganisms. Do this in evening before the procedure.
- Sterilize the trolley to be used.
- Put on a mask and sterile gloves and gown and clean the area around the insertion site with swabs soaked in iodine or methylated spirit, working in a circular motion outward from the site to avoid reintroducing contaminants.
- After the doctor puts on a sterile mask, gown and gloves and drapes the area to create a sterile field, open the packaging of 3 ml syringe and 25G needle and present it to the doctor, using sterile technique.
- Wipe the top of the lignocaine vial with methylated spirit and invert it. The doctor fills the 3 ml syringe and injects the anaesthetic into the site.
- Open the packaging of the catheter and give it to the doctor using sterile technique. The doctor then inserts the catheter.
- During this time, prepare the I.V. administration set for immediate attachment to the catheter hub. Ask the patient to perform Valsalva's manoeuver (forced exhalation against a closed airway) while the doctor attaches the I.V. line to the catheter hub. This increases intrathoracic pressure and reduces the possibility of an air embolus formation during the insertion or removal of a C.V. catheter.
- After the doctor attaches the I.V. line to the catheter hub, set the flow rate at a keep-vein-open rate to maintain venous access. The doctor then sutures the catheter in place
- After an X-ray confirm correct catheter placement, set the flow rate as ordered.
- Use normal saline solution to remove dried blood that could harbour microorganisms and apply iodine over the site. Place antibiotic ointment at the site if hospital policy directs, secure the catheter with adhesive tape, and apply an occlusive, sterile 4" x 4" gauze pad. Expect some serosanguineous drainage during the first 24 hours. Label the dressing with the time and date of catheter insertion and catheter length (if not imprinted).

Teaching Valsalva's manoeuver

Instruct patient to take a deep breath and hold it, and then bear down for 10 seconds. Then tell patient to exhale and breath quietly. This manoeuver raises intrathoracic pressure from normal level of -3 to -4 mmHg to levels of 60 mmHg or higher. It also slows the pulse rate, decreases the return of blood to the heart and increases venous pressure. This is contraindicated in patients with increased intracranial pressure and patients who are not alert or cooperative.

7. Other routes of drug administration

(e) **Intra-arterial administration**

The drug is injected directly into a specific artery to achieve a high drug concentration in a specific tissue before drug distribution occurs throughout the body. This route is used mainly for diagnostic agents and some antineoplastic agents.

(f) **Intrathecal administration**

The drug is injected into the spinal fluid (sometimes used for antibiotics).

(g) **Intra-Osseous administration**

Intraosseous infusion may be indicated in a severe emergency when intravenous access has proved impossible. It can be used to administer anything that would normally be given intravenously, i.e. fluids, whole blood, packed cells, drugs. Drug absorption and effectiveness are the same as by the I. V. route. The use of intraosseous route is usually limited to very young children because the vascular red marrow is replaced by the less vascular yellow marrow at about age 5.

(h) **Intracardiac administration**

The drug is injected directly into the heart.

(i) **Intra-articular administration**

This is injection into a joint space.

(j) **Intrasynovial administration**

This is injection into the joint fluid.

(k) **Intraspinal administration**

This is injection into the spinal column.

(l) **Hypodermoclysis**

This involves injection of large volumes of a solution into subcutaneous tissue to provide a continuous, abundant drug supply; used occasionally for antibiotic administration in children.

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E-mail: greenlife@infoweb.abs.net

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Fax: 234-1-3451175
E-mail: info@cadilanigeria.com
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IPCA PHARMA NIG. LTD
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JAWA INTERNATIONAL LIMITED
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JOHNSON WAX NIGERIA LIMITED
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P.M.B. 21279, Ikeja, Lagos.

JUHEL NIGERIA LTD
35 Nkwubor Road, Emene-Enugu,
P.O. Box 1549 G.P.O. Enugu, Nigeria
Tel: 234-8033478472; 234-42-558898
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JUSTEEN PHARMACEUTICALS LTD
197, Muyibi Street, Olodi-Apapa, Lagos State, Nigeria
57B, Coker Road, Ilupeju, Lagos
Tel: 234-80-34731163, 234-1-7765232.

KAKAKI CHEMISTS LTD
45, Lagos Street, Ebutte-Metta, Lagos State.
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KEZZ KEMISTS LIMITED
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Tel: 234-1-7916758/2669115, 234-80-33101823
Email: kezzpharm@yahoo.co.uk

KINGS CHEMISTS & COSMETICS LTD
33, Idumagbo Avenue (1st Floor), Lagos
Tel: 234-1-2664501, 2636912, 2664846.
Telex: 28315 KINGS NG.

KORLYNS PHARMACEUTICALS LTD
7, Jaiye Oyedotun Street, Magodo GRA, Lagos State, Nigeria.
Tel: 234-1-8958644, 7942990
Fax: 234-1-7912709
Email: korlyns@korlynspharm.com
Website: www.korlynspharm.com

KRSNA PROJECTS LIMITED
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LAHAMS DRUG COMPANY (NIG.) LTD
(Agent to Apotex Phamaceuticals, Canada)
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Tel: 234-1-4973978, 4931935.
Fax: 234-1-823607.

LEADY-PHARMA INDUSTRIES LTD (RC: 26542)
Plots 3&4, Tomori Industrial Estate, Off Idi-Iroko Road, P.O. Box 646, Ota, Ogun State, Nigeria.
Tel: 234-39-722013; 721013
Fax: 234-39-722013.
E-mail: leadypharma@hotmail.com
Lagos: 103, Palm Avenue, Mushin, P.O.Box 611, Oshodi, Lagos State, Nigeria.
Tel: 01- 524784; 524795.

MATBENY MEDICALS LIMITED
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Tel: 234-1-2615280; Fax: 234-1-2622847
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may&baker.lagos@linkserve.com.ng
Website: www.may-baker.com.ng

MEDREICH NIGERIA LTD
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Fax: 234-1-2708866

MOPSON PHARMACEUTICALS LTD
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Tel.: 234-1- 523237, 523056, 4528462.
Fax: 234-1-523237.
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MORISON INDUSTRIES PLC
28/30, Morison Crescent, Oregun, P.M.B. 21290, Ikeja, Lagos State, Nigeria.

NASDMU LIMITED
(Nigerian Army Small Scale Drug Manufacturing Unit)
Bonny Camp, Victoria Island, Lagos.
Tel.: 234-1-613790, 617590.

NEIMETH INT'L PHARMACEUTICALS LTD.
(Formerly Pfizer Products Plc)
1, Henry Carr Street, P.M.B. 2111 Ikeja, Lagos State, Nigeria
Tel: 900370–6
Telex: 26605, Cables: PFIZER Ikeja.

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1, Canal Avenue, Canal Estate, G.P.O Box 7888, Marina, Lagos, Nigeria
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NEW HEALTHWAY COMPANY LTD
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Fax: 4523562, 4523569.

NOVEL DRUGS LIMITED
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OCULUS PHARMACARE LTD (RC. 322110)
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E-mail: oculuspharma@metrong.com

ORANGE DRUGS LIMITED
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Tel: 01-4960036. Fax: 01-967998.

PANVIJ BIOTEC NIGERIA LIMITED
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PEMASON PHARM LTD
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E-mail: phamatex@alpha.linkserve.com

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PHARMA–DEKO PLC
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Tel: 712207, 712350, 712396, 712191.
Fax: 867562, 2647279.

PHARMABOX VENTURES LTD
6, Jejelaiye Street, Olodi-Apapa, Lagos State, Nigeria.
Tel: 234-80-33134443, 234-1-2668115, 2640551, 5556303

PHARMACIA NIGERIA
1, Motorways Avenue, Alausa, Ikeja Lagos State, Nigeria
Tel: 234-1-7942990, 4934188.

P.Z. INDUSTRIES PLC
45/47, Town Planning Way, Ilupeju Industrial Estate, P.M.B. 21132, Ikeja.
Tel: 234-1-4973460-8.
Telex: BODY GUARD LAGOS.

RAJAT PHARMACEUTICALS LTD
69A, Enowa Street, Lagos, Nigeria.
Tel: 234-1-7752856

RAJRAB LIMITED
10 Ogunipebi Street, Off Okilo Road, Ogba Industrial Estate, P.O. Box 1898, Ikeja, Lagos, Nigeria.
Tel: 234-1–920875, 920209.

RANBAXY NIGERIA LIMITED
Plot 5, Block K, Apapa-Isolo Express Way, P.O. Box 4452, Ikeja, Lagos, Nigeria.
Tel: 234-1-4526359, 4527545.
Telex: 20202 IKJ. NG. TDS Box 212.
Fax: 234-1-4526371.

REALS PHARMACEUTICALS LTD
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Fax: +234-1-2630919.
E-mail: reals@skannet.com

RECKITT BENCKISER (NIG.) LTD
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Fax: 234- 1- 5451848.

SAINGENES NIG. LTD
Clannards compound,
Km 16, Ikorodu Road, Ojota.
P.O.Box 18276, Ikeja Lagos, Nigeria.
Tel: 234-1-7756254, 234-80-38192827

SALENAB NIGERIA LIMITED
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Fax: 234-1-4938057, 4964674.
E-mail: salenab@nova.net.ng

SAM PHARMACEUTICAL LTD.
Great Nigeria House (11th Floor)
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Fax: 234-1-2621237 SAM PHARM
E-mail: sampharm@linkserve.com.ng.

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118, Ogudu Road, Ogudu, Ojota, Lagos State, Nigeria.
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55, Urubi Street, P.O.Box 4784, Benin City, Edo State, Nigeria.
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Lagos Office: Falums Healthcare, Kosofe Local Government Shopping Complex, Ogudu Road, Ojota, Lagos State.
Tel.: 234-1-4708112.

SKG–PHARMA LIMITED
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Telefax: 234-1-4962671.
E-mail: customercare@rumon.nigeria.com

SONICX PHARMACEUTICALS & CHEMICAL CO. LTD (RC: 216648)
(Sole Agent for L.B.S. and Union Lab. Products)
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Tel: 234-1-2666999; 080-33085035.
Tel/ Fax: 234-1-4807706.
E-mail: sonicx@onebox.com or sonicx@euroseek.com

ST. MICHAEL PHARMACEUTICALS LTD
17A, Adeola Hopewell Street, Victotia Island, Lagos State, Nigeria.
Tel: 234-1-2668174. Fax: 234-1-2643326

ST. MIRA NIGERIA LIMITED
9 Alhaji Bashorun Street, South–West Ikoyi, Lagos. G.P.O. Box 5197, Marina, Lagos, Nigeria
Tel: 234-1-685748, 685789.
Fax: 234-1-685740

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1, Sumbo-Jibowu Street, Off Ribadu Road, SW Ikoyi, Lagos, Nigeria.
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Fax: 234-1-2672704
Email: stridesnig@hotmail.com
Website: www.stridesarco.com

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32, Sabo Arobiodu Street, G.R.A., Ikeja,
P.O.Box 2680, Yaba, Lagos State.
Tel.: 234-1-4936667, 4967579.
Fax: 234-1-4938142

SUPREME PHARMACEUTICALS LTD.
18, Ilupeju Bye–Pass, Ilupeju, Lagos State, Nigeria. P.O. Box 8366, Shomolu.
Tel: 234-1-4525639, 5870304, 5870307.
E-mail: supreme@nova.net.ng

SWISS PHARMA NIGERIA LTD RC 16806 (SWIPHA)
(Formerly Roche Nigeria Ltd)
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Tel: 234-1-4920543-4, 4921100, 4923444, 4925767; Fax: 234-1-4921974.

TAYLEK DRUGS COMPANY LIMITED
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Tel: 234-1-4525961, 4526037.
Fax: 234-1-4528797.

THERAPEUTIC LABORATORIES LTD
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Tel: 234-1-4973068, 4934445.
E-mail: therapeutic@hyperia.com

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Awaye House, 2nd Floor, Suite 6, Lagos/Badagry Express Way,Orile Iganmu P.O. Box 71323, Victoria Island, Lagos, Nigeria
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Plot 30, Doherty Industrial Estate, Oregun, Ikeja, Lagos State, Nigeria.
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P.O. Box 51564, Ikoyi, Lagos State, Nigeria.
Tel: 234-1-2669679, 2667291, 2632133.
Fax: 234-1-2630096.

TYONEX NIGERIA LIMITED
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Corporate Office: Afripharm Plaza,
15, Kingsway Road, Ikoyi, Lagos, Nigeria.
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E-mail: tyonex@onebox.com

ULTICARE–LYKA PHARMACEUTICALS LIMITED
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Fax: 234-1-5456074.
E-mail: chrismatel@hyperia.com
Factory: Km 10, Ibusa - Asaba Road, Ibusa, Delta State, Nigeria. P.O. Box 308, Ibusa.
Tel.: 234 - 46 - 280046.

UNIQUE PHARMACEUTICALS LTD
11, Fatai Atere Way, Matori, Mushin, Lagos. P.O. Box 71751, Victoria Island, Lagos State, Nigeria.
Tel.: 234-1-4523977, 4520290, 4520658, 7740161, 525678.
Fax: 234-1-4524028, 2615782.
E-mail: unique@cyberspace.net.ng

URASHI PHARMACEUTICALS LTD
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Fax: 234-9-5237009.

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35, Mobolaji Johnson Avenue, Oregun Industrial Estate, P. O. Box 3020 Ikeja, Lagos, Nigeria.
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Fax: 234-1-4960852.

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28, Ajasa Street, Onikan, Lagos, Nigeria.
P.O. Box 51557, Falomo, Ikoyi, Lagos.
Tel.: 234- 1-2636411, 2633485, 2636449.
Fax: 234-1-2636298, 2636678.
E-mail: vitalnig@metrong.com

WYETH/DELPITANO COMPANY LTD
1, Adekunle Odulami Street, Off Ikorodu Road, Ilupeju. Lagos. P.O. Box 3942, Ikeja.
Tel: 234-1-967978, 961594.

ZOOMOTA NIGERIA LIMITED
2B, Ilojo Crescent, Savoil Bus Stop, Ikorodu Road, Obanikoro, P.O.Box 10382 Ikeja, Lagos State, Nigeria.
Tel: 234-1-4976870. Fax: 234-1-4930107.
E-mail: zoomota@beta.linkserve.com

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5FU. *See* Fluorouracil
6-MP. *See* Mercaptopurine

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