BNF 70

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Appendix 1

Interactions | Appendix 1

Interactions

Two or more drugs given at the same time may exert their effects independently or may interact. The interaction may be potentiation or antagonism of one drug by another, or occasionally some other effect. Adverse drug interactions should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA), through the Yellow Card Scheme (see Adverse Reactions to Drugs), as for other adverse drug reactions.

Drug interactions may be pharmacodynamic or

pharmacokinetic.

Pharmacodynamic interactions

These are interactions between drugs which have similar or antagonistic pharmacological effects or side-effects. They may be due to competition at receptor sites, or occur between drugs acting on the same physiological system.

They are usually predictable from a knowledge of the pharmacology of the interacting drugs; in general, those demonstrated with one drug are likely to occur with related drugs. They occur to a greater or lesser extent in most patients who receive the interacting drugs.

Pharmacokinetic interactions

These occur when one drug alters the absorption, distribution, metabolism, or excretion of another, thus increasing or reducing the amount of drug available to produce its pharmacological effects. They are not easily predicted and many of them affect only a small proportion of patients taking the combination of drugs.

Pharmacokinetic interactions occurring with one drug cannot be assumed to occur with related drugs unless their pharmacokinetic properties are known to be similar.

Pharmacokinetic interactions are of several types: Affecting absorption The rate of absorption or the total amount absorbed can both be altered by drug interactions.

Delayed absorption is rarely of clinical importance unless

high peak plasma concentrations are required (e.g. when giving an analgesic). Reduction in the total amount absorbed, however, may result in ineffective therapy.

Due to changes in protein binding To a variable extent most drugs are loosely bound to plasma proteins. Protein-binding sites are non-specific and one drug can displace another thereby increasing its proportion free to diffuse from plasma to its site of action. This only produces a detectable increase in effect if it is an extensively bound drug (more than 90%) that is not widely distributed throughout the body. Even so displacement rarely produces more than transient potentiation because this increased concentration of free drug results in an increased rate of elimination.

Displacement from protein binding plays a part in the potentiation of warfarin by sulfonamides and tolbutamide but the importance of these interactions is due mainly to the fact that warfarin metabolism is also inhibited.

Affecting metabolism Many drugs are metabolised in the liver. Induction of the hepatic microsomal enzyme system by one drug can gradually increase the rate of metabolism of another, resulting in lower plasma concentrations and a reduced effect. On withdrawal of the inducer plasma concentrations increase and toxicity may occur.

Barbiturates, griseofulvin, many antiepileptics, and rifampicin are the most important enzyme inducers. Drugs affected include warfarin and the oral contraceptives.

Conversely when one drug inhibits the metabolism of another higher plasma concentrations are produced, rapidly resulting in an increased effect with risk of toxicity. Some drugs which potentiate warfarin and phenytoin do so by this mechanism.

Isoenzymes of the hepatic cytochrome P450 system interact with a wide range of drugs. Drugs may be substrates, inducers or inhibitors of the different isoenzymes. A great deal of *in-vitro* information is available on the effect of drugs on the isoenzymes; however, since drugs are eliminated by a number of different metabolic routes as well as renal excretion, the clinical effects of interactions cannot be predicted accurately from laboratory data on the cytochrome P450 isoenzymes. Except where a combination of drugs is specifically contra-indicated, the BNF presents only interactions that have been reported in clinical practice. In all cases the possibility of an interaction must be considered if toxic effects occur or if the activity of a drug diminishes.

Affecting renal excretion Drugs are eliminated through the kidney both by glomerular filtration and by active tubular secretion. Competition occurs between those which share active transport mechanisms in the proximal tubule. For example, salicylates and some other NSAIDs delay the excretion of methotrexate; serious methotrexate toxicity is possible.

Relative importance of interactions

Many drug interactions are harmless and many of those which are potentially harmful only occur in a small proportion of patients; moreover, the severity of an interaction varies from one patient to another. Drugs with a small therapeutic ratio (e.g. phenytoin) and those which require careful control of dosage (e.g. anticoagulants, antihypertensives, and antidiabetics) are most often involved.

Patients at increased risk from drug interactions include the elderly and those with impaired renal or liver function.

Serious interactions The symbol l has been placed against interactions that are potentially serious and where concomitant administration of the drugs involved should be avoided (or only undertaken with caution and appropriate monitoring).

Interactions that have no symbol do not usually have serious consequences.

List of drug interactions

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The following is an alphabetical list of drugs and their interactions; to avoid excessive cross-referencing each drug or group is listed twice: in the alphabetical list and also against the drug or group with which it interacts.

Abacavir

▶ Analgesics: abacavir possibly reduces plasma concentration of

METHADONE

▶ Antibacterials: plasma concentration of abacavir possibly reduced by RIFAMPICIN

▶ Antiepileptics: plasma concentration of abacavir possibly reduced by FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Antivirals: abacavir possibly reduces effects of l RIBAVIRIN;

plasma concentration of abacavir reduced by l TIPRANAVIR

l Orlistat: absorption of abacavir possibly reduced by l ORLISTAT

Abatacept

l Cytotoxics: increased risk of side-effects when abatacept given with ADALIMUMAB; avoid concomitant use of abatacept with

l CERTOLIZUMAB PEGOL, l GOLIMUMAB or l INFLIXIMAB

l Etanercept: avoid concomitant use of abatacept with

l ETANERCEPT

l Vaccines: risk of generalised infections when abatacept given with live l VACCINES—avoid concomitant use

Abiraterone

▶ Analgesics: abiraterone increases plasma concentration of

DEXTROMETHORPHAN

l Antibacterials: plasma concentration of abiraterone possibly reduced by l RIFABUTIN—manufacturer of abiraterone advises avoid concomitant use; plasma concentration of abiraterone reduced by l RIFAMPICIN—manufacturer of abiraterone advises avoid concomitant use

l Antidepressants: plasma concentration of abiraterone possibly reduced by l ST JOHN’S WORT—manufacturer of abiraterone advises avoid concomitant use

l Antiepileptics: plasma concentration of abiraterone possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—

manufacturer of abiraterone advises avoid concomitant use

Acarbose *see* Antidiabetics

ACE Inhibitors

▶ Alcohol: enhanced hypotensive effect when ACE inhibitors given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when ACE inhibitors given with ALDESLEUKIN

l Aliskiren: increased risk of hyperkalaemia, hypotension, and impaired renal function when ACE inhibitors given with

l ALISKIREN—avoid concomitant use

▶ Allopurinol: manufacturers state possible increased risk of leucopenia and hypersensitivity reactions when ACE inhibitors given with ALLOPURINOL especially in renal impairment

▶ Alpha-blockers: enhanced hypotensive effect when ACE inhibitors given with ALPHA-BLOCKERS

▶ Anaesthetics, General: enhanced hypotensive effect when ACE inhibitors given with GENERAL ANAESTHETICS

▶ Analgesics: increased risk of renal impairment when ACE inhibitors given with NSAIDS, also hypotensive effect antagonised

l Angiotensin-II Receptor Antagonists: increased risk of hyperkalaemia, hypotension, and impaired renal function when ACE inhibitors given with l ANGIOTENSIN-II RECEPTOR ANTAGONISTS—avoid concomitant use

▶ Antacids: absorption of ACE inhibitors possibly reduced by ANTACIDS; absorption of captopril, enalapril and fosinopril reduced by ANTACIDS

▶ Antibacterials: plasma concentration of active metabolite of imidapril reduced by RIFAMPICIN (reduced antihypertensive effect); quinapril tablets reduce absorption of TETRACYCLINES (quinapril tablets contain magnesium carbonate); possible increased risk of hyperkalaemia when ACE inhibitors given with TRIMETHOPRIM

▶ Anticoagulants: increased risk of hyperkalaemia when ACE inhibitors given with HEPARINS

ACE Inhibitors (continued)

▶ Antidepressants: hypotensive effect of ACE inhibitors possibly enhanced by MAOIS

▶ Antidiabetics: ACE inhibitors possibly enhance hypoglycaemic effect of INSULIN, METFORMIN and SULFONYLUREAS

▶ Antipsychotics: enhanced hypotensive effect when ACE inhibitors given with ANTIPSYCHOTICS

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when ACE inhibitors given with ANXIOLYTICS AND HYPNOTICS

▶ Avanafil: hypotensive effect of enalapril possibly enhanced by

AVANAFIL

▶ Azathioprine: increased risk of anaemia or leucopenia when captopril given with AZATHIOPRINE especially in renal impairment; increased risk of anaemia when enalapril given with AZATHIOPRINE especially in renal impairment

l Bee Venom Extracts: possible severe anaphylactoid reaction when ACE inhibitors given with l BEE VENOM EXTRACTS

▶ Beta-blockers: enhanced hypotensive effect when ACE inhibitors given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when ACE inhibitors given with CALCIUM-CHANNEL BLOCKERS

▶ Cardiac Glycosides: captopril possibly increases plasma concentration of DIGOXIN

l Ciclosporin: increased risk of hyperkalaemia when ACE inhibitors given with l CICLOSPORIN

▶ Clonidine: enhanced hypotensive effect when ACE inhibitors given with CLONIDINE; antihypertensive effect of captopril possibly delayed by previous treatment with CLONIDINE

▶ Corticosteroids: hypotensive effect of ACE inhibitors antagonised by CORTICOSTEROIDS

l Cytotoxics: increased risk of angioedema when ACE inhibitors given with l EVEROLIMUS

▶ Diazoxide: enhanced hypotensive effect when ACE inhibitors given with DIAZOXIDE

l Diuretics: enhanced hypotensive effect when ACE inhibitors given with l DIURETICS; increased risk of severe hyperkalaemia when ACE inhibitors given with l POTASSIUM- SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

▶ Dopaminergics: enhanced hypotensive effect when ACE inhibitors given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

l Lithium: ACE inhibitors reduce excretion of l LITHIUM

(increased plasma concentration)

▶ Methyldopa: enhanced hypotensive effect when ACE inhibitors given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when ACE inhibitors given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when ACE inhibitors given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when ACE inhibitors given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when ACE inhibitors given with NITRATES

▶ Oestrogens: hypotensive effect of ACE inhibitors antagonised by OESTROGENS

l Potassium Salts: increased risk of severe hyperkalaemia when ACE inhibitors given with l POTASSIUM SALTS

▶ Prostaglandins: enhanced hypotensive effect when ACE inhibitors given with ALPROSTADIL

l Sodium Aurothiomalate: flushing and hypotension reported when ACE inhibitors given with l SODIUM AUROTHIOMALATE

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when ACE inhibitors given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

l Wasp Venom Extracts: possible severe anaphylactoid reaction

when ACE inhibitors given with l WASP VENOM EXTRACTS

Acebutolol *see* Beta-blockers Aceclofenac *see* NSAIDs Acemetacin *see* NSAIDs Acenocoumarol *see* Coumarins Acetazolamide *see* Diuretics Aciclovir

NOTE Interactions do not apply to topical aciclovir preparations

▶ Aminophylline: aciclovir possibly increases plasma concentration of AMINOPHYLLINE

Aciclovir (continued)

▶ Ciclosporin: increased risk of nephrotoxicity when aciclovir given with CICLOSPORIN

▶ Mycophenolate: plasma concentration of aciclovir increased by MYCOPHENOLATE, also plasma concentration of inactive metabolite of mycophenolate increased

▶ Tacrolimus: possible increased risk of nephrotoxicity when aciclovir given with TACROLIMUS

▶ Theophylline: aciclovir possibly increases plasma concentration of THEOPHYLLINE

Acitretin *see* Retinoids Aclidinium *see* Antimuscarinics Acrivastine *see* Antihistamines Adalimumab

▶ Abatacept: increased risk of side-effects when adalimumab

given with ABATACEPT

l Anakinra: avoid concomitant use of adalimumab with

l ANAKINRA

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Adefovir

▶ Antivirals: avoidance of adefovir advised by manufacturer of

TENOFOVIR

▶ Interferons: manufacturer of adefovir advises caution with

PEGINTERFERON ALFA

Adenosine

NOTE Possibility of interaction with drugs tending to impair myocardial conduction

▶ Aminophylline: anti-arrhythmic effect of adenosine antagonised by AMINOPHYLLINE—manufacturer of adenosine advises avoid aminophylline for 24 hours before adenosine

▶ Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with BUPIVACAINE, LEVOBUPIVACAINE,

PRILOCAINE or ROPIVACAINE

l Anti-arrhythmics: increased myocardial depression when anti- arrhythmics given with other l ANTI-ARRHYTHMICS

l Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with

l ANTIPSYCHOTICS that prolong the QT interval

l Beta-blockers: increased myocardial depression when anti- arrhythmics given with l BETA-BLOCKERS

▶ Caffeine citrate: anti-arrhythmic effect of adenosine antagonised by CAFFEINE CITRATE—manufacturer of adenosine advises avoid caffeine citrate for at least 12 hours before adenosine

l Dipyridamole: effect of adenosine enhanced and extended by l DIPYRIDAMOLE (important risk of toxicity)—reduce dose of adenosine, see p. 87

▶ Nicotine: effects of adenosine possibly enhanced by NICOTINE

▶ Theophylline: anti-arrhythmic effect of adenosine antagonised by THEOPHYLLINE—manufacturer of adenosine advises avoid theophylline for 24 hours before adenosine

Adrenaline (epinephrine) *see* Sympathomimetics

Adrenergic Neurone Blockers

▶ Alcohol: enhanced hypotensive effect when adrenergic neurone blockers given with ALCOHOL

▶ Alpha-blockers: enhanced hypotensive effect when adrenergic neurone blockers given with ALPHA-BLOCKERS

l Anaesthetics, General: enhanced hypotensive effect when adrenergic neurone blockers given with l GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of adrenergic neurone blockers antagonised by NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when adrenergic neurone blockers given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antidepressants: enhanced hypotensive effect when adrenergic neurone blockers given with MAOIS; hypotensive effect of adrenergic neurone blockers antagonised by TRICYCLICS

▶ Antipsychotics: hypotensive effect of adrenergic neurone blockers antagonised by HALOPERIDOL; hypotensive effect of adrenergic neurone blockers antagonised by higher doses of

Adrenergic Neurone Blockers

Antipsychotics (continued)

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CHLORPROMAZINE; enhanced hypotensive effect when adrenergic neurone blockers given with PHENOTHIAZINES

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when adrenergic neurone blockers given with ANXIOLYTICS AND HYPNOTICS

▶ Beta-blockers: enhanced hypotensive effect when adrenergic neurone blockers given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when adrenergic neurone blockers given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when adrenergic neurone blockers given with CLONIDINE

▶ Corticosteroids: hypotensive effect of adrenergic neurone blockers antagonised by CORTICOSTEROIDS

▶ Diazoxide: enhanced hypotensive effect when adrenergic neurone blockers given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when adrenergic neurone blockers given with DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when adrenergic neurone blockers given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Methyldopa: enhanced hypotensive effect when adrenergic neurone blockers given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when adrenergic neurone blockers given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when adrenergic neurone blockers given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when adrenergic neurone blockers given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when adrenergic neurone blockers given with NITRATES

▶ Oestrogens: hypotensive effect of adrenergic neurone blockers antagonised by OESTROGENS

▶ Pizotifen: hypotensive effect of adrenergic neurone blockers antagonised by PIZOTIFEN

▶ Prostaglandins: enhanced hypotensive effect when adrenergic neurone blockers given with ALPROSTADIL

l Sympathomimetics: increased risk of hypertension when guanethidine given with l ADRENALINE (EPINEPHRINE); hypotensive effect of guanethidine antagonised by

l DEXAMFETAMINE and l LISDEXAMFETAMINE; hypotensive effect of adrenergic neurone blockers antagonised by l EPHEDRINE, l ISOMETHEPTENE, l METARAMINOL, l METHYLPHENIDATE,

l NORADRENALINE (NOREPINEPHRINE), l OXYMETAZOLINE,

l PHENYLEPHRINE, l PSEUDOEPHEDRINE and l XYLOMETAZOLINE

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when adrenergic neurone blockers given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Adsorbents *see* Kaolin

Afatinib

▶ Anti-arrhythmics: plasma concentration of afatinib possibly increased by AMIODARONE—manufacturer of afatinib advises separating administration of amiodarone by 6 to 12 hours

▶ Antibacterials: plasma concentration of afatinib possibly increased by ERYTHROMYCIN—manufacturer of afatinib advises separating administration of erythromycin by 6 to 12 hours; plasma concentration of afatinib reduced by RIFAMPICIN

▶ Antifungals: plasma concentration of afatinib possibly increased by ITRACONAZOLE and KETOCONAZOLE—manufacturer of afatinib advises separating administration of itraconazole and ketoconazole by 6 to 12 hours

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Antivirals: plasma concentration of afatinib increased by RITONAVIR—manufacturer of afatinib advises separating administration of ritonavir by 6 to 12 hours; plasma concentration of afatinib possibly increased by SAQUINAVIR— manufacturer of afatinib advises separating administration of saquinavir by 6 to 12 hours

▶ Calcium-channel Blockers: plasma concentration of afatinib possibly increased by VERAPAMIL—manufacturer of afatinib advises separating administration of verapamil by 6 to 12 hours

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Afatinib (continued)

▶ Ciclosporin: plasma concentration of afatinib possibly increased by CICLOSPORIN—manufacturer of afatinib advises separating administration of ciclosporin by 6 to 12 hours

▶ Tacrolimus: plasma concentration of afatinib possibly increased by TACROLIMUS—manufacturer of afatinib advises separating administration of tacrolimus by 6 to 12 hours

Agalsidase Alfa and Beta

▶ Anti-arrhythmics: effects of agalsidase alfa and beta possibly inhibited by AMIODARONE (manufacturers of agalsidase alfa and beta advise avoid concomitant use)

▶ Antibacterials: effects of agalsidase alfa and beta possibly inhibited by GENTAMICIN (manufacturers of agalsidase alfa and beta advise avoid concomitant use)

▶ Antimalarials: effects of agalsidase alfa and beta possibly inhibited by CHLOROQUINE and HYDROXYCHLOROQUINE (manufacturers of agalsidase alfa and beta advise avoid concomitant use)

Agomelatine

l Antibacterials: manufacturer of agomelatine advises avoid concomitant use with l CIPROFLOXACIN

l Antidepressants: metabolism of agomelatine inhibited by

l FLUVOXAMINE (increased plasma concentration)

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

Albendazole

▶ Anthelmintics: plasma concentration of both drugs possibly reduced when albendazole given with LEVAMISOLE

l Antiepileptics: plasma concentration of albendazole reduced by l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE—consider increasing albendazole dose when given for systemic infections

l Antivirals: plasma concentration of active metabolite of albendazole reduced by l RITONAVIR—consider increasing albendazole dose when given for systemic infections

▶ Corticosteroids: plasma concentration of active metabolite of albendazole increased by DEXAMETHASONE

▶ Grapefruit Juice: plasma concentration of active metabolite of albendazole increased by GRAPEFRUIT JUICE

▶ Ulcer-healing Drugs: effects of albendazole possibly enhanced by CIMETIDINE

Alcohol

▶ ACE Inhibitors: enhanced hypotensive effect when alcohol given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when alcohol given with ADRENERGIC NEURONE BLOCKERS

▶ Alpha-blockers: increased sedative effect when alcohol given with INDORAMIN; enhanced hypotensive effect when alcohol given with ALPHA-BLOCKERS

▶ Analgesics: enhanced hypotensive and sedative effects when alcohol given with OPIOID ANALGESICS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when alcohol given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Anthelmintics: possibility of disulfiram-like reaction when alcohol given with LEVAMISOLE

l Antibacterials: disulfiram-like reaction when alcohol given with METRONIDAZOLE; possibility of disulfiram-like reaction when alcohol given with TINIDAZOLE; increased risk of convulsions when alcohol given with l CYCLOSERINE

l Anticoagulants: major changes in consumption of alcohol may affect anticoagulant control with l COUMARINS or

l PHENINDIONE

l Antidepressants: some beverages containing alcohol and some dealcoholised beverages contain tyramine which interacts with l MAOIS (hypertensive crisis)—if no tyramine, enhanced hypotensive effect; sedative effects possibly increased when alcohol given with SSRIS; increased sedative effect when alcohol given with l MIRTAZAPINE, l TRICYCLIC-RELATED ANTIDEPRESSANTS or l TRICYCLICS

▶ Antidiabetics: alcohol enhances hypoglycaemic effect of ANTIDIABETICS; increased risk of lactic acidosis when alcohol given with METFORMIN

Alcohol (continued)

▶ Antiepileptics: alcohol possibly increases CNS side-effects of CARBAMAZEPINE; chronic heavy consumption of alcohol possibly reduces plasma concentration of FOSPHENYTOIN and PHENYTOIN; increased sedative effect when alcohol given with PHENOBARBITAL or PRIMIDONE; increased risk of blurred vision when alcohol given with RETIGABINE

▶ Antifungals: possibility of disulfiram-like reaction when alcohol given with KETOCONAZOLE; effects of alcohol possibly enhanced by GRISEOFULVIN

▶ Antihistamines: increased sedative effect when alcohol given with ANTIHISTAMINES (possibly less effect with non-sedating antihistamines)

▶ Antimuscarinics: increased sedative effect when alcohol given with HYOSCINE

▶ Antipsychotics: increased sedative effect when alcohol given with ANTIPSYCHOTICS

▶ Anxiolytics and Hypnotics: increased sedative effect when alcohol given with ANXIOLYTICS AND HYPNOTICS

▶ Avanafil: possible enhanced hypotensive effect when alcohol given with AVANAFIL

▶ Beta-blockers: enhanced hypotensive effect when alcohol given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when alcohol given with CALCIUM-CHANNEL BLOCKERS; plasma concentration of alcohol possibly increased by VERAPAMIL

▶ Clonidine: enhanced hypotensive effect when alcohol given with CLONIDINE

l Cytotoxics: disulfiram-like reaction when alcohol given with PROCARBAZINE; avoidance of alcohol advised by manufacturer of l TRABECTEDIN

l Dapoxetine: increased sedative effect when alcohol given with

l DAPOXETINE

▶ Diazoxide: enhanced hypotensive effect when alcohol given with DIAZOXIDE

▶ Disulfiram: disulfiram reaction when alcohol given with

DISULFIRAM

▶ Diuretics: enhanced hypotensive effect when alcohol given with DIURETICS

▶ Dopaminergics: alcohol reduces tolerance to BROMOCRIPTINE

▶ Lipid-regulating Drugs: avoidance of alcohol advised by manufacturer of LOMITAPIDE

▶ Lofexidine: increased sedative effect when alcohol given with

LOFEXIDINE

▶ Methyldopa: enhanced hypotensive effect when alcohol given with METHYLDOPA

▶ Metoclopramide: absorption of alcohol possibly increased by

METOCLOPRAMIDE

▶ Moxonidine: enhanced hypotensive effect when alcohol given with MOXONIDINE

▶ Muscle Relaxants: increased sedative effect when alcohol given with BACLOFEN, METHOCARBAMOL or TIZANIDINE

▶ Nicorandil: alcohol possibly enhances hypotensive effect of

NICORANDIL

▶ Nitrates: enhanced hypotensive effect when alcohol given with NITRATES

l Paraldehyde: increased sedative effect when alcohol given with l PARALDEHYDE

l Retinoids: presence of alcohol causes etretinate to be formed from l ACITRETIN (increased risk of teratogenicity in women of child-bearing potential)

▶ Sympathomimetics: alcohol possibly enhances effects of

METHYLPHENIDATE

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when alcohol given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Aldesleukin

▶ ACE Inhibitors: enhanced hypotensive effect when aldesleukin given with ACE INHIBITORS

▶ Alpha-blockers: enhanced hypotensive effect when aldesleukin given with ALPHA-BLOCKERS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when aldesleukin given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antivirals: aldesleukin possibly increases plasma concentration of INDINAVIR

Aldesleukin (continued)

▶ Beta-blockers: enhanced hypotensive effect when aldesleukin given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when aldesleukin given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when aldesleukin given with CLONIDINE

l Corticosteroids: manufacturer of aldesleukin advises avoid concomitant use with l CORTICOSTEROIDS

l Cytotoxics: manufacturer of aldesleukin advises avoid concomitant use with l CISPLATIN, l DACARBAZINE and l VINBLASTINE

▶ Diazoxide: enhanced hypotensive effect when aldesleukin given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when aldesleukin given with DIURETICS

▶ Methyldopa: enhanced hypotensive effect when aldesleukin given with METHYLDOPA

▶ Moxonidine: enhanced hypotensive effect when aldesleukin given with MOXONIDINE

▶ Nitrates: enhanced hypotensive effect when aldesleukin given with NITRATES

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when aldesleukin given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Alemtuzumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Alendronic Acid *see* Bisphosphonates

Alfacalcidol *see* Vitamins Alfentanil *see* Opioid Analgesics Alfuzosin *see* Alpha-blockers Alimemazine *see* Antihistamines Aliskiren

l ACE Inhibitors: increased risk of hyperkalaemia, hypotension,

and impaired renal function when aliskiren given with l ACE INHIBITORS—avoid concomitant use

▶ Analgesics: hypotensive effect of aliskiren possibly antagonised by NSAIDS

l Angiotensin-II Receptor Antagonists: increased risk of hyperkalaemia, hypotension, and impaired renal function when aliskiren given with l ANGIOTENSIN-II RECEPTOR ANTAGONISTS—avoid concomitant use; plasma concentration of aliskiren possibly reduced by IRBESARTAN

▶ Antibacterials: plasma concentration of aliskiren reduced by

RIFAMPICIN

▶ Anticoagulants: increased risk of hyperkalaemia when aliskiren given with HEPARINS

l Antifungals: plasma concentration of aliskiren increased by KETOCONAZOLE; plasma concentration of aliskiren increased by l ITRACONAZOLE—avoid concomitant use

▶ Calcium-channel Blockers: plasma concentration of aliskiren increased by VERAPAMIL

l Ciclosporin: plasma concentration of aliskiren increased by

l CICLOSPORIN—avoid concomitant use

▶ Diuretics: aliskiren reduces plasma concentration of FUROSEMIDE; increased risk of hyperkalaemia when aliskiren given with POTASSIUM-SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

l Grapefruit Juice: plasma concentration of aliskiren reduced by

l GRAPEFRUIT JUICE—avoid concomitant use

▶ Potassium Salts: increased risk of hyperkalaemia when aliskiren given with POTASSIUM SALTS

Alitretinoin *see* Retinoids

Alkylating Drugs *see* Bendamustine, Busulfan, Carmustine, Cyclophosphamide, Estramustine, Ifosfamide, Lomustine, Melphalan, and Thiotepa

Allopurinol

▶ ACE Inhibitors: manufacturers state possible increased risk of leucopenia and hypersensitivity reactions when allopurinol given with ACE INHIBITORS especially in renal impairment

▶ Aminophylline: allopurinol possibly increases plasma concentration of AMINOPHYLLINE

Allopurinol (continued)

▶ Antibacterials: increased risk of rash when allopurinol given with AMOXICILLIN, AMPICILLIN or CO-AMOXICLAV

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▶ Anticoagulants: allopurinol possibly enhances anticoagulant effect of COUMARINS

l Antivirals: allopurinol increases plasma concentration of

l DIDANOSINE (risk of toxicity)—avoid concomitant use

l Azathioprine: allopurinol enhances effects and increases toxicity of l AZATHIOPRINE (reduce dose of azathioprine to one quarter of usual dose)

▶ Ciclosporin: allopurinol possibly increases plasma concentration of CICLOSPORIN (risk of nephrotoxicity)

l Cytotoxics: avoidance of allopurinol advised by manufacturer of l CAPECITABINE; allopurinol enhances effects and increases toxicity of l MERCAPTOPURINE (reduce dose of mercaptopurine to one quarter of usual dose)

▶ Diuretics: increased risk of hypersensitivity when allopurinol given with THIAZIDES AND RELATED DIURETICS especially in renal impairment

▶ Theophylline: allopurinol possibly increases plasma concentration of THEOPHYLLINE

Almotriptan *see* 5HT1-receptor Agonists (under HT)

Alogliptin *see* Antidiabetics

Alpha2-adrenoceptor Stimulants *see* Apraclonidine, Brimonidine, Clonidine, and Methyldopa

Alpha-blockers

▶ ACE Inhibitors: enhanced hypotensive effect when alpha- blockers given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when alpha-blockers given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when alpha-blockers given with ALCOHOL; increased sedative effect when indoramin given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when alpha- blockers given with ALDESLEUKIN

l Anaesthetics, General: enhanced hypotensive effect when alpha-blockers given with l GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of alpha-blockers antagonised by NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when alpha-blockers given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Antidepressants: manufacturer of indoramin advises avoid

concomitant use with l MAOIS; enhanced hypotensive effect when alpha-blockers given with MAOIS

l Antifungals: plasma concentration of alfuzosin possibly increased by KETOCONAZOLE; plasma concentration of tamsulosin increased by l KETOCONAZOLE

▶ Antipsychotics: enhanced hypotensive effect when alpha- blockers given with ANTIPSYCHOTICS

l Antivirals: plasma concentration of doxazosin and tamsulosin possibly increased by BOCEPREVIR—manufacturer of boceprevir advises avoid concomitant use; plasma concentration of alfuzosin possibly increased by

l RITONAVIR—avoid concomitant use; avoidance of alfuzosin advised by manufacturer of l TELAPREVIR

▶ Anxiolytics and Hypnotics: enhanced hypotensive and sedative effects when alpha-blockers given with ANXIOLYTICS AND HYPNOTICS

l Avanafil: enhanced hypotensive effect when alpha-blockers

given with l AVANAFIL—when patient is stable on the alpha blocker initiate avanafil at the lowest possible dose

l Beta-blockers: enhanced hypotensive effect when alpha- blockers given with l BETA-BLOCKERS, also increased risk of first-dose hypotension with post-synaptic alpha-blockers such as prazosin

l Calcium-channel Blockers: enhanced hypotensive effect when alpha-blockers given with l CALCIUM-CHANNEL BLOCKERS, also increased risk of first-dose hypotension with post-synaptic alpha-blockers such as prazosin; plasma concentration of tamsulosin increased by VERAPAMIL

▶ Cardiac Glycosides: prazosin increases plasma concentration of

DIGOXIN

▶ Clonidine: enhanced hypotensive effect when alpha-blockers given with CLONIDINE

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Alpha-blockers (continued)

l Cobicistat: plasma concentration of alfuzosin possibly increased by l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

▶ Corticosteroids: hypotensive effect of alpha-blockers antagonised by CORTICOSTEROIDS

▶ Cytotoxics: avoidance of alfuzosin advised by manufacturer of

IDELALISIB

▶ Diazoxide: enhanced hypotensive effect when alpha-blockers given with DIAZOXIDE

l Diuretics: enhanced hypotensive effect when alpha-blockers given with l DIURETICS, also increased risk of first-dose hypotension with post-synaptic alpha-blockers such as prazosin

▶ Dopaminergics: enhanced hypotensive effect when alpha- blockers given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Methyldopa: enhanced hypotensive effect when alpha- blockers given with METHYLDOPA

l Moxisylyte: possible severe postural hypotension when alpha- blockers given with l MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when alpha-blockers given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when alpha- blockers given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when alpha-blockers given with NITRATES

▶ Oestrogens: hypotensive effect of alpha-blockers antagonised by OESTROGENS

▶ Prostaglandins: enhanced hypotensive effect when alpha- blockers given with ALPROSTADIL

l Sildenafil: enhanced hypotensive effect when alpha-blockers given with l SILDENAFIL (avoid alpha-blockers for 4 hours after sildenafil)—when patient is stable on the alpha blocker initiate sildenafil at the lowest possible dose

l Sympathomimetics: avoid concomitant use of tolazoline with

l ADRENALINE (EPINEPHRINE) or l DOPAMINE

l Tadalafil: enhanced hypotensive effect when alpha-blockers given with l TADALAFIL—when patient is stable on the alpha blocker initiate tadalafil at the lowest possible dose; enhanced hypotensive effect when doxazosin given with

l TADALAFIL—manufacturer of tadalafil advises avoid concomitant use

l Ulcer-healing Drugs: effects of tolazoline antagonised by

l CIMETIDINE and l RANITIDINE

l Vardenafil: enhanced hypotensive effect when alpha-blockers given with l VARDENAFIL—when patient is stable on the alpha blocker initiate vardenafil at the lowest possible dose— separate doses by 6 hours (except with tamsulosin)

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when alpha-blockers given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Alpha-blockers (post-synaptic) *see* Alpha-blockers Alprazolam *see* Anxiolytics and Hypnotics Alprostadil *see* Prostaglandins

Aluminium Hydroxide *see* Antacids

Amantadine

▶ Antimalarials: plasma concentration of amantadine possibly increased by QUININE

▶ Antipsychotics: increased risk of extrapyramidal side-effects when amantadine given with ANTIPSYCHOTICS

▶ Bupropion: increased risk of side-effects when amantadine given with BUPROPION

l Memantine: increased risk of CNS toxicity when amantadine given with l MEMANTINE (manufacturer of memantine advises avoid concomitant use); effects of dopaminergics possibly enhanced by MEMANTINE

▶ Methyldopa: increased risk of extrapyramidal side-effects when amantadine given with METHYLDOPA; antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Tetrabenazine: increased risk of extrapyramidal side-effects when amantadine given with TETRABENAZINE

Ambrisentan

▶ Antibacterials: plasma concentration of ambrisentan possibly increased by RIFAMPICIN

Ambrisentan (continued)

l Ciclosporin: plasma concentration of ambrisentan increased by

l CICLOSPORIN (see under Ambrisentan, p. 162)

Amikacin *see* Aminoglycosides Amiloride *see* Diuretics Aminoglycosides

▶ Agalsidase Alfa and Beta: gentamicin possibly inhibits effects of AGALSIDASE ALFA AND BETA (manufacturers of agalsidase alfa and beta advise avoid concomitant use)

▶ Analgesics: plasma concentration of amikacin and gentamicin in neonates possibly increased by INDOMETACIN

l Antibacterials: neomycin reduces absorption of PHENOXYMETHYLPENICILLIN; increased risk of nephrotoxicity when aminoglycosides given with COLISTIMETHATE SODIUM or POLYMYXINS; increased risk of nephrotoxicity and ototoxicity when aminoglycosides given with CAPREOMYCIN or

l VANCOMYCIN; possible increased risk of nephrotoxicity when aminoglycosides given with CEPHALOSPORINS

l Anticoagulants: experience in anticoagulant clinics suggests that INR possibly altered when neomycin (given for local action on gut) is given with l COUMARINS or l PHENINDIONE

▶ Antidiabetics: neomycin possibly enhances hypoglycaemic effect of ACARBOSE, also severity of gastro-intestinal effects increased

▶ Antifungals: increased risk of nephrotoxicity when aminoglycosides given with AMPHOTERICIN

▶ Bisphosphonates: increased risk of hypocalcaemia when aminoglycosides given with BISPHOSPHONATES

▶ Cardiac Glycosides: gentamicin possibly increases plasma concentration of DIGOXIN; neomycin reduces absorption of DIGOXIN

l Ciclosporin: increased risk of nephrotoxicity when

aminoglycosides given with l CICLOSPORIN

l Cytotoxics: neomycin possibly reduces absorption of METHOTREXATE; neomycin reduces bioavailability of SORAFENIB; increased risk of nephrotoxicity and possibly of ototoxicity when aminoglycosides given with l PLATINUM COMPOUNDS

l Diuretics: increased risk of otoxicity when aminoglycosides given with l LOOP DIURETICS

▶ Mannitol: manufacturer of tobramycin advises avoid concomitant use with MANNITOL

l Muscle Relaxants: aminoglycosides enhance effects of l NON-

DEPOLARISING MUSCLE RELAXANTS and l SUXAMETHONIUM

l Parasympathomimetics: aminoglycosides antagonise effects of

l NEOSTIGMINE and l PYRIDOSTIGMINE

l Tacrolimus: increased risk of nephrotoxicity when aminoglycosides given with l TACROLIMUS

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

▶ Vitamins: neomycin possibly reduces absorption of VITAMIN A

Aminophylline

▶ Allopurinol: plasma concentration of aminophylline possibly increased by ALLOPURINOL

▶ Anaesthetics, General: increased risk of convulsions when aminophylline given with KETAMINE

▶ Anti-arrhythmics: aminophylline antagonises anti-arrhythmic effect of ADENOSINE—manufacturer of adenosine advises avoid aminophylline for 24 hours before adenosine; plasma concentration of aminophylline increased by PROPAFENONE

l Antibacterials: plasma concentration of aminophylline possibly increased by CLARITHROMYCIN and ISONIAZID; plasma concentration of aminophylline increased by l ERYTHROMYCIN (also aminophylline may reduce absorption of *oral* erythromycin); plasma concentration of aminophylline increased by l CIPROFLOXACIN and l NORFLOXACIN; metabolism of aminophylline accelerated by RIFAMPICIN (reduced plasma concentration); possible increased risk of convulsions when aminophylline given with l QUINOLONES

l Antidepressants: plasma concentration of aminophylline increased by l FLUVOXAMINE (concomitant use should usually be avoided, but where not possible halve aminophylline dose and monitor plasma-aminophylline concentration); plasma concentration of aminophylline possibly reduced by ST JOHN’S WORT

Aminophylline (continued)

l Antiepileptics: metabolism of aminophylline accelerated by

CARBAMAZEPINE, l PHENOBARBITAL and l PRIMIDONE (reduced

effect); plasma concentration of both drugs reduced when aminophylline given with l FOSPHENYTOIN and l PHENYTOIN

l Antifungals: plasma concentration of aminophylline possibly increased by l FLUCONAZOLE and l KETOCONAZOLE

l Antivirals: plasma concentration of aminophylline possibly increased by ACICLOVIR and VALACICLOVIR; metabolism of aminophylline accelerated by l RITONAVIR (reduced plasma concentration)

▶ Anxiolytics and Hypnotics: aminophylline possibly reduces effects of BENZODIAZEPINES

▶ Caffeine citrate: avoidance of aminophylline advised by manufacturer of CAFFEINE CITRATE

l Calcium-channel Blockers: plasma concentration of aminophylline possibly increased by l CALCIUM-CHANNEL BLOCKERS (enhanced effect); plasma concentration of aminophylline increased by DILTIAZEM; plasma concentration of aminophylline increased by l VERAPAMIL (enhanced effect)

▶ Corticosteroids: increased risk of hypokalaemia when aminophylline given with CORTICOSTEROIDS

▶ Cytotoxics: plasma concentration of aminophylline possibly increased by METHOTREXATE

l Deferasirox: plasma concentration of aminophylline increased by l DEFERASIROX (consider reducing dose of aminophylline)

▶ Disulfiram: metabolism of aminophylline inhibited by

DISULFIRAM (increased risk of toxicity)

▶ Diuretics: increased risk of hypokalaemia when aminophylline given with ACETAZOLAMIDE, LOOP DIURETICS or THIAZIDES AND RELATED DIURETICS

▶ Doxapram: increased CNS stimulation when aminophylline given with DOXAPRAM

l Interferons: metabolism of aminophylline inhibited by

l INTERFERON ALFA and l PEGINTERFERON ALFA (consider

reducing dose of aminophylline)

▶ Leukotriene Receptor Antagonists: plasma concentration of aminophylline possibly increased by ZAFIRLUKAST, also plasma concentration of zafirlukast reduced

▶ Lithium: aminophylline increases excretion of LITHIUM

(reduced plasma concentration)

▶ Oestrogens: plasma concentration of aminophylline increased by OESTROGENS (consider reducing dose of aminophylline)

▶ Pentoxifylline: plasma concentration of aminophylline increased by PENTOXIFYLLINE

▶ Roflumilast: avoidance of aminophylline advised by manufacturer of ROFLUMILAST

▶ Sulfinpyrazone: plasma concentration of aminophylline reduced by SULFINPYRAZONE

▶ Sympathomimetics: manufacturer of aminophylline advises avoid concomitant use with EPHEDRINE in children

▶ Sympathomimetics, Beta2: increased risk of hypokalaemia when aminophylline given with high doses of BETA2 SYMPATHOMIMETICS

l Ulcer-healing Drugs: metabolism of aminophylline inhibited by l CIMETIDINE (increased plasma concentration); absorption of aminophylline possibly reduced by SUCRALFATE (give at least 2 hours apart)

▶ Vaccines: plasma concentration of aminophylline possibly increased by INFLUENZA VACCINE

Aminosalicylates *see* individual drugs

Amiodarone

NOTE Amiodarone has a long half-life; there is a potential for drug interactions to occur for several weeks (or even months) after treatment with it has been stopped

▶ Agalsidase Alfa and Beta: amiodarone possibly inhibits effects of AGALSIDASE ALFA AND BETA (manufacturers of agalsidase alfa and beta advise avoid concomitant use)

▶ Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with BUPIVACAINE, LEVOBUPIVACAINE,

PRILOCAINE or ROPIVACAINE

l Anti-arrhythmics: increased myocardial depression when anti- arrhythmics given with other l ANTI-ARRHYTHMICS; increased risk of ventricular arrhythmias when amiodarone given with l DISOPYRAMIDE or l DRONEDARONE—avoid concomitant use;

Amiodarone

l Anti-arrhythmics (continued)

Interactions | Appendix 1

amiodarone increases plasma concentration of l FLECAINIDE

(halve dose of flecainide)

l Antibacterials: increased risk of ventricular arrhythmias when amiodarone given with *parenteral* l ERYTHROMYCIN—avoid concomitant use; increased risk of ventricular arrhythmias when amiodarone given with l LEVOFLOXACIN or

l MOXIFLOXACIN—avoid concomitant use; possible increased risk of ventricular arrhythmias when amiodarone given with SULFAMETHOXAZOLE and TRIMETHOPRIM (as co-trimoxazole)— manufacturer of amiodarone advises avoid concomitant use of co-trimoxazole; increased risk of ventricular arrhythmias when amiodarone given with l DELAMANID; avoidance of amiodarone advised by manufacturer of FIDAXOMICIN; possible increased risk of ventricular arrhythmias when amiodarone given with l TELITHROMYCIN

l Anticoagulants: amiodarone inhibits metabolism of

l COUMARINS and l PHENINDIONE (enhanced anticoagulant effect); amiodarone increases plasma concentration of

l DABIGATRAN (see under Dabigatran Etexilate, p. 117)

l Antidepressants: avoidance of amiodarone advised by manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when amiodarone given with l TRICYCLICS—avoid concomitant use

l Antiepileptics: amiodarone inhibits metabolism of

l FOSPHENYTOIN and l PHENYTOIN (increased plasma concentration)

l Antihistamines: increased risk of ventricular arrhythmias when amiodarone given with l MIZOLASTINE—avoid concomitant use

l Antimalarials: avoidance of amiodarone advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE (risk of ventricular arrhythmias); avoidance of amiodarone advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when amiodarone given with l CHLOROQUINE,

l HYDROXYCHLOROQUINE, l MEFLOQUINE or l QUININE—avoid

concomitant use

l Antimuscarinics: increased risk of ventricular arrhythmias when amiodarone given with l TOLTERODINE

l Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with

l ANTIPSYCHOTICS that prolong the QT interval; increased risk of ventricular arrhythmias when amiodarone given with

l BENPERIDOL—manufacturer of benperidol advises avoid concomitant use; increased risk of ventricular arrhythmias when amiodarone given with l AMISULPRIDE, l DROPERIDOL, l HALOPERIDOL, l PHENOTHIAZINES, l PIMOZIDE or

l ZUCLOPENTHIXOL—avoid concomitant use; increased risk of ventricular arrhythmias when amiodarone given with

l SULPIRIDE

l Antivirals: plasma concentration of amiodarone possibly increased by l ATAZANAVIR; possible increased risk of bradycardia when amiodarone given with l DACLATASVIR and l SIMEPREVIR (with sofosbuvir)—see under Amiodarone,

p. 88; plasma concentration of amiodarone possibly increased by l FOSAMPRENAVIR (increased risk of ventricular arrhythmias—avoid concomitant use); plasma concentration of amiodarone possibly increased by l INDINAVIR—avoid concomitant use; plasma concentration of amiodarone increased by l RITONAVIR (increased risk of ventricular arrhythmias—avoid concomitant use); increased risk of ventricular arrhythmias when amiodarone given with

l SAQUINAVIR—avoid concomitant use; possible increased risk of bradycardia when amiodarone given with l SOFOSBUVIR— see under Amiodarone, p. 88; avoidance of amiodarone advised by manufacturer of l TELAPREVIR (risk of ventricular arrhythmias)

l Atomoxetine: increased risk of ventricular arrhythmias when amiodarone given with l ATOMOXETINE

l Beta-blockers: increased risk of bradycardia, AV block and myocardial depression when amiodarone given with l BETA- BLOCKERS; increased myocardial depression when anti-

Interactions | Appendix 1

Amiodarone

l Beta-blockers (continued)

arrhythmics given with l BETA-BLOCKERS; increased risk of ventricular arrhythmias when amiodarone given with

l SOTALOL—avoid concomitant use

l Calcium-channel Blockers: increased risk of bradycardia, AV block and myocardial depression when amiodarone given with l DILTIAZEM or l VERAPAMIL

l Cardiac Glycosides: amiodarone increases plasma concentration of l DIGOXIN (halve dose of digoxin)

▶ Ciclosporin: amiodarone possibly increases plasma concentration of CICLOSPORIN

l Cobicistat: plasma concentration of amiodarone possibly increased by l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Colchicine: amiodarone possibly increases risk of l COLCHICINE

toxicity

l Cytotoxics: amiodarone possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of amiodarone by 6 to 12 hours; possible increased risk of ventricular arrhythmias when amiodarone given with l BOSUTINIB; amiodarone possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809); avoidance of amiodarone advised by manufacturer of IDELALISIB; possible increased risk of ventricular arrhythmias when amiodarone given with l VANDETANIB—avoid concomitant use; increased risk of ventricular arrhythmias when amiodarone given with l ARSENIC TRIOXIDE

▶ Diuretics: increased cardiac toxicity with amiodarone if hypokalaemia occurs with ACETAZOLAMIDE, LOOP DIURETICS or THIAZIDES AND RELATED DIURETICS; amiodarone increases plasma concentration of EPLERENONE (reduce dose of eplerenone)

l Fingolimod: possible increased risk of bradycardia when amiodarone given with l FINGOLIMOD

▶ Grapefruit Juice: plasma concentration of amiodarone increased by GRAPEFRUIT JUICE

l Ivabradine: increased risk of ventricular arrhythmias when amiodarone given with l IVABRADINE

l Lipid-regulating Drugs: increased risk of myopathy when amiodarone given with l SIMVASTATIN (see under Simvastatin,

p. 181); separating administration from amiodarone by 12 hours advised by manufacturer of LOMITAPIDE

l Lithium: manufacturer of amiodarone advises avoid concomitant use with l LITHIUM (risk of ventricular arrhythmias)

▶ Orlistat: plasma concentration of amiodarone possibly reduced by ORLISTAT

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when amiodarone given with l PENTAMIDINE ISETIONATE—avoid concomitant use

▶ Thyroid Hormones: amiodarone can affect serum concentrations of THYROID HORMONES—monitor thyroid function closely

▶ Ulcer-healing Drugs: plasma concentration of amiodarone increased by CIMETIDINE

Amisulpride *see* Antipsychotics Amitriptyline *see* Antidepressants, Tricyclic Amlodipine *see* Calcium-channel Blockers Amoxicillin *see* Penicillins

Amphotericin

NOTE Close monitoring required with concomitant administration of nephrotoxic drugs or cytotoxics

▶ Antibacterials: increased risk of nephrotoxicity when amphotericin given with AMINOGLYCOSIDES or POLYMYXINS; possible increased risk of nephrotoxicity when amphotericin given with VANCOMYCIN

▶ Antifungals: amphotericin reduces renal excretion and increases cellular uptake of FLUCYTOSINE (toxicity possibly increased); effects of amphotericin possibly antagonised by IMIDAZOLES and TRIAZOLES; plasma concentration of amphotericin possibly increased by MICAFUNGIN

l Cardiac Glycosides: hypokalaemia caused by amphotericin increases cardiac toxicity with l CARDIAC GLYCOSIDES

Amphotericin (continued)

l Ciclosporin: increased risk of nephrotoxicity when amphotericin given with l CICLOSPORIN

l Corticosteroids: increased risk of hypokalaemia when amphotericin given with l CORTICOSTEROIDS—avoid concomitant use unless corticosteroids needed to control reactions

l Cytotoxics: increased risk of ventricular arrhythmias when amphotericin given with l ARSENIC TRIOXIDE

▶ Diuretics: increased risk of hypokalaemia when amphotericin given with LOOP DIURETICS or THIAZIDES AND RELATED DIURETICS

▶ Pentamidine Isetionate: possible increased risk of nephrotoxicity when amphotericin given with PENTAMIDINE ISETIONATE

l Sodium Stibogluconate: possible increased risk of arrhythmias

when amphotericin given after l SODIUM STIBOGLUCONATE— manufacturer of sodium stibogluconate advises giving 14 days apart

l Tacrolimus: increased risk of nephrotoxicity when amphotericin given with l TACROLIMUS

Ampicillin *see* Penicillins

Anabolic Steroids

l Anticoagulants: anabolic steroids enhance anticoagulant effect of l COUMARINS and l PHENINDIONE

▶ Antidiabetics: anabolic steroids possibly enhance hypoglycaemic effect of ANTIDIABETICS

Anaesthetics, General

NOTE *See also* Surgery and Long-term Medication, under General Anaesthesia in BNF

▶ ACE Inhibitors: enhanced hypotensive effect when general anaesthetics given with ACE INHIBITORS

l Adrenergic Neurone Blockers: enhanced hypotensive effect when general anaesthetics given with l ADRENERGIC NEURONE BLOCKERS

l Alpha-blockers: enhanced hypotensive effect when general

anaesthetics given with l ALPHA-BLOCKERS

▶ Aminophylline: increased risk of convulsions when ketamine given with AMINOPHYLLINE

▶ Analgesics: metabolism of etomidate inhibited by FENTANYL (consider reducing dose of etomidate); effects of thiopental possibly enhanced by ASPIRIN; effects of intravenous general anaesthetics and volatile liquid general anaesthetics possibly enhanced by OPIOID ANALGESICS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when general anaesthetics given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antibacterials: increased risk of hepatotoxicity when isoflurane given with ISONIAZID; effects of thiopental enhanced by SULFONAMIDES; hypersensitivity-like reactions can occur when general anaesthetics given with *intravenous* VANCOMYCIN

▶ Antidepressants: increased risk of arrhythmias and

hypotension when general anaesthetics given with TRICYCLICS

l Antipsychotics: enhanced hypotensive effect when general anaesthetics given with l ANTIPSYCHOTICS; effects of thiopental enhanced by DROPERIDOL

▶ Anxiolytics and Hypnotics: increased sedative effect when general anaesthetics given with ANXIOLYTICS AND HYPNOTICS

▶ Beta-blockers: enhanced hypotensive effect when general anaesthetics given with BETA-BLOCKERS

l Calcium-channel Blockers: enhanced hypotensive effect when general anaesthetics or isoflurane given with CALCIUM- CHANNEL BLOCKERS; general anaesthetics enhance hypotensive effect of l VERAPAMIL (also AV delay)

▶ Clonidine: enhanced hypotensive effect when general anaesthetics given with CLONIDINE

l Cytotoxics: nitrous oxide increases antifolate effect of

l METHOTREXATE—avoid concomitant use

▶ Diazoxide: enhanced hypotensive effect when general anaesthetics given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when general anaesthetics given with DIURETICS

l Dopaminergics: increased risk of arrhythmias when volatile liquid general anaesthetics given with l CO-BENELDOPA, l CO- CARELDOPA or l LEVODOPA

Anaesthetics, General (continued)

l Doxapram: increased risk of arrhythmias when volatile liquid general anaesthetics given with l DOXAPRAM (avoid doxapram for at least 10 minutes after volatile liquid general anaesthetics)

l Memantine: increased risk of CNS toxicity when ketamine given with l MEMANTINE (manufacturer of memantine advises avoid concomitant use)

▶ Methyldopa: enhanced hypotensive effect when general anaesthetics given with METHYLDOPA

▶ Metoclopramide: effects of thiopental enhanced by

METOCLOPRAMIDE

▶ Moxonidine: enhanced hypotensive effect when general anaesthetics given with MOXONIDINE

l Muscle Relaxants: increased risk of myocardial depression and bradycardia when propofol given with l SUXAMETHONIUM; volatile liquid general anaesthetics enhance effects of NON- DEPOLARISING MUSCLE RELAXANTS and SUXAMETHONIUM;

ketamine enhances effects of ATRACURIUM

▶ Nitrates: enhanced hypotensive effect when general anaesthetics given with NITRATES

▶ Oxytocin: oxytocic effect possibly reduced, also enhanced hypotensive effect and risk of arrhythmias when volatile liquid general anaesthetics given with OXYTOCIN

l Sympathomimetics: manufacturer of isoflurane advises avoid concomitant use with l SYMPATHOMIMETICS (risk of ventricular arrhythmias); increased risk of arrhythmias when volatile liquid general anaesthetics given with l ADRENALINE (EPINEPHRINE) or l NORADRENALINE (NOREPINEPHRINE);

increased risk of hypertension when volatile liquid general anaesthetics given with l METHYLPHENIDATE

▶ Theophylline: increased risk of convulsions when ketamine given with THEOPHYLLINE

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when general anaesthetics given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Anaesthetics, General (intravenous) *see* Anaesthetics, General

Anaesthetics, General (volatile liquids) *see* Anaesthetics, General

Anaesthetics, Local *see* Bupivacaine, Chloroprocaine, Levobupivacaine, Lidocaine, Prilocaine, and Ropivacaine

Anagrelide

l Cilostazol: manufacturer of anagrelide advises avoid concomitant use with l CILOSTAZOL

l Phosphodiesterase Type-3 Inhibitors: manufacturer of anagrelide advises avoid concomitant use with l ENOXIMONE and

l MILRINONE

Anakinra

l Cytotoxics: avoid concomitant use of anakinra with

l ADALIMUMAB, l CERTOLIZUMAB PEGOL, l GOLIMUMAB or

l INFLIXIMAB

l Etanercept: avoid concomitant use of anakinra with

l ETANERCEPT

l Vaccines: risk of generalised infections when anakinra given with live l VACCINES—avoid concomitant use

Analgesics *see* Aspirin, Nefopam, NSAIDs, Opioid Analgesics, and Paracetamol

Angiotensin-II Receptor Antagonists

l ACE Inhibitors: increased risk of hyperkalaemia, hypotension, and impaired renal function when angiotensin-II receptor antagonists given with l ACE INHIBITORS—avoid concomitant use

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when angiotensin-II receptor antagonists given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when angiotensin-II receptor antagonists given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when angiotensin-II receptor antagonists given with ALDESLEUKIN

l Aliskiren: increased risk of hyperkalaemia, hypotension, and impaired renal function when angiotensin-II receptor antagonists given with l ALISKIREN—avoid concomitant use; irbesartan possibly reduces plasma concentration of ALISKIREN

Angiotensin-II Receptor Antagonists (continued)

▶ Alpha-blockers: enhanced hypotensive effect when angiotensin-II receptor antagonists given with ALPHA- BLOCKERS

Interactions | Appendix 1

▶ Anaesthetics, General: enhanced hypotensive effect when angiotensin-II receptor antagonists given with GENERAL ANAESTHETICS

▶ Analgesics: increased risk of renal impairment when angiotensin-II receptor antagonists given with NSAIDS, also hypotensive effect antagonised

▶ Antibacterials: plasma concentration of losartan and its active metabolite reduced by RIFAMPICIN; possible increased risk of hyperkalaemia when angiotensin-II receptor antagonists given with TRIMETHOPRIM

▶ Anticoagulants: increased risk of hyperkalaemia when angiotensin-II receptor antagonists given with HEPARINS

▶ Antidepressants: hypotensive effect of angiotensin-II receptor antagonists possibly enhanced by MAOIS

▶ Antipsychotics: enhanced hypotensive effect when angiotensin-II receptor antagonists given with ANTIPSYCHOTICS

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when angiotensin-II receptor antagonists given with ANXIOLYTICS AND HYPNOTICS

▶ Beta-blockers: enhanced hypotensive effect when

angiotensin-II receptor antagonists given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when angiotensin-II receptor antagonists given with CALCIUM- CHANNEL BLOCKERS

l Ciclosporin: increased risk of hyperkalaemia when

angiotensin-II receptor antagonists given with l CICLOSPORIN

▶ Clonidine: enhanced hypotensive effect when angiotensin-II receptor antagonists given with CLONIDINE

▶ Corticosteroids: hypotensive effect of angiotensin-II receptor antagonists antagonised by CORTICOSTEROIDS

▶ Diazoxide: enhanced hypotensive effect when angiotensin-II receptor antagonists given with DIAZOXIDE

l Diuretics: enhanced hypotensive effect when angiotensin-II receptor antagonists given with l DIURETICS; increased risk of hyperkalaemia when angiotensin-II receptor antagonists given with l POTASSIUM-SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

▶ Dopaminergics: enhanced hypotensive effect when angiotensin-II receptor antagonists given with CO-BENELDOPA,

CO-CARELDOPA or LEVODOPA

l Lithium: angiotensin-II receptor antagonists reduce excretion of l LITHIUM (increased plasma concentration)

▶ Methyldopa: enhanced hypotensive effect when angiotensin-II receptor antagonists given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when angiotensin-II receptor antagonists given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when angiotensin-II receptor antagonists given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when angiotensin-II receptor antagonists given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when angiotensin-II receptor antagonists given with NITRATES

▶ Oestrogens: hypotensive effect of angiotensin-II receptor antagonists antagonised by OESTROGENS

l Potassium Salts: increased risk of hyperkalaemia when angiotensin-II receptor antagonists given with l POTASSIUM SALTS

▶ Prostaglandins: enhanced hypotensive effect when angiotensin-II receptor antagonists given with ALPROSTADIL

▶ Tacrolimus: increased risk of hyperkalaemia when angiotensin-II receptor antagonists given with TACROLIMUS

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when angiotensin-II receptor antagonists given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Antacids

NOTE Antacids should preferably not be taken at the same time as other drugs since they may impair absorption

▶ ACE Inhibitors: antacids possibly reduce absorption of ACE INHIBITORS; antacids reduce absorption of CAPTOPRIL, ENALAPRIL and FOSINOPRIL

Interactions | Appendix 1

Antacids (continued)

▶ Analgesics: antacids possibly reduce absorption of ACEMETACIN; alkaline urine due to some antacids increases excretion of ASPIRIN

▶ Anthelmintics: sodium bicarbonate increases the excretion of

DIETHYLCARBAMAZINE

▶ Antibacterials: antacids reduce absorption of AZITHROMYCIN, CEFACLOR, CIPROFLOXACIN, ISONIAZID, LEVOFLOXACIN, MOXIFLOXACIN, NORFLOXACIN, OFLOXACIN, RIFAMPICIN and

TETRACYCLINES; avoid concomitant use of antacids with METHENAMINE; oral magnesium salts (as magnesium trisilicate) reduce absorption of NITROFURANTOIN

▶ Antiepileptics: antacids reduce absorption of FOSPHENYTOIN, GABAPENTIN and PHENYTOIN

▶ Antifungals: antacids reduce absorption of ITRACONAZOLE and

KETOCONAZOLE

▶ Antihistamines: antacids reduce absorption of FEXOFENADINE

▶ Antimalarials: antacids reduce absorption of CHLOROQUINE and HYDROXYCHLOROQUINE; oral magnesium salts (as magnesium trisilicate) reduce absorption of PROGUANIL

▶ Antipsychotics: antacids reduce absorption of PHENOTHIAZINES

and SULPIRIDE

▶ Antivirals: antacids reduce absorption of ATAZANAVIR (give at least 2 hours before or 1 hour after antacids); aluminium hydroxide reduces absorption of DOLUTEGRAVIR— manufacturer of dolutegravir advises give at least 2 hours before or 6 hours after aluminium hydroxide; oral magnesium salts reduce absorption of DOLUTEGRAVIR— manufacturer of dolutegravir advises give at least 2 hours before or 6 hours after oral magnesium salts; aluminium hydroxide reduces absorption of ELVITEGRAVIR (give at least 4 hours apart); oral magnesium salts reduce absorption of ELVITEGRAVIR (give at least 4 hours apart); aluminium hydroxide reduces plasma concentration of RALTEGRAVIR— manufacturer of raltegravir advises avoid concomitant use; oral magnesium salts reduce plasma concentration of RALTEGRAVIR—manufacturer of raltegravir advises avoid concomitant use; manufacturer of rilpivirine advises give antacids 2 hours before or 4 hours after RILPIVIRINE; antacids reduce absorption of TIPRANAVIR (give at least 2 hours apart)

▶ Bile Acids: antacids possibly reduce absorption of BILE ACIDS

▶ Bisphosphonates: antacids reduce absorption of

BISPHOSPHONATES

▶ Cardiac Glycosides: antacids possibly reduce absorption of

DIGOXIN

▶ Corticosteroids: antacids reduce absorption of DEFLAZACORT

l Cytotoxics: aluminium hydroxide and oral magnesium salts possibly reduce absorption of ESTRAMUSTINE—manufacturer of estramustine advises avoid concomitant administration; separating administration with antacids by about 12 hours advised by manufacturer of BOSUTINIB; antacids possibly reduce plasma concentration of l ERLOTINIB—give antacids at least 4 hours before or 2 hours after erlotinib

▶ Deferasirox: antacids containing aluminium possibly reduce absorption of DEFERASIROX (manufacturer of deferasirox advises avoid concomitant use)

▶ Deferiprone: antacids containing aluminium possibly reduce absorption of DEFERIPRONE (manufacturer of deferiprone advises avoid concomitant use)

▶ Dipyridamole: antacids possibly reduce absorption of

DIPYRIDAMOLE

▶ Eltrombopag: antacids reduce absorption of ELTROMBOPAG

(give at least 4 hours apart)

▶ Folates: antacids possibly reduce absorption of FOLIC ACID

(manufacturer of folic acid advises give at least 2 hours apart)

▶ Iron Salts: oral magnesium salts (as magnesium trisilicate) reduce absorption of *oral* IRON SALTS

▶ Lipid-regulating Drugs: antacids reduce absorption of

ROSUVASTATIN

▶ Lithium: sodium bicarbonate increases excretion of LITHIUM

(reduced plasma concentration)

▶ Mycophenolate: antacids reduce absorption of MYCOPHENOLATE

▶ Penicillamine: antacids reduce absorption of PENICILLAMINE

▶ Polystyrene Sulfonate Resins: risk of intestinal obstruction when aluminium hydroxide given with POLYSTYRENE

Antacids

Polystyrene Sulfonate Resins (continued)

SULFONATE RESINS; risk of metabolic alkalosis when oral magnesium salts given with POLYSTYRENE SULFONATE RESINS

▶ Riociguat: antacids reduce absorption of RIOCIGUAT (give at least 2 hours before or 1 hour after riociguat)

▶ Sympathomimetics: aluminium hydroxide possibly increases absorption of PSEUDOEPHEDRINE

▶ Thyroid Hormones: antacids possibly reduce absorption of

LEVOTHYROXINE

▶ Ulcer-healing Drugs: antacids possibly reduce absorption of

LANSOPRAZOLE

Antazoline *see* Antihistamines Anthelmintics *see* individual drugs Anthrax Vaccine *see* Vaccines

Anti-D Immunoglobulins *see* Immunoglobulins

Anti-arrhythmics *see* Adenosine, Amiodarone, Disopyramide, Dronedarone, Flecainide, Lidocaine, and Propafenone

Antibacterials *see* individual drugs

Antibiotics (cytotoxic) *see* Bleomycin, Doxorubicin, Epirubicin, Idarubicin, Mitomycin, Mitoxantrone, and Pixantrone

Anticoagulants *see* Apixaban, Argatroban, Bivalirudin, Coumarins, Dabigatran, Danaparoid, Fondaparinux, Heparins, Phenindione, and Rivaroxaban

Antidepressants *see* Agomelatine; Antidepressants, SSRI; Antidepressants, Tricyclic; Antidepressants, Tricyclic (related); MAOIs; Mirtazapine; Moclobemide; Reboxetine; St John’s Wort; Venlafaxine

Antidepressants, Noradrenaline Re-uptake Inhibitors *see*

Reboxetine

Antidepressants, SSRI

NOTE *see also* Dapoxetine

▶ Alcohol: sedative effects possibly increased when SSRIs given with ALCOHOL

l Aminophylline: fluvoxamine increases plasma concentration of l AMINOPHYLLINE (concomitant use should usually be avoided, but where not possible halve aminophylline dose and monitor plasma-aminophylline concentration)

▶ Anaesthetics, Local: fluvoxamine inhibits metabolism of

ROPIVACAINE—avoid prolonged administration of ropivacaine

l Analgesics: increased risk of bleeding when SSRIs given with l NSAIDS or l ASPIRIN; possible increased serotonergic effects when SSRIs given with FENTANYL; fluoxetine, fluvoxamine, paroxetine and sertraline possibly increase plasma concentration of METHADONE; increased risk of CNS toxicity when SSRIs given with l TRAMADOL

l Anti-arrhythmics: manufacturer of citalopram and escitalopram advises avoid concomitant use with

l AMIODARONE (risk of ventricular arrhythmias); manufacturer of citalopram and escitalopram advises avoid concomitant use with l DISOPYRAMIDE (risk of ventricular arrhythmias); manufacturer of citalopram and escitalopram advises avoid concomitant use with l DRONEDARONE (risk of ventricular arrhythmias); fluoxetine increases plasma concentration of FLECAINIDE; fluoxetine and paroxetine possibly inhibit metabolism of PROPAFENONE

l Antibacterials: manufacturer of citalopram and escitalopram advises avoid concomitant use with *intravenous*

l ERYTHROMYCIN (risk of ventricular arrhythmias); manufacturer of citalopram and escitalopram advises avoid concomitant use with l MOXIFLOXACIN (risk of ventricular arrhythmias); possible increased risk of ventricular arrhythmias when citalopram given with l TELITHROMYCIN

l Anticoagulants: SSRIs possibly enhance anticoagulant effect of l COUMARINS; possible increased risk of bleeding when SSRIs given with l DABIGATRAN

l Antidepressants: avoidance of fluvoxamine advised by manufacturer of l REBOXETINE; possible increased serotonergic effects when SSRIs given with DULOXETINE; fluvoxamine inhibits metabolism of l DULOXETINE—avoid concomitant use; citalopram, escitalopram, fluvoxamine, paroxetine or sertraline should not be started until 2 weeks after stopping l MAOIS, also MAOIs should not be started until at least 1 week after stopping citalopram, escitalopram, fluvoxamine, paroxetine or sertraline; fluoxetine should not

Antidepressants, SSRI

l Antidepressants (continued)

be started until 2 weeks after stopping l MAOIS, also MAOIs should not be started until at least 5 weeks after stopping fluoxetine; CNS effects of SSRIs increased by l MAOIS (risk of serious toxicity); increased risk of CNS toxicity when escitalopram given with l MOCLOBEMIDE, preferably avoid concomitant use; after stopping citalopram, fluvoxamine, paroxetine or sertraline do not start l MOCLOBEMIDE for at least 1 week; after stopping fluoxetine do not start

l MOCLOBEMIDE for 5 weeks; increased serotonergic effects when SSRIs given with l ST JOHN’S WORT—avoid concomitant use; fluvoxamine inhibits metabolism of l AGOMELATINE (increased plasma concentration); possible increased serotonergic effects when fluoxetine or fluvoxamine given with MIRTAZAPINE; SSRIs increase plasma concentration of some l TRICYCLICS; manufacturer of citalopram and escitalopram advises avoid concomitant use with l TRICYCLICS (risk of ventricular arrhythmias)

l Antiepileptics: SSRIs antagonise anticonvulsant effect of

l ANTIEPILEPTICS (convulsive threshold lowered); fluoxetine and fluvoxamine increase plasma concentration of

l CARBAMAZEPINE; fluoxetine and fluvoxamine increase plasma concentration of l FOSPHENYTOIN; plasma concentration of sertraline possibly reduced by FOSPHENYTOIN and PHENYTOIN, also plasma concentration of fosphenytoin and phenytoin possibly increased; plasma concentration of paroxetine reduced by FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE; fluoxetine and fluvoxamine increase plasma concentration of l PHENYTOIN

▶ Antifungals: plasma concentration of paroxetine possibly increased by TERBINAFINE

l Antihistamines: manufacturer of citalopram and escitalopram advises avoid concomitant use with l MIZOLASTINE (risk of ventricular arrhythmias); antidepressant effect of SSRIs possibly antagonised by CYPROHEPTADINE

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and

l ARTENIMOL WITH PIPERAQUINE; possible increased risk of ventricular arrhythmias when citalopram or escitalopram given with l ARTEMETHER WITH LUMEFANTRINE—avoid concomitant use; possible increased risk of ventricular arrhythmias when citalopram or escitalopram given with l ARTENIMOL WITH PIPERAQUINE—avoid concomitant use; possible increased risk of ventricular arrhythmias when citalopram and escitalopram given with l CHLOROQUINE; possible increased risk of ventricular arrhythmias when citalopram or escitalopram given with l QUININE—avoid concomitant use

▶ Antimuscarinics: paroxetine increases plasma concentration of

DARIFENACIN and PROCYCLIDINE

l Antipsychotics: avoidance of fluoxetine, fluvoxamine and sertraline advised by manufacturer of l DROPERIDOL (risk of ventricular arrhythmias); manufacturer of citalopram and escitalopram advises avoid concomitant use with

l HALOPERIDOL (risk of ventricular arrhythmias); fluoxetine increases plasma concentration of l CLOZAPINE,

l HALOPERIDOL and RISPERIDONE; fluvoxamine possibly increases plasma concentration of ASENAPINE and HALOPERIDOL; paroxetine inhibits metabolism of PERPHENAZINE (reduce dose of perphenazine); fluoxetine and paroxetine possibly increase plasma concentration of

l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); plasma concentration of paroxetine possibly increased by ASENAPINE; fluvoxamine, paroxetine and sertraline increase plasma concentration of l CLOZAPINE; citalopram possibly increases plasma concentration of CLOZAPINE (increased risk of toxicity); fluvoxamine increases plasma concentration of OLANZAPINE; manufacturer of citalopram and escitalopram advises avoid concomitant use with l PHENOTHIAZINES (risk of ventricular arrhythmias); manufacturer of citalopram and escitalopram advises avoid concomitant use with l PIMOZIDE (risk of ventricular arrhythmias); SSRIs possibly increase plasma concentration of l PIMOZIDE (increased risk of ventricular

Antidepressants, SSRI

l Antipsychotics (continued)

Interactions | Appendix 1

arrhythmias—avoid concomitant use); paroxetine possibly increases plasma concentration of RISPERIDONE (increased risk of toxicity)

l Antivirals: plasma concentration of paroxetine and sertraline possibly reduced by DARUNAVIR; plasma concentration of SSRIs possibly increased by l RITONAVIR; plasma concentration of paroxetine possibly reduced by RITONAVIR

l Anxiolytics and Hypnotics: fluoxetine increases plasma concentration of ALPRAZOLAM; fluvoxamine increases plasma concentration of some BENZODIAZEPINES; fluvoxamine increases plasma concentration of l MELATONIN—avoid concomitant use; sedative effects possibly increased when sertraline given with ZOLPIDEM

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE; fluoxetine and paroxetine possibly inhibit metabolism of ATOMOXETINE

l Beta-blockers: citalopram and escitalopram increase plasma concentration of METOPROLOL; paroxetine possibly increases the plasma concentration of l METOPROLOL—increased risk of AV block (manufacturer of paroxetine advises avoid concomitant use in cardiac insufficiency); fluvoxamine increases plasma concentration of PROPRANOLOL; increased risk of ventricular arrhythmias when citalopram given with

l SOTALOL—avoid concomitant use; manufacturer of escitalopram advises avoid concomitant use with l SOTALOL (risk of ventricular arrhythmias)

▶ Bupropion: plasma concentration of citalopram possibly increased by BUPROPION

▶ Calcium-channel Blockers: fluoxetine possibly inhibits metabolism of NIFEDIPINE (increased plasma concentration)

l Clopidogrel: fluoxetine and fluvoxamine possibly reduce antiplatelet effect of l CLOPIDOGREL

l Dapoxetine: possible increased risk of serotonergic effects when SSRIs given with l DAPOXETINE (manufacturer of dapoxetine advises SSRIs should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping SSRIs)

l Dopaminergics: increased risk of CNS toxicity when SSRIs given with l RASAGILINE; fluvoxamine should not be started until 2 weeks after stopping l RASAGILINE; fluoxetine should not be started until 2 weeks after stopping l RASAGILINE, also rasagiline should not be started until at least 5 weeks after stopping fluoxetine; avoidance of citalopram and escitalopram advised by manufacturer of SELEGILINE; increased risk of hypertension and CNS excitation when fluvoxamine or sertraline given with l SELEGILINE (selegiline should not be started until 1 week after stopping fluvoxamine or sertraline, avoid fluvoxamine or sertraline for 2 weeks after stopping selegiline); increased risk of hypertension and CNS excitation when paroxetine given with l SELEGILINE (selegiline should not be started until 2 weeks after stopping paroxetine, avoid paroxetine for 2 weeks after stopping selegiline); increased risk of hypertension and CNS excitation when fluoxetine given with l SELEGILINE (selegiline should not be started until 5 weeks after stopping fluoxetine, avoid fluoxetine for 2 weeks after stopping selegiline)

▶ Grapefruit Juice: plasma concentration of sertraline possibly increased by GRAPEFRUIT JUICE

l Hormone Antagonists: fluoxetine and paroxetine possibly inhibit metabolism of l TAMOXIFEN to active metabolite (avoid concomitant use)

l 5HT1-receptor Agonists: increased risk of CNS toxicity when citalopram given with l 5HT1 AGONISTS (manufacturer of citalopram advises avoid concomitant use); fluvoxamine inhibits the metabolism of FROVATRIPTAN; possible increased serotonergic effects when SSRIs given with NARATRIPTAN; CNS toxicity reported when sertraline given with

SUMATRIPTAN; increased risk of CNS toxicity when citalopram, escitalopram, fluoxetine, fluvoxamine or paroxetine given with l SUMATRIPTAN; fluvoxamine possibly inhibits metabolism of ZOLMITRIPTAN (reduce dose of zolmitriptan)

▶ 5HT3-receptor Antagonists: possible increased serotonergic effects when SSRIs given with 5HT3 ANTAGONISTS

Interactions | Appendix 1

Antidepressants, SSRI (continued)

▶ Lipid-regulating Drugs: separating administration from fluoxetine and fluvoxamine by 12 hours advised by manufacturer of LOMITAPIDE

l Lithium: Increased risk of CNS effects when SSRIs given with

l LITHIUM (lithium toxicity reported)

l Methylthioninium: risk of CNS toxicity when SSRIs given with l METHYLTHIONINIUM—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

▶ Metoclopramide: CNS toxicity reported when SSRIs given with

METOCLOPRAMIDE

l Muscle Relaxants: fluvoxamine increases plasma concentration of l TIZANIDINE (increased risk of toxicity)—avoid concomitant use

▶ Parasympathomimetics: paroxetine increases plasma concentration of GALANTAMINE

l Pentamidine Isetionate: manufacturer of citalopram and escitalopram advises avoid concomitant use with

l PENTAMIDINE ISETIONATE (risk of ventricular arrhythmias)

l Pirfenidone: fluvoxamine increases plasma concentration of l PIRFENIDONE—manufacturer of pirfenidone advises avoid concomitant use

l Pomalidomide: fluvoxamine increases plasma concentration of

l POMALIDOMIDE

▶ Ranolazine: paroxetine increases plasma concentration of

RANOLAZINE

▶ Roflumilast: fluvoxamine inhibits the metabolism of

ROFLUMILAST

▶ Sympathomimetics: metabolism of SSRIs possibly inhibited by

METHYLPHENIDATE

l Theophylline: fluvoxamine increases plasma concentration of l THEOPHYLLINE (concomitant use should usually be avoided, but where not possible halve theophylline dose and monitor plasma-theophylline concentration)

▶ Ticagrelor: possible increased risk of bleeding when citalopram, paroxetine or sertraline given with TICAGRELOR

▶ Ulcer-healing Drugs: plasma concentration of citalopram, escitalopram and sertraline increased by CIMETIDINE; fluvoxamine possibly increases plasma concentration of LANSOPRAZOLE; plasma concentration of escitalopram increased by OMEPRAZOLE

Antidepressants, SSRI (related) *see* Duloxetine and Venlafaxine

Antidepressants, Tricyclic

▶ Adrenergic Neurone Blockers: tricyclics antagonise hypotensive effect of ADRENERGIC NEURONE BLOCKERS

l Alcohol: increased sedative effect when tricyclics given with

l ALCOHOL

▶ Alpha2-adrenoceptor Stimulants: avoidance of tricyclics advised by manufacturer of APRACLONIDINE and BRIMONIDINE

▶ Anaesthetics, General: increased risk of arrhythmias and hypotension when tricyclics given with GENERAL ANAESTHETICS

l Analgesics: increased risk of CNS toxicity when tricyclics given

with l TRAMADOL; side-effects possibly increased when tricyclics given with NEFOPAM; sedative effects possibly increased when tricyclics given with OPIOID ANALGESICS

l Anti-arrhythmics: increased risk of ventricular arrhythmias when tricyclics given with l AMIODARONE—avoid concomitant use; increased risk of ventricular arrhythmias when tricyclics given with l DISOPYRAMIDE or l FLECAINIDE; avoidance of tricyclics advised by manufacturer of l DRONEDARONE (risk of ventricular arrhythmias); increased risk of arrhythmias when tricyclics given with l PROPAFENONE

l Antibacterials: increased risk of ventricular arrhythmias when tricyclics given with l MOXIFLOXACIN—avoid concomitant use; possible increased risk of ventricular arrhythmias when tricyclics that prolong the QT interval given with

l DELAMANID; possible increased risk of ventricular arrhythmias when tricyclics given with l TELITHROMYCIN

l Anticoagulants: tricyclics may enhance or reduce anticoagulant effect of l COUMARINS

l Antidepressants: avoidance of tricyclics advised by manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); possible increased serotonergic

Antidepressants, Tricyclic

l Antidepressants (continued)

effects when amitriptyline or clomipramine given with DULOXETINE; increased risk of hypertension and CNS excitation when tricyclics given with l MAOIS, tricyclics should not be started until 2 weeks after stopping MAOIs (3 weeks if starting clomipramine or imipramine), also MAOIs should not be started for at least 1–2 weeks after stopping tricyclics (3 weeks in the case of clomipramine or imipramine); after stopping tricyclics do not start

l MOCLOBEMIDE for at least 1 week; plasma concentration of some tricyclics increased by l SSRIS; plasma concentration of amitriptyline reduced by ST JOHN’S WORT

l Antiepileptics: tricyclics antagonise anticonvulsant effect of

l ANTIEPILEPTICS (convulsive threshold lowered); metabolism of tricyclics accelerated by l CARBAMAZEPINE (reduced plasma concentration and reduced effect); plasma concentration of tricyclics possibly reduced by l FOSPHENYTOIN and

l PHENYTOIN; metabolism of tricyclics possibly accelerated by l PHENOBARBITAL and l PRIMIDONE (reduced plasma concentration)

▶ Antifungals: plasma concentration of amitriptyline and nortriptyline possibly increased by FLUCONAZOLE; plasma concentration of tricyclics possibly increased by TERBINAFINE

▶ Antihistamines: increased antimuscarinic and sedative effects when tricyclics given with ANTIHISTAMINES

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

▶ Antimuscarinics: increased risk of antimuscarinic side-effects when tricyclics given with ANTIMUSCARINICS

l Antipsychotics: avoidance of tricyclics advised by manufacturer of l DROPERIDOL, l FLUPHENAZINE,

l HALOPERIDOL, l SULPIRIDE and l ZUCLOPENTHIXOL (risk of

ventricular arrhythmias); possible increased antimuscarinic side-effects when tricyclics given with CLOZAPINE; increased risk of antimuscarinic side-effects when tricyclics given with PHENOTHIAZINES; possible increased risk of ventricular arrhythmias when tricyclics given with l RISPERIDONE

l Antivirals: plasma concentration of tricyclics possibly increased by l RITONAVIR; increased risk of ventricular arrhythmias when tricyclics given with l SAQUINAVIR—avoid concomitant use

▶ Anxiolytics and Hypnotics: increased sedative effect when tricyclics given with ANXIOLYTICS AND HYPNOTICS

l Atomoxetine: increased risk of ventricular arrhythmias when tricyclics given with l ATOMOXETINE; possible increased risk of convulsions when antidepressants given with ATOMOXETINE

l Beta-blockers: plasma concentration of imipramine increased by LABETALOL and PROPRANOLOL; increased risk of ventricular arrhythmias when tricyclics given with l SOTALOL

▶ Bupropion: plasma concentration of tricyclics possibly increased by BUPROPION (possible increased risk of convulsions)

▶ Calcium-channel Blockers: plasma concentration of imipramine increased by DILTIAZEM and VERAPAMIL; plasma concentration of tricyclics possibly increased by DILTIAZEM and VERAPAMIL

▶ Cannabis Extract: possible increased risk of hypertension and tachycardia when tricyclics given with CANNABIS EXTRACT

l Clonidine: tricyclics antagonise hypotensive effect of

l CLONIDINE, also increased risk of hypertension on clonidine withdrawal

l Cytotoxics: increased risk of ventricular arrhythmias when amitriptyline or clomipramine given with l ARSENIC TRIOXIDE

l Dapoxetine: possible increased risk of serotonergic effects when tricyclics given with l DAPOXETINE (manufacturer of dapoxetine advises tricyclics should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping tricyclics)

▶ Disulfiram: metabolism of tricyclics inhibited by DISULFIRAM (increased plasma concentration); concomitant amitriptyline reported to increase DISULFIRAM reaction with alcohol

▶ Diuretics: increased risk of postural hypotension when tricyclics given with DIURETICS

l Dopaminergics: caution with tricyclics advised by manufacturer of ENTACAPONE; increased risk of CNS toxicity

Antidepressants, Tricyclic

l Dopaminergics (continued)

when tricyclics given with l RASAGILINE; CNS toxicity reported when tricyclics given with l SELEGILINE

▶ Histamine: tricyclics theoretically antagonise effects of HISTAMINE—manufacturer of histamine advises avoid concomitant use

▶ Lithium: risk of toxicity when tricyclics given with LITHIUM

l Methylthioninium: risk of CNS toxicity when clomipramine given with l METHYLTHIONINIUM—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

▶ Moxonidine: tricyclics possibly antagonise hypotensive effect of MOXONIDINE (manufacturer of moxonidine advises avoid concomitant use)

▶ Muscle Relaxants: tricyclics enhance muscle relaxant effect of

BACLOFEN

▶ Nicorandil: tricyclics possibly enhance hypotensive effect of

NICORANDIL

▶ Nitrates: tricyclics reduce effects of sublingual tablets of NITRATES (failure to dissolve under tongue owing to dry mouth)

▶ Oestrogens: antidepressant effect of tricyclics antagonised by OESTROGENS (but side-effects of tricyclics possibly increased due to increased plasma concentration)

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when tricyclics given with l PENTAMIDINE ISETIONATE

▶ Sodium Oxybate: increased risk of side-effects when tricyclics given with SODIUM OXYBATE

l Sympathomimetics: increased risk of hypertension and arrhythmias when tricyclics given with l ADRENALINE (EPINEPHRINE) (but local anaesthetics with adrenaline appear to be safe); metabolism of tricyclics possibly inhibited by METHYLPHENIDATE; increased risk of hypertension and arrhythmias when tricyclics given with l NORADRENALINE (NOREPINEPHRINE) or PHENYLEPHRINE

▶ Thyroid Hormones: effects of tricyclics possibly enhanced by THYROID HORMONES; effects of amitriptyline and imipramine enhanced by THYROID HORMONES

▶ Ulcer-healing Drugs: plasma concentration of tricyclics possibly increased by CIMETIDINE; metabolism of amitriptyline, doxepin, imipramine and nortriptyline inhibited by CIMETIDINE (increased plasma concentration)

Antidepressants, Tricyclic (related)

l Alcohol: increased sedative effect when tricyclic-related antidepressants given with l ALCOHOL

▶ Alpha2-adrenoceptor Stimulants: avoidance of tricyclic-related antidepressants advised by manufacturer of APRACLONIDINE and BRIMONIDINE

▶ Antibacterials: plasma concentration of trazodone possibly increased by CLARITHROMYCIN

▶ Anticoagulants: trazodone may enhance or reduce anticoagulant effect of WARFARIN

l Antidepressants: tricyclic-related antidepressants should not be started until 2 weeks after stopping l MAOIS, also MAOIs should not be started until at least 1–2 weeks after stopping tricyclic-related antidepressants; after stopping tricyclic- related antidepressants do not start l MOCLOBEMIDE for at least 1 week

l Antiepileptics: tricyclic-related antidepressants possibly antagonise anticonvulsant effect of l ANTIEPILEPTICS (convulsive threshold lowered); plasma concentration of mianserin and trazodone reduced by l CARBAMAZEPINE; plasma concentration of mianserin reduced by

l FOSPHENYTOIN and l PHENYTOIN; metabolism of mianserin accelerated by l PHENOBARBITAL and l PRIMIDONE (reduced plasma concentration)

▶ Antihistamines: possible increased antimuscarinic and sedative effects when tricyclic-related antidepressants given with ANTIHISTAMINES

l Antimalarials: avoidance of antidepressants advised by

manufacturer of l ARTEMETHER WITH LUMEFANTRINE and

l ARTENIMOL WITH PIPERAQUINE

Antidepressants, Tricyclic (related) (continued)

▶ Antimuscarinics: possible increased antimuscarinic side-effects when tricyclic-related antidepressants given with ANTIMUSCARINICS

Interactions | Appendix 1

l Antivirals: plasma concentration of trazodone increased by

l RITONAVIR (increased risk of toxicity); increased risk of ventricular arrhythmias when trazodone given with

l SAQUINAVIR—avoid concomitant use; plasma concentration of trazodone possibly increased by TELAPREVIR

▶ Anxiolytics and Hypnotics: increased sedative effect when tricyclic-related antidepressants given with ANXIOLYTICS AND HYPNOTICS

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

▶ Diazoxide: enhanced hypotensive effect when tricyclic-related antidepressants given with DIAZOXIDE

▶ Nitrates: tricyclic-related antidepressants possibly reduce effects of sublingual tablets of NITRATES (failure to dissolve under tongue owing to dry mouth)

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when tricyclic-related antidepressants given with HYDRALAZINE or SODIUM NITROPRUSSIDE

Antidiabetics

NOTE Other drugs administered orally may need to be taken at least 1 hour before or 4 hours after lixisenatide injection, or taken with a meal when lixisenatide is not administered, to minimise possible interference with absorption

NOTE Other drugs administered orally may need to be taken at least 1 hour before or 4 hours after exenatide injection, or taken with a meal when exenatide is not administered, to minimise possible interference with absorption

▶ ACE Inhibitors: hypoglycaemic effect of insulin, metformin and sulfonylureas possibly enhanced by ACE INHIBITORS

▶ Alcohol: hypoglycaemic effect of antidiabetics enhanced by ALCOHOL; increased risk of lactic acidosis when metformin given with ALCOHOL

▶ Anabolic Steroids: hypoglycaemic effect of antidiabetics possibly enhanced by ANABOLIC STEROIDS

l Analgesics: effects of sulfonylureas possibly enhanced by

l NSAIDS; lixisenatide possibly reduces the absorption of

PARACETAMOL when given 1 to 4 hours before paracetamol

▶ Anti-arrhythmics: hypoglycaemic effect of gliclazide, insulin and metformin possibly enhanced by DISOPYRAMIDE

l Antibacterials: hypoglycaemic effect of acarbose possibly enhanced by NEOMYCIN, also severity of gastro-intestinal effects increased; effects of repaglinide enhanced by CLARITHROMYCIN; effects of glibenclamide possibly enhanced by NORFLOXACIN; plasma concentration of canagliflozin and nateglinide reduced by l RIFAMPICIN; effects of linagliptin possibly reduced by RIFAMPICIN; hypoglycaemic effect of repaglinide possibly antagonised by RIFAMPICIN; effects of sulfonylureas enhanced by l CHLORAMPHENICOL; metabolism of tolbutamide accelerated by l RIFAMYCINS (reduced effect); metabolism of sulfonylureas possibly accelerated by

l RIFAMYCINS (reduced effect); effects of sulfonylureas rarely enhanced by SULFONAMIDES and TRIMETHOPRIM; hypoglycaemic effect of sulfonylureas possibly enhanced by TETRACYCLINES; hypoglycaemic effect of repaglinide possibly enhanced by TRIMETHOPRIM—manufacturer advises avoid concomitant use

l Anticoagulants: exenatide possibly enhances anticoagulant effect of WARFARIN; hypoglycaemic effect of sulfonylureas possibly enhanced by l COUMARINS, also possible changes to anticoagulant effect

▶ Antidepressants: hypoglycaemic effect of antidiabetics possibly enhanced by MAOIS; hypoglycaemic effect of insulin, metformin and sulfonylureas enhanced by MAOIS

▶ Antidiabetics: manufacturer of dapagliflozin advises avoid concomitant use with PIOGLITAZONE

▶ Antiepileptics: tolbutamide transiently increases plasma concentration of FOSPHENYTOIN and PHENYTOIN (possibility of toxicity); plasma concentration of glibenclamide possibly reduced by TOPIRAMATE; plasma concentration of metformin possibly increased by TOPIRAMATE

l Antifungals: plasma concentration of pioglitazone, saxagliptin and tolbutamide increased by KETOCONAZOLE; plasma

Interactions | Appendix 1

Antidiabetics

l Antifungals (continued)

concentration of sulfonylureas increased by l FLUCONAZOLE and l MICONAZOLE; hypoglycaemic effect of gliclazide and glipizide enhanced by l MICONAZOLE—avoid concomitant use; hypoglycaemic effect of nateglinide possibly enhanced by FLUCONAZOLE; hypoglycaemic effect of repaglinide possibly enhanced by ITRACONAZOLE; hypoglycaemic effect of glipizide possibly enhanced by POSACONAZOLE; plasma concentration of sulfonylureas possibly increased by VORICONAZOLE

▶ Antihistamines: thrombocyte count depressed when metformin given with KETOTIFEN (manufacturer of ketotifen advises avoid concomitant use)

▶ Antipsychotics: hypoglycaemic effect of sulfonylureas possibly antagonised by PHENOTHIAZINES

▶ Antivirals: plasma concentration of tolbutamide possibly increased by RITONAVIR; plasma concentration of metformin increased by TELAPREVIR (consider reducing dose of metformin)

▶ Aprepitant: plasma concentration of tolbutamide reduced by

APREPITANT

▶ Beta-blockers: warning signs of hypoglycaemia (such as tremor) with antidiabetics may be masked when given with BETA-BLOCKERS; hypoglycaemic effect of insulin enhanced by BETA-BLOCKERS

l Bosentan: increased risk of hepatotoxicity when glibenclamide given with l BOSENTAN—avoid concomitant use

▶ Calcium-channel Blockers: glucose tolerance occasionally impaired when insulin given with NIFEDIPINE

▶ Cardiac Glycosides: canagliflozin and sitagliptin increase plasma concentration of DIGOXIN; acarbose possibly reduces plasma concentration of DIGOXIN

▶ Ciclosporin: hypoglycaemic effect of repaglinide possibly enhanced by CICLOSPORIN

▶ Corticosteroids: hypoglycaemic effect of antidiabetics antagonised by CORTICOSTEROIDS

l Cytotoxics: avoidance of repaglinide advised by manufacturer of l LAPATINIB; plasma concentration of metformin possibly increased by VANDETANIB (consider reducing dose of metformin)

▶ Deferasirox: plasma concentration of repaglinide increased by

DEFERASIROX

▶ Diazoxide: hypoglycaemic effect of antidiabetics antagonised by DIAZOXIDE

▶ Diuretics: canagliflozin possibly enhances diuretic effect of DIURETICS; manufacturer of canagliflozin advises avoid concomitant use with LOOP DIURETICS; hypoglycaemic effect of antidiabetics antagonised by LOOP DIURETICS and THIAZIDES AND RELATED DIURETICS; dapagliflozin possibly enhances diuretic effect of LOOP DIURETICS and THIAZIDES AND RELATED DIURETICS

▶ Fosaprepitant: plasma concentration of tolbutamide reduced by FOSAPREPITANT

▶ Hormone Antagonists: requirements for antidiabetics possibly reduced by LANREOTIDE, OCTREOTIDE and PASIREOTIDE

▶ Leflunomide: hypoglycaemic effect of tolbutamide possibly enhanced by LEFLUNOMIDE

l Lipid-regulating Drugs: absorption of glibenclamide and glipizide reduced by COLESEVELAM; absorption of glimepiride reduced by COLESEVELAM—manufacturer of glimepiride advises give at least 4 hours before colesevelam; hypoglycaemic effect of acarbose possibly enhanced by COLESTYRAMINE; hypoglycaemic effect of nateglinide possibly enhanced by GEMFIBROZIL; increased risk of severe hypoglycaemia when repaglinide given with l GEMFIBROZIL— avoid concomitant use; plasma concentration of glibenclamide possibly increased by FLUVASTATIN; manufacturer of canagliflozin advises give at least 1 hour before or 4–6 hours after BILE ACID SEQUESTRANTS; may be improved glucose tolerance and an additive effect when insulin or sulfonylureas given with FIBRATES; separating administration from linagliptin by 12 hours advised by manufacturer of LOMITAPIDE

▶ Oestrogens: hypoglycaemic effect of antidiabetics antagonised

by OESTROGENS

Antidiabetics (continued)

▶ Orlistat: avoidance of acarbose advised by manufacturer of

ORLISTAT

▶ Pancreatin: hypoglycaemic effect of acarbose antagonised by

PANCREATIN

▶ Progestogens: hypoglycaemic effect of antidiabetics antagonised by PROGESTOGENS

l Sulfinpyrazone: effects of sulfonylureas enhanced by

l SULFINPYRAZONE

▶ Teriflunomide: plasma concentration of repaglinide increased by TERIFLUNOMIDE

▶ Testosterone: hypoglycaemic effect of antidiabetics possibly enhanced by TESTOSTERONE

▶ Ulcer-healing Drugs: excretion of metformin reduced by CIMETIDINE (increased plasma concentration); hypoglycaemic effect of sulfonylureas enhanced by CIMETIDINE

Antiepileptics *see* Carbamazepine, Eslicarbazepine, Ethosuximide, Fosphenytoin, Gabapentin, Lacosamide, Lamotrigine, Levetiracetam, Oxcarbazepine, Perampanel, Phenobarbital, Phenytoin, Pregabalin, Primidone, Retigabine, Rufinamide, Sodium valproate, Stiripentol, Tiagabine, Topiramate, Valproic acid, Vigabatrin, and Zonisamide

Antifungals *see* Amphotericin; Antifungals, Imidazole; Antifungals, Triazole; Caspofungin; Flucytosine; Griseofulvin; Micafungin; Terbinafine

Antifungals, Imidazole

▶ Alcohol: possibility of disulfiram-like reaction when ketoconazole given with ALCOHOL

▶ Aliskiren: ketoconazole increases plasma concentration of

ALISKIREN

l Alpha-blockers: ketoconazole possibly increases plasma concentration of ALFUZOSIN; ketoconazole increases plasma concentration of l TAMSULOSIN

l Aminophylline: ketoconazole possibly increases plasma concentration of l AMINOPHYLLINE

l Analgesics: ketoconazole inhibits metabolism of

l BUPRENORPHINE (reduce dose of buprenorphine); possible increased risk of ventricular arrhythmias when ketoconazole given with l METHADONE—manufacturer of ketoconazole advises avoid concomitant use; ketoconazole increases plasma concentration of OXYCODONE; manufacturer of ketoconazole advises avoid concomitant use with PARACETAMOL

▶ Antacids: absorption of ketoconazole reduced by ANTACIDS

▶ Anthelmintics: ketoconazole increases plasma concentration of PRAZIQUANTEL

l Anti-arrhythmics: increased risk of ventricular arrhythmias when ketoconazole given with l DISOPYRAMIDE—avoid concomitant use; ketoconazole increases plasma concentration of l DRONEDARONE—avoid concomitant use

l Antibacterials: manufacturer of ketoconazole advises avoid concomitant l CLARITHROMYCIN in severe renal impairment; metabolism of ketoconazole accelerated by l RIFAMPICIN (reduced plasma concentration), also plasma concentration of rifampicin may be reduced by ketoconazole; ketoconazole increases plasma concentration of BEDAQUILINE—avoid concomitant use if ketoconazole given for more than 14 days; avoidance of ketoconazole advised by manufacturer of FIDAXOMICIN; plasma concentration of ketoconazole possibly reduced by ISONIAZID; ketoconazole increases the plasma concentration of l TELITHROMYCIN—avoid in severe renal and hepatic impairment

l Anticoagulants: ketoconazole increases plasma concentration

of l APIXABAN—manufacturer of apixaban advises avoid concomitant use; miconazole enhances anticoagulant effect of l COUMARINS (miconazole oral gel and possibly vaginal and topical formulations absorbed); ketoconazole enhances anticoagulant effect of l COUMARINS; ketoconazole increases plasma concentration of l DABIGATRAN and l RIVAROXABAN— avoid concomitant use

l Antidepressants: avoidance of imidazoles advised by manufacturer of l REBOXETINE; ketoconazole increases plasma concentration of MIRTAZAPINE

l Antidiabetics: miconazole enhances hypoglycaemic effect of

l GLICLAZIDE and l GLIPIZIDE—avoid concomitant use;

Antifungals, Imidazole

l Antidiabetics (continued)

ketoconazole increases plasma concentration of

PIOGLITAZONE, SAXAGLIPTIN and TOLBUTAMIDE; miconazole

increases plasma concentration of l SULFONYLUREAS

l Antiepileptics: miconazole possibly increases plasma concentration of CARBAMAZEPINE; plasma concentration of ketoconazole possibly reduced by CARBAMAZEPINE, also plasma concentration of carbamazepine possibly increased; plasma concentration of ketoconazole reduced by

l FOSPHENYTOIN and l PHENYTOIN; miconazole enhances anticonvulsant effect of l FOSPHENYTOIN and l PHENYTOIN (plasma concentration of fosphenytoin and phenytoin increased); ketoconazole increases plasma concentration of PERAMPANEL

▶ Antifungals: imidazoles possibly antagonise effects of

AMPHOTERICIN

l Antihistamines: imidazoles possibly inhibit metabolism of

l MIZOLASTINE (avoid concomitant use)

l Antimalarials: avoidance of imidazoles advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; avoidance of imidazoles advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias); ketoconazole increases plasma concentration of MEFLOQUINE

l Antimuscarinics: absorption of ketoconazole reduced by ANTIMUSCARINICS; ketoconazole increases plasma concentration of DARIFENACIN—avoid concomitant use; manufacturer of fesoterodine advises dose reduction when ketoconazole given with FESOTERODINE—consult fesoterodine product literature; ketoconazole increases plasma concentration of OXYBUTYNIN; ketoconazole increases plasma concentration of l SOLIFENACIN—see under Solifenacin,

p. 670; avoidance of ketoconazole advised by manufacturer of l TOLTERODINE

l Antipsychotics: ketoconazole inhibits metabolism of

l ARIPIPRAZOLE (reduce dose of aripiprazole); ketoconazole increases plasma concentration of l LURASIDONE—avoid concomitant use; increased risk of ventricular arrhythmias when imidazoles given with l PIMOZIDE—avoid concomitant use; imidazoles possibly increase plasma concentration of l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: ketoconazole increases plasma concentration of l BOCEPREVIR; ketoconazole increases the plasma concentration of l DACLATASVIR—reduce dose of daclatasvir

(see under Daclatasvir, p. 544); plasma concentration of both drugs increased when ketoconazole given with DARUNAVIR; plasma concentration of ketoconazole reduced by

l EFAVIRENZ; plasma concentration of ketoconazole increased by FOSAMPRENAVIR (also plasma concentration of fosamprenavir possibly increased); ketoconazole increases plasma concentration of l INDINAVIR and l MARAVIROC (consider reducing dose of indinavir and maraviroc); plasma concentration of ketoconazole reduced by l NEVIRAPINE— avoid concomitant use; plasma concentration of ketoconazole increased by l RITONAVIR (reduce dose of ketoconazole); imidazoles possibly increase plasma concentration of SAQUINAVIR; ketoconazole increases plasma concentration of l SAQUINAVIR—manufacturer of ketoconazole advises avoid concomitant use; avoidance of ketoconazole advised by manufacturer of l SIMEPREVIR; plasma concentration of both drugs possibly increased when ketoconazole given with TELAPREVIR (increased risk of ventricular arrhythmias)—reduce dose of ketoconazole

l Anxiolytics and Hypnotics: ketoconazole increases plasma concentration of l ALPRAZOLAM—manufacturer of ketoconazole advises avoid concomitant use; ketoconazole increases plasma concentration of l MIDAZOLAM (risk of prolonged sedation—avoid concomitant use of *oral* midazolam); ketoconazole increases plasma concentration of ZOLPIDEM

▶ Aprepitant: ketoconazole increases plasma concentration of

APREPITANT

l Avanafil: ketoconazole increases plasma concentration of

l AVANAFIL—avoid concomitant use

Antifungals, Imidazole (continued)

▶ Beta-blockers: ketoconazole possibly increases plasma concentration of NADOLOL

Interactions | Appendix 1

▶ Bosentan: ketoconazole increases plasma concentration of

BOSENTAN

l Calcium-channel Blockers: ketoconazole inhibits metabolism of l FELODIPINE (increased plasma concentration)— manufacturer of ketoconazole advises avoid concomitant use; avoidance of ketoconazole advised by manufacturer of LERCANIDIPINE; ketoconazole possibly inhibits metabolism of DIHYDROPYRIDINES (increased plasma concentration)

▶ Cannabis Extract: ketoconazole increases plasma concentration of CANNABIS EXTRACT

l Ciclosporin: ketoconazole inhibits metabolism of

l CICLOSPORIN (increased plasma concentration); miconazole possibly inhibits metabolism of l CICLOSPORIN (increased plasma concentration)

l Cilostazol: ketoconazole increases plasma concentration of

l CILOSTAZOL (see under Cilostazol, p. 206)

▶ Cinacalcet: ketoconazole inhibits metabolism of CINACALCET

(increased plasma concentration)

l Clopidogrel: ketoconazole possibly reduces antiplatelet effect of l CLOPIDOGREL

▶ Cobicistat: plasma concentration of ketoconazole possibly increased by COBICISTAT—manufacturer of cobicistat advises reduce dose of ketoconazole

l Colchicine: ketoconazole possibly increases risk of

l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Corticosteroids: ketoconazole possibly inhibits metabolism of CORTICOSTEROIDS; ketoconazole increases the plasma concentration of *inhaled* and *oral* (and possibly also *intranasal* and *rectal*) l BUDESONIDE; ketoconazole increases plasma concentration of active metabolite of l CICLESONIDE; ketoconazole possibly increases plasma concentration of *inhaled* FLUTICASONE; ketoconazole inhibits the metabolism of METHYLPREDNISOLONE; ketoconazole increases plasma concentration of *inhaled* MOMETASONE

l Cytotoxics: ketoconazole inhibits the metabolism of IFOSFAMIDE; possible increased risk of neutropenia when ketoconazole given with l BRENTUXIMAB VEDOTIN; ketoconazole possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of ketoconazole by 6 to 12 hours; ketoconazole increases plasma concentration of AXITINIB (reduce dose of axitinib—consult axitinib product literature); ketoconazole increases the plasma concentration of

l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; ketoconazole increases plasma concentration of BORTEZOMIB, CABOZANTINIB, DABRAFENIB, ETOPOSIDE, IDELALISIB, IMATINIB and PONATINIB;

ketoconazole increases plasma concentration of l CRIZOTINIB,

l LAPATINIB, l NILOTINIB and l REGORAFENIB—avoid

concomitant use; ketoconazole possibly increases plasma concentration of DASATINIB; ketoconazole inhibits metabolism of ERLOTINIB and SUNITINIB (increased plasma concentration); ketoconazole increases plasma concentration of l EVEROLIMUS—manufacturer of ketoconazole advises avoid concomitant use; ketoconazole increases plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809); ketoconazole increases plasma concentration of l PAZOPANIB (reduce dose of pazopanib); manufacturer of ruxolitinib advises dose reduction when ketoconazole given with l RUXOLITINIB—consult ruxolitinib product literature; ketoconazole increases plasma concentration of active metabolite of l TEMSIROLIMUS—avoid concomitant use; avoidance of ketoconazole advised by manufacturer of l CABAZITAXEL; *in vitro* studies suggest a possible interaction between ketoconazole and DOCETAXEL (consult docetaxel product literature); ketoconazole reduces plasma concentration of l IRINOTECAN (but concentration of active metabolite of irinotecan increased)—avoid concomitant use; ketoconazole increases plasma concentration of l VINFLUNINE—manufacturer of vinflunine advises avoid concomitant use

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Antifungals, Imidazole (continued)

l Dapoxetine: ketoconazole increases plasma concentration of l DAPOXETINE—manufacturer of dapoxetine advises avoid concomitant use

l Diuretics: ketoconazole increases plasma concentration of

l EPLERENONE—avoid concomitant use

l Domperidone: manufacturer of ketoconazole advises avoid concomitant use with l DOMPERIDONE (risk of ventricular arrhythmias)

l Ergot Alkaloids: manufacturer of ketoconazole advises avoid concomitant use with l ERGOT ALKALOIDS; increased risk of ergotism when imidazoles given with l ERGOTAMINE—avoid concomitant use

l Fingolimod: ketoconazole increases plasma concentration of

l FINGOLIMOD

▶ Fosaprepitant: ketoconazole increases plasma concentration of FOSAPREPITANT

▶ Hormone Antagonists: manufacturer of ketoconazole advises avoid concomitant use with PASIREOTIDE

l 5HT1-receptor Agonists: ketoconazole increases plasma concentration of ALMOTRIPTAN (increased risk of toxicity); ketoconazole increases plasma concentration of l ELETRIPTAN (risk of toxicity)—avoid concomitant use

l Ivabradine: ketoconazole increases plasma concentration of

l IVABRADINE—avoid concomitant use

l Ivacaftor: ketoconazole increases plasma concentration of

l IVACAFTOR (see under Ivacaftor, p. 257)

▶ Lanthanum: absorption of ketoconazole possibly reduced by

LANTHANUM (give at least 2 hours apart)

l Lenalidomide: ketoconazole possibly increases plasma concentration of l LENALIDOMIDE (increased risk of toxicity)

l Lipid-regulating Drugs: possible increased risk of myopathy when imidazoles given with ATORVASTATIN; possible increased risk of myopathy when ketoconazole given with

l ATORVASTATIN—manufacturer of ketoconazole advises avoid concomitant use; increased risk of myopathy when ketoconazole given with l SIMVASTATIN (avoid concomitant use); possible increased risk of myopathy when miconazole given with l SIMVASTATIN; ketoconazole increases plasma concentration of l LOMITAPIDE—avoid concomitant use

▶ Macitentan: ketoconazole increases plasma concentration of

MACITENTAN

▶ Mirabegron: when given with ketoconazole avoid or reduce dose of MIRABEGRON in hepatic or renal impairment—see Mirabegron, p. 671

l Nintedanib: ketoconazole increases plasma concentration of

l NINTEDANIB

▶ Oestrogens: anecdotal reports of contraceptive failure when imidazoles given with OESTROGENS

▶ Parasympathomimetics: ketoconazole increases plasma concentration of GALANTAMINE

l Ranolazine: ketoconazole increases plasma concentration of

l RANOLAZINE—avoid concomitant use

l Retinoids: ketoconazole increases plasma concentration of

ALITRETINOIN; ketoconazole possibly increases risk of

l TRETINOIN toxicity

▶ Riociguat: avoidance of ketoconazole advised by manufacturer of RIOCIGUAT

l Sildenafil: ketoconazole increases plasma concentration of l SILDENAFIL—reduce initial dose of sildenafil for erectile dysfunction and avoid concomitant use of sildenafil for pulmonary hypertension

l Sirolimus: ketoconazole increases plasma concentration of l SIROLIMUS—avoid concomitant use; miconazole increases plasma concentration of l SIROLIMUS

l Sympathomimetics, Beta2: ketoconazole increases plasma concentration of OLODATEROL; ketoconazole inhibits metabolism of l SALMETEROL (increased plasma concentration)

l Tacrolimus: ketoconazole increases plasma concentration of l TACROLIMUS (consider reducing dose of tacrolimus); miconazole *oral gel* possibly increases plasma concentration of l TACROLIMUS

l Tadalafil: ketoconazole increases plasma concentration of l TADALAFIL—avoid concomitant use of tadalafil for pulmonary hypertension

Antifungals, Imidazole (continued)

l Theophylline: ketoconazole possibly increases plasma concentration of l THEOPHYLLINE

l Ticagrelor: ketoconazole increases plasma concentration of l TICAGRELOR—manufacturer of ticagrelor advises avoid concomitant use

▶ Tolvaptan: ketoconazole increases plasma concentration of TOLVAPTAN—manufacturer of ketoconazole advises avoid concomitant use

▶ Ulcer-healing Drugs: absorption of ketoconazole reduced by HISTAMINE H2-ANTAGONISTS, PROTON PUMP INHIBITORS and SUCRALFATE

▶ Ulipristal: ketoconazole increases plasma concentration of *low-dose* ULIPRISTAL—manufacturer of *low-dose* ulipristal advises avoid concomitant use

l Vardenafil: ketoconazole increases plasma concentration of

l VARDENAFIL—avoid concomitant use

▶ Vitamins: miconazole possibly reduces effects of ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL and

VITAMIN D; ketoconazole possibly increases plasma concentration of PARICALCITOL

Antifungals, Polyene *see* Amphotericin

Antifungals, Triazole

NOTE In general, fluconazole interactions relate to multiple- dose treatment

l Aliskiren: itraconazole increases plasma concentration of

l ALISKIREN—avoid concomitant use

l Aminophylline: fluconazole possibly increases plasma concentration of l AMINOPHYLLINE

l Analgesics: fluconazole increases plasma concentration of CELECOXIB (halve dose of celecoxib); voriconazole increases plasma concentration of DICLOFENAC, IBUPROFEN and

l OXYCODONE; fluconazole increases plasma concentration of FLURBIPROFEN, IBUPROFEN and METHADONE; fluconazole increases plasma concentration of PARECOXIB (reduce dose of parecoxib); voriconazole increases plasma concentration of l ALFENTANIL and l METHADONE (consider reducing dose of alfentanil and methadone); fluconazole inhibits metabolism of ALFENTANIL (risk of prolonged or delayed respiratory depression); itraconazole possibly inhibits metabolism of ALFENTANIL; triazoles possibly increase plasma concentration of l FENTANYL; itraconazole possibly increases plasma concentration of l METHADONE (increased risk of ventricular

arrhythmias); itraconazole increases plasma concentration of

OXYCODONE

▶ Antacids: absorption of itraconazole reduced by ANTACIDS

l Anti-arrhythmics: manufacturer of itraconazole advises avoid concomitant use with l DISOPYRAMIDE; avoidance of itraconazole, posaconazole and voriconazole advised by manufacturer of l DRONEDARONE

l Antibacterials: plasma concentration of itraconazole increased by CLARITHROMYCIN; manufacturer of fluconazole advises avoid concomitant use with ERYTHROMYCIN; triazoles possibly increase plasma concentration of l RIFABUTIN (increased risk of uveitis—reduce rifabutin dose); posaconazole increases plasma concentration of l RIFABUTIN (also plasma concentration of posaconazole reduced); voriconazole increases plasma concentration of l RIFABUTIN, also rifabutin reduces plasma concentration of voriconazole (increase dose of voriconazole and also monitor for rifabutin toxicity); fluconazole increases plasma concentration of l RIFABUTIN (increased risk of uveitis—reduce rifabutin dose); plasma concentration of itraconazole reduced by l RIFABUTIN and

l RIFAMPICIN—manufacturer of itraconazole advises avoid concomitant use; plasma concentration of posaconazole reduced by l RIFAMPICIN; plasma concentration of voriconazole reduced by l RIFAMPICIN—avoid concomitant use; metabolism of fluconazole accelerated by l RIFAMPICIN (reduced plasma concentration); fluconazole possibly increases plasma concentration of BEDAQUILINE—avoid concomitant use if fluconazole given for more than 14 days

l Anticoagulants: avoidance of itraconazole, posaconazole and voriconazole advised by manufacturer of APIXABAN; fluconazole, itraconazole and voriconazole enhance

Antifungals, Triazole

l Anticoagulants (continued)

anticoagulant effect of l COUMARINS; avoidance of itraconazole advised by manufacturer of DABIGATRAN and RIVAROXABAN; avoidance of posaconazole and voriconazole advised by manufacturer of RIVAROXABAN

l Antidepressants: avoidance of triazoles advised by manufacturer of l REBOXETINE; fluconazole possibly increases plasma concentration of AMITRIPTYLINE and NORTRIPTYLINE; plasma concentration of voriconazole reduced by l ST JOHN’S WORT—avoid concomitant use

l Antidiabetics: posaconazole possibly enhances hypoglycaemic effect of GLIPIZIDE; fluconazole possibly enhances hypoglycaemic effect of NATEGLINIDE; itraconazole possibly enhances hypoglycaemic effect of REPAGLINIDE; fluconazole increases plasma concentration of l SULFONYLUREAS; voriconazole possibly increases plasma concentration of SULFONYLUREAS

l Antiepileptics: fluconazole possibly increases plasma concentration of CARBAMAZEPINE; plasma concentration of voriconazole possibly reduced by l CARBAMAZEPINE,

l PHENOBARBITAL and l PRIMIDONE—avoid concomitant use; plasma concentration of itraconazole and posaconazole possibly reduced by l CARBAMAZEPINE; voriconazole increases plasma concentration of l FOSPHENYTOIN and l PHENYTOIN, also fosphenytoin and phenytoin reduces plasma concentration of voriconazole (increase dose of voriconazole and also monitor for fosphenytoin and phenytoin toxicity); plasma concentration of posaconazole reduced by

l FOSPHENYTOIN and l PHENYTOIN; plasma concentration of itraconazole reduced by l FOSPHENYTOIN and l PHENYTOIN— avoid concomitant use; fluconazole increases plasma concentration of l FOSPHENYTOIN and l PHENYTOIN (consider reducing dose of fosphenytoin and phenytoin); plasma concentration of itraconazole and posaconazole possibly reduced by l PHENOBARBITAL; plasma concentration of itraconazole and posaconazole possibly reduced by

l PRIMIDONE

▶ Antifungals: triazoles possibly antagonise effects of AMPHOTERICIN; monitoring for increased voriconazole side effects advised by manufacturer of FLUCONAZOLE if voriconazole given after fluconazole; plasma concentration of itraconazole increased by MICAFUNGIN (consider reducing dose of itraconazole); plasma concentration of fluconazole increased by TERBINAFINE

l Antihistamines: itraconazole inhibits metabolism of

l MIZOLASTINE—avoid concomitant use

l Antimalarials: avoidance of triazoles advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; avoidance of triazoles advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

l Antimuscarinics: avoidance of itraconazole advised by manufacturer of DARIFENACIN and TOLTERODINE; manufacturer of fesoterodine advises dose reduction when itraconazole given with FESOTERODINE—consult fesoterodine product literature; itraconazole possibly increases plasma concentration of l SOLIFENACIN—see under Solifenacin,

p. 670

l Antipsychotics: itraconazole possibly increases plasma concentration of HALOPERIDOL; itraconazole possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); itraconazole, posaconazole and voriconazole possibly increase plasma concentration of l LURASIDONE—avoid concomitant use; fluconazole possibly increases the plasma concentration of l LURASIDONE (see under Lurasidone,

p. 315); increased risk of ventricular arrhythmias when triazoles given with l PIMOZIDE—avoid concomitant use; triazoles possibly increase plasma concentration of

l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use; itraconazole possibly increases side-effects of RISPERIDONE

l Antivirals: plasma concentration of voriconazole increased or decreased by l ATAZANAVIR and plasma concentration of atazanavir also reduced; posaconazole increases plasma

Antifungals, Triazole

l Antivirals (continued)

Interactions | Appendix 1

concentration of l ATAZANAVIR; itraconazole, posaconazole and voriconazole possibly increase the plasma concentration of l DACLATASVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); plasma concentration of voriconazole reduced by l EFAVIRENZ, also plasma concentration of efavirenz increased (increase voriconazole dose and reduce efavirenz dose); plasma concentration of itraconazole and posaconazole reduced by l EFAVIRENZ; plasma concentration of both drugs may increase when itraconazole given with FOSAMPRENAVIR; plasma concentration of posaconazole possibly reduced by FOSAMPRENAVIR; itraconazole increases plasma concentration of l INDINAVIR (consider reducing dose of indinavir); fluconazole increases plasma concentration of l NEVIRAPINE, RITONAVIR and TIPRANAVIR; plasma

concentration of itraconazole possibly reduced by NEVIRAPINE—consider increasing dose of itraconazole; plasma concentration of voriconazole reduced by l RITONAVIR—avoid concomitant use; combination of itraconazole with

l RITONAVIR may increase plasma concentration of either drug (or both); triazoles possibly increase plasma concentration of SAQUINAVIR; fluconazole, itraconazole, posaconazole and voriconazole possibly increase plasma concentration of

l SIMEPREVIR—manufacturer of simeprevir advises avoid concomitant use; plasma concentration of voriconazole possibly affected by l TELAPREVIR (possible increased risk of ventricular arrhythmias); plasma concentration of posaconazole possibly increased by l TELAPREVIR (increased risk of ventricular arrhythmias); plasma concentration of itraconazole possibly increased by TELAPREVIR; fluconazole increases plasma concentration of l ZIDOVUDINE (increased risk of toxicity)

l Anxiolytics and Hypnotics: itraconazole increases plasma concentration of ALPRAZOLAM; fluconazole and voriconazole increase plasma concentration of l DIAZEPAM (risk of prolonged sedation); fluconazole, itraconazole, posaconazole and voriconazole increase plasma concentration of

l MIDAZOLAM (risk of prolonged sedation); itraconazole increases plasma concentration of BUSPIRONE (reduce dose of buspirone)

l Avanafil: itraconazole and voriconazole possibly increase plasma concentration of l AVANAFIL—manufacturer of avanafil advises avoid concomitant use; fluconazole possibly increases plasma concentration of l AVANAFIL—see under Avanafil, p. 698

l Bosentan: fluconazole possibly increases plasma concentration of l BOSENTAN—avoid concomitant use; itraconazole possibly increases plasma concentration of BOSENTAN

l Calcium-channel Blockers: negative inotropic effect possibly increased when itraconazole given with CALCIUM-CHANNEL BLOCKERS; itraconazole inhibits metabolism of l FELODIPINE (increased plasma concentration); avoidance of itraconazole advised by manufacturer of LERCANIDIPINE; itraconazole possibly inhibits metabolism of DIHYDROPYRIDINES (increased plasma concentration)

l Cardiac Glycosides: itraconazole increases plasma

concentration of l DIGOXIN

l Ciclosporin: fluconazole, itraconazole, posaconazole and voriconazole inhibit metabolism of l CICLOSPORIN (increased plasma concentration)

l Cilostazol: itraconazole possibly increases plasma concentration of l CILOSTAZOL (see under Cilostazol, p. 206)

l Clopidogrel: fluconazole, itraconazole and voriconazole possibly reduce antiplatelet effect of l CLOPIDOGREL

▶ Cobicistat: plasma concentration of itraconazole possibly increased by COBICISTAT—manufacturer of cobicistat advises reduce dose of itraconazole

l Colchicine: itraconazole possibly increases risk of l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Corticosteroids: itraconazole possibly inhibits metabolism of CORTICOSTEROIDS and METHYLPREDNISOLONE; itraconazole increases the plasma concentration of *inhaled* and *oral* (and

Interactions | Appendix 1

Antifungals, Triazole

l Corticosteroids (continued)

possibly also *intranasal* and *rectal*) l BUDESONIDE; itraconazole increases plasma concentration of *inhaled* FLUTICASONE

l Cytotoxics: itraconazole inhibits metabolism of BUSULFAN (increased risk of toxicity); fluconazole and itraconazole possibly increase side-effects of CYCLOPHOSPHAMIDE; itraconazole possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of itraconazole by 6 to 12 hours; itraconazole possibly increases plasma concentration of AXITINIB (reduce dose of axitinib—consult axitinib product literature); fluconazole, itraconazole, posaconazole and voriconazole possibly increase the plasma concentration of l BOSUTINIB— manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; itraconazole possibly increases plasma concentration of CABOZANTINIB; itraconazole and voriconazole possibly increase plasma concentration of

l CRIZOTINIB—manufacturer of crizotinib advises avoid concomitant use; avoidance of itraconazole advised by manufacturer of DASATINIB and l TEMSIROLIMUS (plasma concentration of dasatinib and temsirolimus possibly increased); itraconazole, posaconazole and voriconazole possibly increase plasma concentration of l EVEROLIMUS— manufacturer of everolimus advises avoid concomitant use; itraconazole increases plasma concentration of GEFITINIB; fluconazole, itraconazole and voriconazole possibly increase the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809); avoidance of itraconazole, posaconazole and voriconazole advised by manufacturer of l LAPATINIB; avoidance of itraconazole and voriconazole advised by manufacturer of l NILOTINIB; itraconazole and voriconazole possibly increase plasma concentration of l PAZOPANIB (reduce dose of pazopanib); itraconazole and voriconazole possibly increase plasma concentration of PONATINIB—consider reducing initial dose of ponatinib (see under Ponatinib, p. 814); manufacturer of ruxolitinib advises dose reduction when fluconazole, itraconazole, posaconazole and voriconazole given with

l RUXOLITINIB—consult ruxolitinib product literature; itraconazole and voriconazole possibly increase the plasma concentration of l CABAZITAXEL—manufacturer of cabazitaxel advises avoid or consider reducing dose of cabazitaxel; itraconazole and voriconazole possibly increase plasma concentration of l DOCETAXEL—manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose; increased risk of toxicity when itraconazole given with l IRINOTECAN—avoid concomitant use; itraconazole possibly increases risk of l VINBLASTINE,

l VINDESINE, l VINFLUNINE and l VINORELBINE toxicity; posaconazole possibly inhibits metabolism of l VINBLASTINE and l VINCRISTINE (increased risk of neurotoxicity); itraconazole increases risk of l VINCRISTINE toxicity

l Dapoxetine: manufacturer of dapoxetine advises dose reduction when fluconazole given with DAPOXETINE (see under Dapoxetine, p. 703); avoidance of itraconazole advised by manufacturer of l DAPOXETINE (increased risk of toxicity)

l Diuretics: fluconazole increases plasma concentration of EPLERENONE (reduce dose of eplerenone); itraconazole increases plasma concentration of l EPLERENONE—avoid concomitant use; plasma concentration of fluconazole increased by HYDROCHLOROTHIAZIDE

l Domperidone: possible increased risk of ventricular arrhythmias when itraconazole or voriconazole given with l DOMPERIDONE—avoid concomitant use

l Ergot Alkaloids: increased risk of ergotism when voriconazole given with l ERGOMETRINE—avoid concomitant use; manufacturer of itraconazole advises avoid concomitant use with l ERGOMETRINE (increased risk of ergotism); increased risk of ergotism when triazoles given with l ERGOTAMINE— avoid concomitant use

l 5HT1-receptor Agonists: itraconazole increases plasma concentration of l ELETRIPTAN (risk of toxicity)—avoid concomitant use

Antifungals, Triazole (continued)

l Ivabradine: fluconazole increases plasma concentration of IVABRADINE—reduce initial dose of ivabradine; itraconazole possibly increases plasma concentration of l IVABRADINE— avoid concomitant use

l Ivacaftor: itraconazole, posaconazole and voriconazole

possibly increase plasma concentration of l IVACAFTOR (see under Ivacaftor, p. 257); fluconazole increases plasma concentration of l IVACAFTOR (see under Ivacaftor, p. 257)

l Lenalidomide: itraconazole possibly increases plasma concentration of l LENALIDOMIDE (increased risk of toxicity)

▶ Leukotriene Receptor Antagonists: fluconazole increases plasma concentration of ZAFIRLUKAST

l Lipid-regulating Drugs: increased risk of myopathy when itraconazole, posaconazole or voriconazole given with

l ATORVASTATIN; possible increased risk of myopathy when fluconazole given with l ATORVASTATIN or l SIMVASTATIN; fluconazole increases plasma concentration of FLUVASTATIN— possible increased risk of myopathy; itraconazole increases plasma concentration of l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature); increased risk of myopathy when itraconazole or posaconazole given with

l SIMVASTATIN (avoid concomitant use); increased risk of myopathy when voriconazole given with l SIMVASTATIN; avoidance of triazoles advised by manufacturer of

l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

▶ Mirabegron: when given with itraconazole avoid or reduce dose of MIRABEGRON in hepatic or renal impairment—see Mirabegron, p. 671

▶ Oestrogens: plasma concentration of voriconazole increased by OESTROGENS

▶ Progestogens: plasma concentration of voriconazole possibly increased by PROGESTOGENS

l Ranolazine: itraconazole, posaconazole and voriconazole possibly increase plasma concentration of l RANOLAZINE— manufacturer of ranolazine advises avoid concomitant use

l Retinoids: fluconazole and voriconazole possibly increase risk of l TRETINOIN toxicity

▶ Riociguat: avoidance of itraconazole and voriconazole advised by manufacturer of RIOCIGUAT

▶ Sildenafil: itraconazole increases plasma concentration of

SILDENAFIL—reduce initial dose of sildenafil

l Sirolimus: fluconazole and posaconazole possibly increase plasma concentration of SIROLIMUS; itraconazole and voriconazole increase plasma concentration of l SIROLIMUS— avoid concomitant use

l Tacrolimus: fluconazole, itraconazole, posaconazole and voriconazole increase plasma concentration of l TACROLIMUS (consider reducing dose of tacrolimus)

▶ Tadalafil: itraconazole possibly increases plasma concentration of TADALAFIL

l Theophylline: fluconazole possibly increases plasma concentration of l THEOPHYLLINE

l Ulcer-healing Drugs: plasma concentration of posaconazole reduced by l CIMETIDINE and l ESOMEPRAZOLE—manufacturer of posaconazole *suspension* advises avoid concomitant use; plasma concentration of posaconazole possibly reduced by

l FAMOTIDINE, l LANSOPRAZOLE, l NIZATIDINE, l OMEPRAZOLE, l PANTOPRAZOLE, l RABEPRAZOLE and l RANITIDINE—

manufacturer of posaconazole *suspension* advises avoid concomitant use; voriconazole possibly increases plasma concentration of ESOMEPRAZOLE; voriconazole increases plasma concentration of OMEPRAZOLE (consider reducing dose of omeprazole); absorption of itraconazole reduced by HISTAMINE H2-ANTAGONISTS and PROTON PUMP INHIBITORS

▶ Ulipristal: avoidance of itraconazole advised by manufacturer

of ULIPRISTAL

l Vardenafil: itraconazole possibly increases plasma concentration of l VARDENAFIL—avoid concomitant use

Antihistamines

NOTE Sedative interactions apply to a lesser extent to the non-sedating antihistamines. Interactions do not generally apply to antihistamines used for topical action (including inhalation)

Antihistamines (continued)

▶ Alcohol: increased sedative effect when antihistamines given with ALCOHOL (possibly less effect with non-sedating antihistamines)

l Analgesics: sedative effects possibly increased when sedating antihistamines given with l OPIOID ANALGESICS

▶ Antacids: absorption of fexofenadine reduced by ANTACIDS

l Anti-arrhythmics: increased risk of ventricular arrhythmias when mizolastine given with l AMIODARONE, l DISOPYRAMIDE or l FLECAINIDE—avoid concomitant use; manufacturer of mizolastine advises avoid concomitant use with PROPAFENONE (possible risk of ventricular arrhythmias)

l Antibacterials: manufacturer of loratadine advises plasma concentration possibly increased by ERYTHROMYCIN; metabolism of mizolastine inhibited by l ERYTHROMYCIN— avoid concomitant use; increased risk of ventricular arrhythmias when mizolastine given with l MOXIFLOXACIN— avoid concomitant use; effects of fexofenadine possibly reduced by RIFAMPICIN; metabolism of mizolastine possibly inhibited by l MACROLIDES (avoid concomitant use)

l Antidepressants: avoidance of mizolastine advised by

manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); increased antimuscarinic and sedative effects when antihistamines given with MAOIS or TRICYCLICS; manufacturer of promethazine advises avoid for 2 weeks after stopping MAOIS; manufacturer of hydroxyzine advises avoid concomitant use with MAOIS; cyproheptadine possibly antagonises antidepressant effect of SSRIS; possible increased antimuscarinic and sedative effects when antihistamines given with TRICYCLIC-RELATED ANTIDEPRESSANTS

▶ Antidiabetics: thrombocyte count depressed when ketotifen

given with METFORMIN (manufacturer of ketotifen advises avoid concomitant use)

l Antifungals: metabolism of mizolastine inhibited by

l ITRACONAZOLE—avoid concomitant use; metabolism of mizolastine possibly inhibited by l IMIDAZOLES (avoid concomitant use)

l Antimalarials: avoidance of mizolastine advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

▶ Antimuscarinics: increased risk of antimuscarinic side-effects when antihistamines given with ANTIMUSCARINICS

l Antivirals: plasma concentration of chlorphenamine possibly increased by LOPINAVIR; plasma concentration of non- sedating antihistamines possibly increased by RITONAVIR; increased risk of ventricular arrhythmias when mizolastine given with l SAQUINAVIR—avoid concomitant use

▶ Anxiolytics and Hypnotics: increased sedative effect when antihistamines given with ANXIOLYTICS AND HYPNOTICS

l Beta-blockers: increased risk of ventricular arrhythmias when mizolastine given with l SOTALOL—avoid concomitant use

▶ Betahistine: antihistamines theoretically antagonise effect of

BETAHISTINE

l Cytotoxics: possible increased risk of ventricular arrhythmias when mizolastine given with l VANDETANIB—avoid concomitant use

▶ Grapefruit Juice: plasma concentration of bilastine reduced by

GRAPEFRUIT JUICE

▶ Histamine: antihistamines theoretically antagonise effects of HISTAMINE—manufacturer of histamine advises avoid concomitant use

▶ Ulcer-healing Drugs: manufacturer of loratadine advises plasma concentration possibly increased by CIMETIDINE; plasma concentration of hydroxyzine increased by CIMETIDINE

▶ Ulipristal: manufacturer of ulipristal advises give fexofenadine at least 1.5 hours before or after ULIPRISTAL

Antihistamines, Non-sedating *see* Antihistamines

Antihistamines, Sedating *see* Antihistamines

Antimalarials *see* Artemether with Lumefantrine, Artenimol with Piperaquine, Chloroquine, Hydroxychloroquine, Mefloquine, Primaquine, Proguanil, Pyrimethamine, and Quinine

Antimetabolites *see* Capecitabine, Cladribine, Cytarabine, Decitabine, Fludarabine, Fluorouracil, Gemcitabine,

Antimetabolites (continued)

Mercaptopurine, Methotrexate, Pemetrexed, Raltitrexed, Tegafur, and Tioguanine

Interactions | Appendix 1

Antimuscarinics

NOTE Many drugs have antimuscarinic effects; concomitant use of two or more such drugs can increase side-effects such as dry mouth, urine retention, and constipation; concomitant use can also lead to confusion in the elderly. Interactions do not generally apply to antimuscarinics used by inhalation

▶ Alcohol: increased sedative effect when hyoscine given with

ALCOHOL

▶ Analgesics: possible increased risk of antimuscarinic side- effects when antimuscarinics given with CODEINE; increased risk of antimuscarinic side-effects when antimuscarinics given with NEFOPAM

l Anti-arrhythmics: increased risk of ventricular arrhythmias when tolterodine given with l AMIODARONE, l DISOPYRAMIDE or l FLECAINIDE; increased risk of antimuscarinic side-effects when antimuscarinics given with DISOPYRAMIDE

▶ Antibacterials: manufacturer of fesoterodine advises dose reduction when fesoterodine given with CLARITHROMYCIN and TELITHROMYCIN—consult fesoterodine product literature; manufacturer of tolterodine advises avoid concomitant use with CLARITHROMYCIN and ERYTHROMYCIN; plasma concentration of darifenacin possibly increased by ERYTHROMYCIN; plasma concentration of active metabolite of fesoterodine reduced by RIFAMPICIN

▶ Antidepressants: plasma concentration of darifenacin and procyclidine increased by PAROXETINE; increased risk of antimuscarinic side-effects when antimuscarinics given with MAOIS or TRICYCLICS; possible increased antimuscarinic side- effects when antimuscarinics given with TRICYCLIC-RELATED ANTIDEPRESSANTS

l Antifungals: antimuscarinics reduce absorption of KETOCONAZOLE; manufacturer of fesoterodine advises dose reduction when fesoterodine given with ITRACONAZOLE and KETOCONAZOLE—consult fesoterodine product literature; plasma concentration of darifenacin increased by KETOCONAZOLE—avoid concomitant use; plasma concentration of solifenacin increased by l KETOCONAZOLE— see under Solifenacin, p. 670; plasma concentration of oxybutynin increased by KETOCONAZOLE; manufacturer of tolterodine advises avoid concomitant use with ITRACONAZOLE and l KETOCONAZOLE; manufacturer of darifenacin advises avoid concomitant use with ITRACONAZOLE; plasma concentration of solifenacin possibly increased by

l ITRACONAZOLE—see under Solifenacin, p. 670

▶ Antihistamines: increased risk of antimuscarinic side-effects when antimuscarinics given with ANTIHISTAMINES

▶ Antipsychotics: antimuscarinics possibly reduce effects of HALOPERIDOL; increased risk of antimuscarinic side-effects when antimuscarinics given with CLOZAPINE; antimuscarinics reduce plasma concentration of PHENOTHIAZINES, but risk of antimuscarinic side-effects increased

l Antivirals: manufacturer of fesoterodine advises dose reduction when fesoterodine given with ATAZANAVIR, INDINAVIR, RITONAVIR and SAQUINAVIR—consult fesoterodine product literature; manufacturer of darifenacin advises avoid concomitant use with ATAZANAVIR, FOSAMPRENAVIR, INDINAVIR, LOPINAVIR, RITONAVIR, SAQUINAVIR and TIPRANAVIR;

manufacturer of tolterodine advises avoid concomitant use with FOSAMPRENAVIR, INDINAVIR, LOPINAVIR, RITONAVIR and

SAQUINAVIR; plasma concentration of solifenacin possibly increased by l RITONAVIR—see under Solifenacin, p. 670

l Beta-blockers: increased risk of ventricular arrhythmias when tolterodine given with l SOTALOL

▶ Calcium-channel Blockers: plasma concentration of solifenacin increased by VERAPAMIL; manufacturer of darifenacin advises avoid concomitant use with VERAPAMIL

▶ Cardiac Glycosides: darifenacin possibly increases plasma concentration of DIGOXIN

▶ Ciclosporin: manufacturer of darifenacin advises avoid concomitant use with CICLOSPORIN

▶ Domperidone: antimuscarinics antagonise effects of

DOMPERIDONE on gastro-intestinal activity

Interactions | Appendix 1

Antimuscarinics (continued)

▶ Dopaminergics: antimuscarinics possibly reduce absorption of

CO-BENELDOPA, CO-CARELDOPA and LEVODOPA

▶ Hormone Antagonists: possible increased risk of bradycardia when ipratropium or oxybutynin given with PASIREOTIDE

▶ Memantine: effects of antimuscarinics possibly enhanced by

MEMANTINE

▶ Metoclopramide: antimuscarinics antagonise effects of

METOCLOPRAMIDE on gastro-intestinal activity

▶ Nitrates: antimuscarinics possibly reduce effects of sublingual tablets of NITRATES (failure to dissolve under tongue owing to dry mouth)

▶ Parasympathomimetics: antimuscarinics antagonise effects of

PARASYMPATHOMIMETICS

Antipsychotics

NOTE Increased risk of toxicity with myelosuppressive drugs NOTE Avoid concomitant use of clozapine with drugs that have a substantial potential for causing agranulocytosis

▶ ACE Inhibitors: enhanced hypotensive effect when antipsychotics given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when phenothiazines given with ADRENERGIC NEURONE BLOCKERS; higher doses of chlorpromazine antagonise hypotensive effect of ADRENERGIC NEURONE BLOCKERS; haloperidol antagonises hypotensive effect of ADRENERGIC NEURONE BLOCKERS

▶ Adsorbents: absorption of phenothiazines possibly reduced by

KAOLIN

▶ Alcohol: increased sedative effect when antipsychotics given with ALCOHOL

▶ Alpha-blockers: enhanced hypotensive effect when antipsychotics given with ALPHA-BLOCKERS

l Anaesthetics, General: droperidol enhances effects of THIOPENTAL; enhanced hypotensive effect when antipsychotics given with l GENERAL ANAESTHETICS

l Analgesics: possible severe drowsiness when haloperidol given with ACEMETACIN or INDOMETACIN; increased risk of ventricular arrhythmias when antipsychotics that prolong the QT interval given with l METHADONE; increased risk of ventricular arrhythmias when amisulpride given with l METHADONE— avoid concomitant use; increased risk of convulsions when antipsychotics given with TRAMADOL; enhanced hypotensive and sedative effects when antipsychotics given with OPIOID ANALGESICS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when antipsychotics given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antacids: absorption of phenothiazines and sulpiride reduced by ANTACIDS

l Anti-arrhythmics: increased risk of ventricular arrhythmias when antipsychotics that prolong the QT interval given with l ANTI-ARRHYTHMICS that prolong the QT interval; increased risk of ventricular arrhythmias when amisulpride, droperidol, haloperidol, phenothiazines, pimozide or zuclopenthixol given with l AMIODARONE—avoid concomitant use; increased risk of ventricular arrhythmias when benperidol given with

l AMIODARONE—manufacturer of benperidol advises avoid concomitant use; increased risk of ventricular arrhythmias when sulpiride given with l AMIODARONE or l DISOPYRAMIDE; increased risk of ventricular arrhythmias when amisulpride, droperidol, pimozide or zuclopenthixol given with

l DISOPYRAMIDE—avoid concomitant use; possible increased risk of ventricular arrhythmias when haloperidol given with l DISOPYRAMIDE—avoid concomitant use; increased risk of ventricular arrhythmias when phenothiazines given with

l DISOPYRAMIDE; avoidance of phenothiazines advised by manufacturer of l DRONEDARONE (risk of ventricular arrhythmias); increased risk of arrhythmias when clozapine given with l FLECAINIDE

l Antibacterials: plasma concentration of lurasidone possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN—avoid concomitant use; increased risk of ventricular arrhythmias when pimozide given with l CLARITHROMYCIN, l MOXIFLOXACIN or l TELITHROMYCIN—avoid concomitant use; plasma concentration of quetiapine possibly increased by

l CLARITHROMYCIN—manufacturer of quetiapine advises avoid

Antipsychotics

l Antibacterials (continued)

concomitant use; plasma concentration of lurasidone possibly increased by l ERYTHROMYCIN (see under Lurasidone,

p. 315); increased risk of ventricular arrhythmias when amisulpride given with l ERYTHROMYCIN—avoid concomitant use; plasma concentration of clozapine possibly increased by l ERYTHROMYCIN (possible increased risk of convulsions); possible increased risk of ventricular arrhythmias when pimozide given with l ERYTHROMYCIN—avoid concomitant use; plasma concentration of quetiapine increased by

l ERYTHROMYCIN—manufacturer of quetiapine advises avoid concomitant use; increased risk of ventricular arrhythmias when sulpiride given with *parenteral* l ERYTHROMYCIN; increased risk of ventricular arrhythmias when zuclopenthixol given with *parenteral* l ERYTHROMYCIN—avoid concomitant use; plasma concentration of clozapine increased by CIPROFLOXACIN; plasma concentration of olanzapine possibly increased by CIPROFLOXACIN; increased risk of ventricular arrhythmias when droperidol, haloperidol, phenothiazines or zuclopenthixol given with

l MOXIFLOXACIN—avoid concomitant use; increased risk of ventricular arrhythmias when benperidol given with

l MOXIFLOXACIN—manufacturer of benperidol advises avoid concomitant use; plasma concentration of aripiprazole possibly reduced by l RIFABUTIN and l RIFAMPICIN (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); plasma concentration of lurasidone reduced by l RIFAMPICIN—avoid concomitant use; plasma concentration of clozapine possibly reduced by RIFAMPICIN; metabolism of haloperidol accelerated by l RIFAMPICIN (reduced plasma concentration); avoid concomitant use of clozapine with l CHLORAMPHENICOL or

l SULFONAMIDES (increased risk of agranulocytosis); increased risk of ventricular arrhythmias when droperidol, haloperidol or pimozide given with l DELAMANID; increased risk of ventricular arrhythmias when phenothiazines that prolong the QT interval given with l DELAMANID; manufacturer of droperidol advises avoid concomitant use with l MACROLIDES (risk of ventricular arrhythmias); possible increased risk of ventricular arrhythmias when chlorpromazine given with

l TELITHROMYCIN; plasma concentration of quetiapine possibly increased by TELITHROMYCIN

l Antidepressants: plasma concentration of clozapine possibly increased by CITALOPRAM (increased risk of toxicity); avoidance of haloperidol, phenothiazines and pimozide advised by manufacturer of l CITALOPRAM (risk of ventricular arrhythmias); avoidance of haloperidol, phenothiazines and pimozide advised by manufacturer of l ESCITALOPRAM (risk of ventricular arrhythmias); plasma concentration of aripiprazole possibly increased by l FLUOXETINE and

l PAROXETINE (reduce dose of aripiprazole—consult aripiprazole product literature); plasma concentration of clozapine, haloperidol and risperidone increased by

l FLUOXETINE; manufacturer of droperidol advises avoid concomitant use with l FLUOXETINE, l FLUVOXAMINE,

l SERTRALINE and l TRICYCLICS (risk of ventricular arrhythmias); plasma concentration of asenapine and haloperidol possibly increased by FLUVOXAMINE; plasma concentration of clozapine and olanzapine increased by l FLUVOXAMINE; asenapine possibly increases plasma concentration of PAROXETINE; plasma concentration of clozapine increased by l PAROXETINE and l SERTRALINE;

plasma concentration of risperidone possibly increased by PAROXETINE (increased risk of toxicity); metabolism of perphenazine inhibited by PAROXETINE (reduce dose of perphenazine); plasma concentration of haloperidol increased by VENLAFAXINE; clozapine possibly increases CNS effects of l MAOIS; plasma concentration of pimozide possibly increased by l SSRIS (increased risk of ventricular arrhythmias—avoid concomitant use); plasma concentration of lurasidone possibly reduced by l ST JOHN’S WORT—avoid concomitant use; plasma concentration of aripiprazole possibly reduced by l ST JOHN’S WORT (avoid concomitant use or consider increasing the dose of aripiprazole—consult

Antipsychotics

l Antidepressants (continued)

aripiprazole product literature); manufacturer of fluphenazine, haloperidol, sulpiride and zuclopenthixol advises avoid concomitant use with l TRICYCLICS (risk of ventricular arrhythmias); increased risk of antimuscarinic side-effects when phenothiazines given with TRICYCLICS; possible increased risk of ventricular arrhythmias when risperidone given with l TRICYCLICS; possible increased antimuscarinic side-effects when clozapine given with TRICYCLICS

▶ Antidiabetics: phenothiazines possibly antagonise hypoglycaemic effect of SULFONYLUREAS

l Antiepileptics: antipsychotics antagonise anticonvulsant effect of l ANTIEPILEPTICS (convulsive threshold lowered); metabolism of haloperidol, olanzapine, quetiapine and risperidone accelerated by CARBAMAZEPINE (reduced plasma concentration); metabolism of clozapine accelerated by

l CARBAMAZEPINE (reduced plasma concentration), also avoid concomitant use of drugs with substantial potential for causing agranulocytosis; plasma concentration of aripiprazole reduced by l CARBAMAZEPINE (avoid concomitant use or consider increasing the dose of aripiprazole —consult aripiprazole product literature); plasma concentration of paliperidone reduced by CARBAMAZEPINE; plasma concentration of lurasidone possibly reduced by

l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE—avoid concomitant use; chlorpromazine possibly increases or decreases plasma concentration of FOSPHENYTOIN and PHENYTOIN; metabolism of clozapine and quetiapine accelerated by FOSPHENYTOIN (reduced plasma concentration); plasma concentration of aripiprazole possibly reduced by l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE (avoid

concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); plasma concentration of haloperidol reduced by FOSPHENYTOIN and PHENYTOIN; metabolism of haloperidol accelerated by PHENOBARBITAL and PRIMIDONE (reduced plasma concentration); plasma concentration of both drugs reduced when chlorpromazine given with PHENOBARBITAL and PRIMIDONE; plasma concentration of clozapine possibly reduced by PHENOBARBITAL and PRIMIDONE; metabolism of clozapine and quetiapine accelerated by PHENYTOIN (reduced plasma concentration); increased risk of side-effects including neutropenia when olanzapine given with l SODIUM VALPROATE and l VALPROIC ACID; plasma concentration of clozapine possibly increased or decreased by SODIUM VALPROATE and VALPROIC ACID

l Antifungals: plasma concentration of lurasidone increased by l KETOCONAZOLE—avoid concomitant use; metabolism of aripiprazole inhibited by l KETOCONAZOLE (reduce dose of aripiprazole); plasma concentration of lurasidone possibly increased by l FLUCONAZOLE (see under Lurasidone, p. 315); plasma concentration of lurasidone possibly increased by

l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE—avoid

concomitant use; plasma concentration of aripiprazole possibly increased by l ITRACONAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); side- effects of risperidone possibly increased by ITRACONAZOLE; plasma concentration of haloperidol possibly increased by ITRACONAZOLE; increased risk of ventricular arrhythmias when pimozide given with l IMIDAZOLES or l TRIAZOLES—avoid concomitant use; plasma concentration of quetiapine possibly increased by l IMIDAZOLES and l TRIAZOLES— manufacturer of quetiapine advises avoid concomitant use

l Antimalarials: avoidance of antipsychotics advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; avoidance of droperidol, haloperidol, phenothiazines and pimozide advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when droperidol given with

l CHLOROQUINE, l HYDROXYCHLOROQUINE or l QUININE—avoid

concomitant use; possible increased risk of ventricular arrhythmias when haloperidol given with l MEFLOQUINE or

Antipsychotics

l Antimalarials (continued)

Interactions | Appendix 1

l QUININE—avoid concomitant use; manufacturer of risperidone advises possible risk of ventricular arrhythmias when risperidone given with l MEFLOQUINE; increased risk of ventricular arrhythmias when pimozide given with

l MEFLOQUINE or l QUININE—avoid concomitant use; manufacturer of amisulpride advises avoid concomitant use with MEFLOQUINE; possible increased risk of ventricular arrhythmias when risperidone given with l QUININE

▶ Antimuscarinics: increased risk of antimuscarinic side-effects when clozapine given with ANTIMUSCARINICS; plasma concentration of phenothiazines reduced by ANTIMUSCARINICS, but risk of antimuscarinic side-effects increased; effects of haloperidol possibly reduced by ANTIMUSCARINICS

l Antipsychotics: increased risk of ventricular arrhythmias when amisulpride, pimozide or sulpiride given with l DROPERIDOL— avoid concomitant use; increased risk of ventricular arrhythmias when phenothiazines that prolong the QT interval given with l DROPERIDOL—avoid concomitant use; avoid concomitant use of clozapine with depot formulation of l FLUPENTIXOL, l FLUPHENAZINE, l HALOPERIDOL,

l PIPOTIAZINE, l RISPERIDONE or l ZUCLOPENTHIXOL as cannot

be withdrawn quickly if neutropenia occurs; increased risk of ventricular arrhythmias when sulpiride given with

l HALOPERIDOL; chlorpromazine possibly increases plasma concentration of HALOPERIDOL; increased risk of ventricular arrhythmias when droperidol given with l HALOPERIDOL— avoid concomitant use; increased risk of ventricular arrhythmias when pimozide given with l PHENOTHIAZINES— avoid concomitant use; lurasidone possibly increases plasma concentration of PIMOZIDE (increased risk of toxicity); possible increased risk of ventricular arrhythmias when antipsychotics that prolong the QT interval given with

l RISPERIDONE; increased risk of ventricular arrhythmias when pimozide given with l SULPIRIDE

l Antivirals: plasma concentration of aripiprazole possibly increased by l ATAZANAVIR, l DARUNAVIR, l FOSAMPRENAVIR, l INDINAVIR, l LOPINAVIR, l RITONAVIR, l SAQUINAVIR and

l TIPRANAVIR (reduce dose of aripiprazole—consult aripiprazole product literature); plasma concentration of quetiapine possibly increased by l ATAZANAVIR, l BOCEPREVIR, l DARUNAVIR, l FOSAMPRENAVIR, l INDINAVIR, l LOPINAVIR,

l RITONAVIR, l SAQUINAVIR, l TELAPREVIR and l TIPRANAVIR—

manufacturer of quetiapine advises avoid concomitant use; plasma concentration of pimozide possibly increased by

l ATAZANAVIR—avoid concomitant use; avoidance of pimozide advised by manufacturer of l BOCEPREVIR and l TELAPREVIR; plasma concentration of lurasidone possibly increased by

l BOCEPREVIR, l INDINAVIR, l RITONAVIR, l SAQUINAVIR and

l TELAPREVIR—avoid concomitant use; plasma concentration of aripiprazole possibly reduced by l EFAVIRENZ and

l NEVIRAPINE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); plasma concentration of pimozide possibly increased by l EFAVIRENZ, l INDINAVIR and l SAQUINAVIR (increased risk of ventricular arrhythmias—avoid concomitant use); plasma concentration of pimozide increased by l FOSAMPRENAVIR and l RITONAVIR (increased risk of ventricular arrhythmias—avoid concomitant use); plasma concentration of antipsychotics possibly increased by

l RITONAVIR; plasma concentration of olanzapine reduced by RITONAVIR—consider increasing dose of olanzapine; avoidance of clozapine advised by manufacturer of

l RITONAVIR (increased risk of toxicity); increased risk of ventricular arrhythmias when clozapine, haloperidol or phenothiazines given with l SAQUINAVIR—avoid concomitant use

l Anxiolytics and Hypnotics: increased sedative effect when antipsychotics given with ANXIOLYTICS AND HYPNOTICS; plasma concentration of haloperidol possibly increased by ALPRAZOLAM; lurasidone increases plasma concentration of MIDAZOLAM; serious adverse events reported with concomitant use of clozapine and

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Antipsychotics

l Anxiolytics and Hypnotics (continued)

l BENZODIAZEPINES (causality not established); increased risk of hypotension, bradycardia and respiratory depression when *intramuscular* olanzapine given with *parenteral*

l BENZODIAZEPINES; plasma concentration of haloperidol increased by BUSPIRONE

l Aprepitant: avoidance of pimozide advised by manufacturer of

l APREPITANT

l Atomoxetine: increased risk of ventricular arrhythmias when antipsychotics that prolong the QT interval given with

l ATOMOXETINE

l Beta-blockers: enhanced hypotensive effect when phenothiazines given with BETA-BLOCKERS; plasma concentration of both drugs may increase when chlorpromazine given with l PROPRANOLOL; increased risk of ventricular arrhythmias when droperidol or zuclopenthixol given with l SOTALOL—avoid concomitant use; increased risk of ventricular arrhythmias when amisulpride, phenothiazines, pimozide or sulpiride given with l SOTALOL; possible increased risk of ventricular arrhythmias when risperidone given with l SOTALOL; possible increased risk of ventricular arrhythmias when haloperidol given with

l SOTALOL—avoid concomitant use

l Calcium-channel Blockers: enhanced hypotensive effect when antipsychotics given with CALCIUM-CHANNEL BLOCKERS; plasma concentration of lurasidone increased by l DILTIAZEM (see under Lurasidone, p. 315); plasma concentration of lurasidone possibly increased by l VERAPAMIL (see under Lurasidone, p. 315)

▶ Clonidine: enhanced hypotensive effect when phenothiazines given with CLONIDINE

l Cobicistat: plasma concentration of lurasidone possibly increased by l COBICISTAT—avoid concomitant use; plasma concentration of pimozide possibly increased by

l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Cytotoxics: avoid concomitant use of clozapine with

l CYTOTOXICS (increased risk of agranulocytosis); possible increased risk of ventricular arrhythmias when haloperidol given with l BOSUTINIB; caution with pimozide advised by manufacturer of l CRIZOTINIB; avoidance of pimozide and quetiapine advised by manufacturer of IDELALISIB; avoidance of pimozide advised by manufacturer of l LAPATINIB; possible increased risk of ventricular arrhythmias when amisulpride, chlorpromazine, haloperidol, pimozide, sulpiride or zuclopenthixol given with l VANDETANIB—avoid concomitant use; increased risk of ventricular arrhythmias when antipsychotics that prolong the QT interval given with

l ARSENIC TRIOXIDE; increased risk of ventricular arrhythmias when haloperidol given with l ARSENIC TRIOXIDE

▶ Deferasirox: avoidance of clozapine advised by manufacturer of DEFERASIROX

▶ Desferrioxamine: manufacturer of levomepromazine advises avoid concomitant use with DESFERRIOXAMINE; avoidance of prochlorperazine advised by manufacturer of DESFERRIOXAMINE

▶ Diazoxide: enhanced hypotensive effect when phenothiazines given with DIAZOXIDE

l Diuretics: risk of ventricular arrhythmias with amisulpride increased by hypokalaemia caused by l DIURETICS; risk of ventricular arrhythmias with pimozide increased by hypokalaemia caused by l DIURETICS (avoid concomitant use); enhanced hypotensive effect when phenothiazines given with DIURETICS

▶ Dopaminergics: increased risk of extrapyramidal side-effects when antipsychotics given with AMANTADINE; antipsychotics antagonise effects of APOMORPHINE, CO-BENELDOPA, CO- CARELDOPA, LEVODOPA and PERGOLIDE; antipsychotics antagonise hypoprolactinaemic and antiparkinsonian effects of BROMOCRIPTINE and CABERGOLINE; manufacturer of amisulpride advises avoid concomitant use of CO-BENELDOPA, CO-CARELDOPA and LEVODOPA (antagonism of effect); avoidance of antipsychotics advised by manufacturer of PRAMIPEXOLE, ROPINIROLE and ROTIGOTINE (antagonism of effect)

Antipsychotics (continued)

▶ Ergot Alkaloids: lurasidone possibly increases plasma concentration of ERGOT ALKALOIDS (increased risk of toxicity)

l Fosaprepitant: avoidance of pimozide advised by manufacturer of l FOSAPREPITANT

l Grapefruit Juice: manufacturer of lurasidone and pimozide advises avoid concomitant use with GRAPEFRUIT JUICE; plasma concentration of quetiapine possibly increased by

l GRAPEFRUIT JUICE—manufacturer of quetiapine advises avoid concomitant use

▶ Histamine: antipsychotics theoretically antagonise effects of HISTAMINE—manufacturer of histamine advises avoid concomitant use

l Hormone Antagonists: manufacturer of droperidol advises avoid concomitant use with l TAMOXIFEN (risk of ventricular arrhythmias)

l Ivabradine: increased risk of ventricular arrhythmias when pimozide given with l IVABRADINE

l Lithium: increased risk of extrapyramidal side-effects and possibly neurotoxicity when clozapine, flupentixol, haloperidol, phenothiazines, risperidone or zuclopenthixol given with l LITHIUM; possible risk of toxicity when olanzapine given with LITHIUM; extrapyramidal side-effects of quetiapine possibly increased by LITHIUM; increased risk of extrapyramidal side-effects when sulpiride given with LITHIUM

▶ Memantine: effects of antipsychotics possibly reduced by

MEMANTINE

▶ Methyldopa: enhanced hypotensive effect when antipsychotics given with METHYLDOPA (also increased risk of extrapyramidal effects)

▶ Metoclopramide: increased risk of extrapyramidal side-effects when antipsychotics given with METOCLOPRAMIDE

▶ Moxonidine: enhanced hypotensive effect when phenothiazines given with MOXONIDINE

▶ Muscle Relaxants: promazine possibly enhances effects of

SUXAMETHONIUM

▶ Nitrates: enhanced hypotensive effect when phenothiazines given with NITRATES

l Penicillamine: avoid concomitant use of clozapine with

l PENICILLAMINE (increased risk of agranulocytosis)

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when amisulpride or droperidol given with

l PENTAMIDINE ISETIONATE—avoid concomitant use; increased risk of ventricular arrhythmias when phenothiazines given with l PENTAMIDINE ISETIONATE

▶ Sodium Benzoate: haloperidol possibly reduces effects of

SODIUM BENZOATE

▶ Sodium Oxybate: antipsychotics possibly enhance effects of

SODIUM OXYBATE

▶ Sodium Phenylbutyrate: haloperidol possibly reduces effects of

SODIUM PHENYLBUTYRATE

▶ Sympathomimetics: antipsychotics antagonise hypertensive effect of SYMPATHOMIMETICS; antipsychotic effects of chlorpromazine possibly antagonised by DEXAMFETAMINE; chlorpromazine possibly reduces effects of LISDEXAMFETAMINE; side-effects of risperidone possibly increased by METHYLPHENIDATE

l Tacrolimus: manufacturer of droperidol advises avoid concomitant use with l TACROLIMUS (risk of ventricular arrhythmias)

▶ Tetrabenazine: increased risk of extrapyramidal side-effects when antipsychotics given with TETRABENAZINE

▶ Ulcer-healing Drugs: effects of antipsychotics, chlorpromazine and clozapine possibly enhanced by CIMETIDINE; plasma concentration of clozapine possibly reduced by OMEPRAZOLE; absorption of sulpiride reduced by SUCRALFATE

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when phenothiazines given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Antivirals *see* individual drugs

Anxiolytics and Hypnotics

▶ ACE Inhibitors: enhanced hypotensive effect when anxiolytics and hypnotics given with ACE INHIBITORS

Anxiolytics and Hypnotics (continued)

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when anxiolytics and hypnotics given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: increased sedative effect when anxiolytics and hypnotics given with ALCOHOL

▶ Alpha-blockers: enhanced hypotensive and sedative effects when anxiolytics and hypnotics given with ALPHA-BLOCKERS

▶ Aminophylline: effects of benzodiazepines possibly reduced by

AMINOPHYLLINE

▶ Anaesthetics, General: increased sedative effect when anxiolytics and hypnotics given with GENERAL ANAESTHETICS

▶ Analgesics: metabolism of midazolam possibly inhibited by FENTANYL; increased sedative effect when anxiolytics and hypnotics given with OPIOID ANALGESICS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when anxiolytics and hypnotics given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Antibacterials: metabolism of midazolam inhibited by

l CLARITHROMYCIN, l ERYTHROMYCIN and l TELITHROMYCIN

(increased plasma concentration with increased sedation); plasma concentration of buspirone increased by ERYTHROMYCIN (reduce dose of buspirone); metabolism of zopiclone inhibited by ERYTHROMYCIN; manufacturer of zolpidem advises avoid concomitant use with CIPROFLOXACIN; metabolism of benzodiazepines possibly accelerated by RIFAMPICIN (reduced plasma concentration); metabolism of diazepam and zaleplon accelerated by RIFAMPICIN (reduced plasma concentration); metabolism of buspirone possibly accelerated by RIFAMPICIN; metabolism of zolpidem accelerated by RIFAMPICIN (reduced plasma concentration and reduced effect); plasma concentration of zopiclone significantly reduced by RIFAMPICIN; metabolism of diazepam inhibited by ISONIAZID

▶ Anticoagulants: chloral may transiently enhance anticoagulant effect of COUMARINS

l Antidepressants: plasma concentration of alprazolam increased by FLUOXETINE; plasma concentration of melatonin increased by l FLUVOXAMINE—avoid concomitant use; plasma concentration of some benzodiazepines increased by FLUVOXAMINE; sedative effects possibly increased when zolpidem given with SERTRALINE; manufacturer of buspirone advises avoid concomitant use with MAOIS; avoidance of buspirone for 14 days after stopping l TRANYLCYPROMINE advised by manufacturer of tranylcypromine; plasma concentration of *oral* midazolam possibly reduced by ST JOHN’S WORT; increased sedative effect when anxiolytics and hypnotics given with MIRTAZAPINE, TRICYCLIC-RELATED ANTIDEPRESSANTS or TRICYCLICS

▶ Antiepileptics: plasma concentration of midazolam reduced by CARBAMAZEPINE and PERAMPANEL; plasma concentration of clonazepam often reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE; benzodiazepines possibly increase or decrease plasma concentration of FOSPHENYTOIN and PHENYTOIN; diazepam increases or decreases plasma concentration of FOSPHENYTOIN and PHENYTOIN; increased sedative effect when anxiolytics and hypnotics given with PHENOBARBITAL or PRIMIDONE; clobazam possibly increases plasma concentration of SODIUM VALPROATE and VALPROIC ACID; plasma concentration of diazepam and lorazepam possibly increased by SODIUM VALPROATE; increased risk of side-effects when clonazepam given with SODIUM VALPROATE or VALPROIC ACID; plasma concentration of clobazam increased by STIRIPENTOL; plasma concentration of diazepam and lorazepam possibly increased by VALPROIC ACID

l Antifungals: plasma concentration of alprazolam increased by

l KETOCONAZOLE—manufacturer of ketoconazole advises avoid concomitant use; plasma concentration of midazolam increased by l KETOCONAZOLE (risk of prolonged sedation— avoid concomitant use of *oral* midazolam); plasma concentration of zolpidem increased by KETOCONAZOLE; plasma concentration of diazepam and midazolam increased by l FLUCONAZOLE (risk of prolonged sedation); plasma concentration of alprazolam increased by ITRACONAZOLE; plasma concentration of midazolam increased by

l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE (risk of

Anxiolytics and Hypnotics

l Antifungals (continued)

Interactions | Appendix 1

prolonged sedation); plasma concentration of buspirone increased by ITRACONAZOLE (reduce dose of buspirone); plasma concentration of diazepam increased by

l VORICONAZOLE (risk of prolonged sedation)

▶ Antihistamines: increased sedative effect when anxiolytics and hypnotics given with ANTIHISTAMINES

l Antipsychotics: increased sedative effect when anxiolytics and hypnotics given with ANTIPSYCHOTICS; alprazolam possibly increases plasma concentration of HALOPERIDOL; buspirone increases plasma concentration of HALOPERIDOL; serious adverse events reported with concomitant use of benzodiazepines and l CLOZAPINE (causality not established); plasma concentration of midazolam increased by LURASIDONE; increased risk of hypotension, bradycardia and respiratory depression when *parenteral* benzodiazepines given with *intramuscular* l OLANZAPINE

l Antivirals: plasma concentration of midazolam possibly increased by l ATAZANAVIR—avoid concomitant use of *oral* midazolam; plasma concentration of *oral* midazolam increased by l BOCEPREVIR—manufacturer of boceprevir advises avoid concomitant use; increased risk of prolonged sedation when midazolam given with l EFAVIRENZ—avoid concomitant use; plasma concentration of midazolam possibly increased by l FOSAMPRENAVIR, l INDINAVIR,

l RITONAVIR and l TELAPREVIR (risk of prolonged sedation— avoid concomitant use of *oral* midazolam); increased risk of prolonged sedation when alprazolam given with

l INDINAVIR—avoid concomitant use; plasma concentration of anxiolytics and hypnotics possibly increased by l RITONAVIR; plasma concentration of alprazolam, diazepam, flurazepam and zolpidem possibly increased by l RITONAVIR (risk of extreme sedation and respiratory depression—avoid concomitant use); plasma concentration of buspirone increased by RITONAVIR (increased risk of toxicity); plasma concentration of midazolam increased by l SAQUINAVIR (risk of prolonged sedation—avoid concomitant use of *oral* midazolam); plasma concentration of *oral* midazolam increased by SIMEPREVIR

▶ Aprepitant: plasma concentration of midazolam increased by

APREPITANT (risk of prolonged sedation)

▶ Beta-blockers: enhanced hypotensive effect when anxiolytics and hypnotics given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when anxiolytics and hypnotics given with CALCIUM-CHANNEL BLOCKERS; midazolam increases absorption of LERCANIDIPINE; metabolism of midazolam inhibited by DILTIAZEM and VERAPAMIL (increased plasma concentration with increased sedation); plasma concentration of buspirone increased by DILTIAZEM and VERAPAMIL (reduce dose of buspirone)

▶ Cardiac Glycosides: alprazolam increases plasma concentration of DIGOXIN (increased risk of toxicity)

▶ Clonidine: enhanced hypotensive effect when anxiolytics and hypnotics given with CLONIDINE

l Cobicistat: avoidance of *oral* midazolam advised by manufacturer of l COBICISTAT

l Cytotoxics: plasma concentration of midazolam increased by l CRIZOTINIB and NILOTINIB; avoidance of *oral* midazolam advised by manufacturer of IDELALISIB

▶ Deferasirox: plasma concentration of midazolam possibly reduced by DEFERASIROX

▶ Diazoxide: enhanced hypotensive effect when anxiolytics and hypnotics given with DIAZOXIDE

▶ Disulfiram: metabolism of benzodiazepines inhibited by DISULFIRAM (increased sedative effects); increased risk of temazepam toxicity when given with DISULFIRAM

▶ Diuretics: enhanced hypotensive effect when anxiolytics and hypnotics given with DIURETICS; administration of chloral with *parenteral* FUROSEMIDE may displace thyroid hormone from binding sites

▶ Dopaminergics: benzodiazepines possibly antagonise effects of

CO-BENELDOPA, CO-CARELDOPA and LEVODOPA

▶ Fosaprepitant: plasma concentration of midazolam increased by FOSAPREPITANT (risk of prolonged sedation)

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Anxiolytics and Hypnotics (continued)

▶ Grapefruit Juice: plasma concentration of *oral* midazolam possibly increased by GRAPEFRUIT JUICE; plasma concentration of buspirone increased by GRAPEFRUIT JUICE

▶ Ivacaftor: plasma concentration of midazolam increased by

IVACAFTOR

▶ Lipid-regulating Drugs: plasma concentration of midazolam possibly increased by ATORVASTATIN; separating administration from alprazolam by 12 hours advised by manufacturer of LOMITAPIDE

▶ Lithium: increased risk of neurotoxicity when clonazepam given with LITHIUM

▶ Lofexidine: increased sedative effect when anxiolytics and hypnotics given with LOFEXIDINE

▶ Methyldopa: enhanced hypotensive effect when anxiolytics and hypnotics given with METHYLDOPA

l Methylthioninium: possible risk of CNS toxicity when buspirone given with l METHYLTHIONINIUM—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

▶ Moxonidine: enhanced hypotensive effect when anxiolytics and hypnotics given with MOXONIDINE; sedative effects possibly increased when benzodiazepines given with MOXONIDINE

▶ Muscle Relaxants: increased sedative effect when anxiolytics and hypnotics given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when anxiolytics and hypnotics given with NITRATES

▶ Oestrogens: plasma concentration of melatonin increased by OESTROGENS; plasma concentration of chlordiazepoxide, diazepam and nitrazepam possibly increased by OESTROGENS; plasma concentration of lorazepam, oxazepam and temazepam possibly reduced by OESTROGENS

▶ Progestogens: plasma concentration of chlordiazepoxide, diazepam and nitrazepam possibly increased by PROGESTOGENS; plasma concentration of lorazepam, oxazepam and temazepam possibly reduced by PROGESTOGENS

l Sodium Oxybate: benzodiazepines enhance effects of l SODIUM OXYBATE (avoid concomitant use)

▶ Theophylline: effects of benzodiazepines possibly reduced by

THEOPHYLLINE

▶ Ulcer-healing Drugs: plasma concentration of melatonin increased by CIMETIDINE; metabolism of benzodiazepines, clomethiazole and zaleplon inhibited by CIMETIDINE (increased plasma concentration); metabolism of diazepam possibly inhibited by ESOMEPRAZOLE and OMEPRAZOLE (increased plasma concentration)

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when anxiolytics and hypnotics given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Apixaban

l Analgesics: increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins)

l Antibacterials: manufacturer of apixaban advises avoid concomitant use with CLARITHROMYCIN and TELITHROMYCIN; plasma concentration of apixaban possibly reduced by

l RIFAMPICIN—manufacturer of apixaban advises avoid concomitant use when given for treatment of deep-vein thrombosis or pulmonary embolism

l Anticoagulants: increased risk of haemorrhage when apixaban given with other l ANTICOAGULANTS (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency); increased risk of haemorrhage when other anticoagulants given with

l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

l Antidepressants: plasma concentration of apixaban possibly reduced by l ST JOHN’S WORT—manufacturer of apixaban advises avoid concomitant use when given for treatment of deep-vein thrombosis or pulmonary embolism

Apixaban (continued)

l Antiepileptics: plasma concentration of apixaban possibly reduced by l CARBAMAZEPINE—manufacturer of apixaban advises avoid concomitant use when given for treatment of deep-vein thrombosis or pulmonary embolism; plasma concentration of apixaban possibly reduced by

l FOSPHENYTOIN, l PHENOBARBITAL, l PHENYTOIN and

l PRIMIDONE

l Antifungals: plasma concentration of apixaban increased by l KETOCONAZOLE—manufacturer of apixaban advises avoid concomitant use; manufacturer of apixaban advises avoid concomitant use with ITRACONAZOLE, POSACONAZOLE and VORICONAZOLE

▶ Antivirals: manufacturer of apixaban advises avoid concomitant use with ATAZANAVIR, BOCEPREVIR, DARUNAVIR, FOSAMPRENAVIR, INDINAVIR, LOPINAVIR, RITONAVIR, SAQUINAVIR, TELAPREVIR and TIPRANAVIR

▶ Cobicistat: manufacturer of apixaban advises avoid concomitant use with COBICISTAT

▶ Sulfinpyrazone: increased risk of bleeding when apixaban given with SULFINPYRAZONE

Apomorphine

▶ Antipsychotics: effects of apomorphine antagonised by

ANTIPSYCHOTICS

▶ Dopaminergics: effects of apomorphine possibly enhanced by

ENTACAPONE

l 5HT3-receptor Antagonists: possible increased hypotensive effect when apomorphine given with l ONDANSETRON—avoid concomitant use

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

Apraclonidine

▶ Antidepressants: manufacturer of apraclonidine advises avoid concomitant use with MAOIS, TRICYCLIC-RELATED ANTIDEPRESSANTS and TRICYCLICS

▶ Sympathomimetics: manufacturer of apraclonidine advises avoid concomitant use with SYMPATHOMIMETICS

Aprepitant

▶ Antibacterials: plasma concentration of aprepitant possibly increased by CLARITHROMYCIN and TELITHROMYCIN; plasma concentration of aprepitant reduced by RIFAMPICIN

▶ Anticoagulants: aprepitant possibly reduces anticoagulant effect of WARFARIN

l Antidepressants: manufacturer of aprepitant advises avoid concomitant use with l ST JOHN’S WORT

▶ Antidiabetics: aprepitant reduces plasma concentration of

TOLBUTAMIDE

▶ Antiepileptics: plasma concentration of aprepitant possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

▶ Antifungals: plasma concentration of aprepitant increased by

KETOCONAZOLE

l Antipsychotics: manufacturer of aprepitant advises avoid concomitant use with l PIMOZIDE

▶ Antivirals: plasma concentration of aprepitant possibly increased by RITONAVIR

▶ Anxiolytics and Hypnotics: aprepitant increases plasma concentration of MIDAZOLAM (risk of prolonged sedation)

l Avanafil: aprepitant possibly increases plasma concentration of l AVANAFIL—see under Avanafil, p. 698

▶ Calcium-channel Blockers: plasma concentration of both drugs may increase when aprepitant given with DILTIAZEM

▶ Corticosteroids: aprepitant inhibits metabolism of DEXAMETHASONE and METHYLPREDNISOLONE (reduce dose of dexamethasone and methylprednisolone)

l Cytotoxics: aprepitant possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; aprepitant possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

▶ Dapoxetine: manufacturer of dapoxetine advises dose reduction when aprepitant given with DAPOXETINE (see under Dapoxetine, p. 703)

Aprepitant (continued)

l Oestrogens: aprepitant possibly causes contraceptive failure of hormonal contraceptives containing l OESTROGENS (alternative contraception recommended)

l Progestogens: aprepitant possibly causes contraceptive failure of hormonal contraceptives containing l PROGESTOGENS (alternative contraception recommended)

Argatroban

l Analgesics: increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins)

l Anticoagulants: increased risk of haemorrhage when other anticoagulants given with l APIXABAN, l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

Aripiprazole *see* Antipsychotics

Arsenic Trioxide

l Anti-arrhythmics: increased risk of ventricular arrhythmias when arsenic trioxide given with l AMIODARONE or

l DISOPYRAMIDE

l Antibacterials: increased risk of ventricular arrhythmias when arsenic trioxide given with l DELAMANID, l ERYTHROMYCIN,

l LEVOFLOXACIN or l MOXIFLOXACIN

l Antidepressants: increased risk of ventricular arrhythmias when arsenic trioxide given with l AMITRIPTYLINE or

l CLOMIPRAMINE

l Antifungals: increased risk of ventricular arrhythmias when arsenic trioxide given with l AMPHOTERICIN

l Antimalarials: avoidance of arsenic trioxide advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

l Antipsychotics: increased risk of ventricular arrhythmias when arsenic trioxide given with l ANTIPSYCHOTICS that prolong the QT interval; increased risk of ventricular arrhythmias when arsenic trioxide given with l HALOPERIDOL; avoid concomitant use of cytotoxics with l CLOZAPINE (increased risk of agranulocytosis)

l Beta-blockers: increased risk of ventricular arrhythmias when arsenic trioxide given with l SOTALOL

l Cytotoxics: possible increased risk of ventricular arrhythmias when arsenic trioxide given with l VANDETANIB—avoid concomitant use

l Diuretics: risk of ventricular arrhythmias with arsenic trioxide increased by hypokalaemia caused by l ACETAZOLAMIDE,

l LOOP DIURETICS or l THIAZIDES AND RELATED DIURETICS

l Lithium: increased risk of ventricular arrhythmias when arsenic trioxide given with l LITHIUM

Artemether with Lumefantrine

l Anti-arrhythmics: manufacturer of artemether with lumefantrine advises avoid concomitant use with

l AMIODARONE, l DISOPYRAMIDE and l FLECAINIDE (risk of

ventricular arrhythmias)

l Antibacterials: manufacturer of artemether with lumefantrine advises avoid concomitant use with l MACROLIDES and

l QUINOLONES

l Antidepressants: possible increased risk of ventricular arrhythmias when artemether with lumefantrine given with l CITALOPRAM or l ESCITALOPRAM—avoid concomitant use; manufacturer of artemether with lumefantrine advises avoid concomitant use with l ANTIDEPRESSANTS

l Antifungals: manufacturer of artemether with lumefantrine

advises avoid concomitant use with l IMIDAZOLES and

l TRIAZOLES

l Antimalarials: manufacturer of artemether with lumefantrine advises avoid concomitant use with l ANTIMALARIALS; increased risk of ventricular arrhythmias when artemether with lumefantrine given with l QUININE

l Antipsychotics: manufacturer of artemether with lumefantrine advises avoid concomitant use with l ANTIPSYCHOTICS

l Antivirals: manufacturer of artemether with lumefantrine advises caution with ATAZANAVIR, FOSAMPRENAVIR, INDINAVIR,

Artemether with Lumefantrine

l Antivirals (continued)

Interactions | Appendix 1

LOPINAVIR, RITONAVIR, SAQUINAVIR and TIPRANAVIR; avoidance

of artemether with lumefantrine advised by manufacturer of l BOCEPREVIR; plasma concentration of lumefantrine increased when artemether with lumefantrine given with DARUNAVIR; plasma concentration of artemether with lumefantrine reduced by l EFAVIRENZ and ETRAVIRINE

l Beta-blockers: manufacturer of artemether with lumefantrine advises avoid concomitant use with l METOPROLOL and

l SOTALOL

l Cytotoxics: possible increased risk of ventricular arrhythmias when artemether with lumefantrine given with

l VANDETANIB—avoid concomitant use

▶ Grapefruit Juice: plasma concentration of artemether with lumefantrine possibly increased by GRAPEFRUIT JUICE

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

l Ulcer-healing Drugs: manufacturer of artemether with lumefantrine advises avoid concomitant use with

l CIMETIDINE

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Artenimol with Piperaquine

NOTE Piperaquine has a long half-life; there is a potential for drug interactions to occur for up to 3 months after treatment has been stopped

l Analgesics: manufacturer of artenimol with piperaquine advises avoid concomitant use with l METHADONE (possible risk of ventricular arrhythmias)

l Anti-arrhythmics: manufacturer of artenimol with piperaquine advises avoid concomitant use with l AMIODARONE and

l DISOPYRAMIDE (possible risk of ventricular arrhythmias)

l Antibacterials: manufacturer of artenimol with piperaquine advises avoid concomitant use with l MACROLIDES and

l MOXIFLOXACIN (possible risk of ventricular arrhythmias); manufacturer of artenimol with piperaquine advises avoid concomitant use with RIFAMPICIN

l Antidepressants: possible increased risk of ventricular arrhythmias when artenimol with piperaquine given with l CITALOPRAM or l ESCITALOPRAM—avoid concomitant use; manufacturer of artenimol with piperaquine advises avoid concomitant use with l ANTIDEPRESSANTS

▶ Antiepileptics: manufacturer of artenimol with piperaquine advises avoid concomitant use with CARBAMAZEPINE,

FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Antifungals: manufacturer of artenimol with piperaquine advises avoid concomitant use with l IMIDAZOLES and

l TRIAZOLES (possible risk of ventricular arrhythmias)

l Antihistamines: manufacturer of artenimol with piperaquine advises avoid concomitant use with l MIZOLASTINE (possible risk of ventricular arrhythmias)

l Antimalarials: avoidance of antimalarials advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE

l Antipsychotics: manufacturer of artenimol with piperaquine advises avoid concomitant use with l DROPERIDOL,

l HALOPERIDOL, l PHENOTHIAZINES and l PIMOZIDE (possible

risk of ventricular arrhythmias)

l Antivirals: manufacturer of artenimol with piperaquine advises avoid concomitant use with l SAQUINAVIR (possible risk of ventricular arrhythmias)

l Beta-blockers: manufacturer of artenimol with piperaquine advises avoid concomitant use with l SOTALOL (possible risk of ventricular arrhythmias)

l Cytotoxics: manufacturer of artenimol with piperaquine advises avoid concomitant use with l ARSENIC TRIOXIDE (possible risk of ventricular arrhythmias); manufacturer of artenimol with piperaquine advises avoid concomitant use with l VINBLASTINE, l VINCRISTINE, l VINFLUNINE and

l VINORELBINE

l Domperidone: manufacturer of artenimol with piperaquine advises avoid concomitant use with l DOMPERIDONE (possible risk of ventricular arrhythmias)

▶ Grapefruit Juice: manufacturer of artenimol with piperaquine advises avoid concomitant use with GRAPEFRUIT JUICE

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Artenimol with Piperaquine (continued)

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

l Pentamidine Isetionate: manufacturer of artenimol with piperaquine advises avoid concomitant use with

l PENTAMIDINE ISETIONATE (possible risk of ventricular arrhythmias)

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Ascorbic acid *see* Vitamins Asenapine *see* Antipsychotics Aspirin

▶ Adsorbents: absorption of aspirin possibly reduced by KAOLIN

▶ Anaesthetics, General: aspirin possibly enhances effects of

THIOPENTAL

l Analgesics: avoid concomitant use of aspirin with l NSAIDS (increased side-effects); antiplatelet effect of aspirin possibly reduced by IBUPROFEN

▶ Antacids: excretion of aspirin increased by alkaline urine due to some ANTACIDS

l Anticoagulants: increased risk of bleeding when aspirin given with l COUMARINS or l PHENINDIONE (due to antiplatelet effect); aspirin enhances anticoagulant effect of l HEPARINS

l Antidepressants: increased risk of bleeding when aspirin given with l SSRIS or l VENLAFAXINE

▶ Antiepileptics: aspirin enhances effects of FOSPHENYTOIN, PHENYTOIN, SODIUM VALPROATE and VALPROIC ACID

▶ Clopidogrel: increased risk of bleeding when aspirin given with

CLOPIDOGREL

▶ Corticosteroids: increased risk of gastro-intestinal bleeding and ulceration when aspirin given with CORTICOSTEROIDS, also corticosteroids reduce plasma concentration of salicylate

l Cytotoxics: aspirin reduces excretion of l METHOTREXATE (increased risk of toxicity); aspirin possibly reduces renal excretion of PEMETREXED—consult product literature

l Diuretics: increased risk of toxicity when high-dose aspirin given with l ACETAZOLAMIDE; aspirin antagonises diuretic effect of SPIRONOLACTONE; possible increased risk of toxicity when high-dose aspirin given with LOOP DIURETICS (also possible reduced effect of loop diuretics)

▶ Iloprost: increased risk of bleeding when aspirin given with

ILOPROST

▶ Leukotriene Receptor Antagonists: aspirin increases plasma concentration of ZAFIRLUKAST

▶ Metoclopramide: rate of absorption of aspirin increased by

METOCLOPRAMIDE (enhanced effect)

▶ Sulfinpyrazone: aspirin antagonises effects of SULFINPYRAZONE

Atazanavir

▶ Antacids: absorption of atazanavir reduced by ANTACIDS (give at least 2 hours before or 1 hour after antacids)

l Anti-arrhythmics: atazanavir possibly increases plasma concentration of l AMIODARONE and l LIDOCAINE

l Antibacterials: plasma concentration of both drugs increased when atazanavir given with CLARITHROMYCIN; atazanavir increases plasma concentration of l RIFABUTIN (reduce dose of rifabutin); plasma concentration of atazanavir reduced by l RIFAMPICIN—avoid concomitant use; avoidance of concomitant atazanavir in severe renal and hepatic impairment advised by manufacturer of l TELITHROMYCIN

▶ Anticoagulants: atazanavir may enhance or reduce anticoagulant effect of WARFARIN; avoidance of atazanavir advised by manufacturer of APIXABAN and RIVAROXABAN

l Antidepressants: plasma concentration of atazanavir reduced by l ST JOHN’S WORT—avoid concomitant use

l Antifungals: plasma concentration of atazanavir increased by l POSACONAZOLE; atazanavir increases or decreases the plasma concentration of l VORICONAZOLE and plasma concentration of atazanavir also reduced

l Antimalarials: caution with atazanavir advised by manufacturer of ARTEMETHER WITH LUMEFANTRINE; atazanavir possibly increases plasma concentration of l QUININE (increased risk of toxicity)

▶ Antimuscarinics: avoidance of atazanavir advised by manufacturer of DARIFENACIN; manufacturer of fesoterodine advises dose reduction when atazanavir given with FESOTERODINE—consult fesoterodine product literature

Atazanavir (continued)

l Antipsychotics: atazanavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); atazanavir possibly increases plasma concentration of

l PIMOZIDE—avoid concomitant use; atazanavir possibly increases plasma concentration of l QUETIAPINE— manufacturer of quetiapine advises avoid concomitant use

l Antivirals: plasma concentration of atazanavir reduced by

l BOCEPREVIR; atazanavir increases the plasma concentration of l DACLATASVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); absorption of atazanavir reduced by DIDANOSINE *tablets* (give at least 2 hours before or 1 hour after didanosine *tablets*); manufacturer of atazanavir advises avoid concomitant use with l EFAVIRENZ (plasma concentration of atazanavir reduced); atazanavir boosted with ritonavir increases plasma concentration of l ELVITEGRAVIR (reduce dose of elvitegravir); avoid concomitant use of atazanavir with l INDINAVIR; atazanavir increases plasma concentration of l MARAVIROC (consider reducing dose of maraviroc); plasma concentration of atazanavir possibly reduced by

l NEVIRAPINE—avoid concomitant use; increased risk of ventricular arrhythmias when atazanavir given with

l SAQUINAVIR—avoid concomitant use; atazanavir possibly reduces plasma concentration of TELAPREVIR, also plasma concentration of atazanavir possibly increased; plasma concentration of atazanavir reduced by TENOFOVIR, also plasma concentration of tenofovir possibly increased; atazanavir increases plasma concentration of TIPRANAVIR (also plasma concentration of atazanavir reduced)

l Anxiolytics and Hypnotics: atazanavir possibly increases plasma concentration of l MIDAZOLAM—avoid concomitant use of *oral* midazolam

l Avanafil: atazanavir possibly increases plasma concentration of l AVANAFIL—manufacturer of avanafil advises avoid concomitant use

l Calcium-channel Blockers: atazanavir increases plasma concentration of l DILTIAZEM (reduce dose of diltiazem); atazanavir possibly increases plasma concentration of VERAPAMIL

l Ciclosporin: atazanavir possibly increases plasma concentration of l CICLOSPORIN

l Colchicine: atazanavir possibly increases risk of l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Cytotoxics: atazanavir possibly increases plasma concentration of AXITINIB (reduce dose of axitinib—consult axitinib product literature); atazanavir possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; atazanavir possibly increases plasma concentration of l CRIZOTINIB and l EVEROLIMUS— manufacturer of crizotinib and everolimus advises avoid concomitant use; atazanavir possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809); atazanavir possibly increases plasma concentration of l PAZOPANIB (reduce dose of pazopanib); avoidance of atazanavir advised by manufacturer of l CABAZITAXEL; atazanavir possibly inhibits metabolism of l IRINOTECAN (increased risk of toxicity)

l Dapoxetine: avoidance of atazanavir advised by manufacturer

of l DAPOXETINE (increased risk of toxicity)

l Ergot Alkaloids: atazanavir possibly increases plasma concentration of l ERGOT ALKALOIDS—avoid concomitant use

l Lipid-regulating Drugs: possible increased risk of myopathy when atazanavir given with l ATORVASTATIN or PRAVASTATIN; atazanavir increases plasma concentration of

l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature); increased risk of myopathy when atazanavir given with l SIMVASTATIN (avoid concomitant use)

▶ Oestrogens: atazanavir increases plasma concentration of

ETHINYLESTRADIOL

l Orlistat: absorption of atazanavir possibly reduced by

l ORLISTAT

▶ Progestogens: atazanavir increases plasma concentration of

NORETHISTERONE

Atazanavir (continued)

l Ranolazine: atazanavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

l Sildenafil: atazanavir possibly increases side-effects of

l SILDENAFIL

l Sirolimus: atazanavir possibly increases plasma concentration of l SIROLIMUS

l Tacrolimus: atazanavir possibly increases plasma concentration of l TACROLIMUS

l Ticagrelor: atazanavir possibly increases plasma concentration of l TICAGRELOR—manufacturer of ticagrelor advises avoid concomitant use

l Ulcer-healing Drugs: manufacturer of atazanavir advises adjust doses of both drugs when atazanavir given with CIMETIDINE and NIZATIDINE—consult atazanavir product literature; plasma concentration of atazanavir reduced by l FAMOTIDINE and l RANITIDINE (adjust doses of both drugs—consult atazanavir product literature); plasma concentration of atazanavir reduced by l PROTON PUMP INHIBITORS—avoid or adjust dose of both drugs (consult product literature)

Atenolol *see* Beta-blockers

Atomoxetine

l Analgesics: increased risk of ventricular arrhythmias when atomoxetine given with l METHADONE; possible increased risk of convulsions when atomoxetine given with TRAMADOL

l Anti-arrhythmics: increased risk of ventricular arrhythmias when atomoxetine given with l AMIODARONE or

l DISOPYRAMIDE

l Antibacterials: increased risk of ventricular arrhythmias when atomoxetine given with *parenteral* l ERYTHROMYCIN; increased risk of ventricular arrhythmias when atomoxetine given with l MOXIFLOXACIN

l Antidepressants: metabolism of atomoxetine possibly inhibited by FLUOXETINE and PAROXETINE; possible increased risk of convulsions when atomoxetine given with ANTIDEPRESSANTS; atomoxetine should not be started until 2 weeks after stopping l MAOIS, also MAOIs should not be started until at least 2 weeks after stopping atomoxetine; increased risk of ventricular arrhythmias when atomoxetine given with l TRICYCLICS

l Antimalarials: increased risk of ventricular arrhythmias when atomoxetine given with l MEFLOQUINE

l Antipsychotics: increased risk of ventricular arrhythmias when atomoxetine given with l ANTIPSYCHOTICS that prolong the QT interval

l Beta-blockers: increased risk of ventricular arrhythmias when atomoxetine given with l SOTALOL

▶ Bupropion: possible increased risk of convulsions when atomoxetine given with BUPROPION

l Diuretics: risk of ventricular arrhythmias with atomoxetine increased by hypokalaemia caused by l DIURETICS

▶ Sympathomimetics, Beta2: Increased risk of cardiovascular side- effects when atomoxetine given with *parenteral* SALBUTAMOL

Atorvastatin *see* Statins

Atovaquone

l Antibacterials: manufacturer of atovaquone advises avoid concomitant use with RIFABUTIN (plasma concentration of both drugs reduced); plasma concentration of atovaquone reduced by l RIFAMPICIN (and concentration of rifampicin increased)—avoid concomitant use; plasma concentration of atovaquone reduced by TETRACYCLINE

l Antivirals: plasma concentration of atovaquone reduced by l EFAVIRENZ—avoid concomitant use; atovaquone possibly reduces plasma concentration of INDINAVIR; plasma

concentration of atovaquone possibly reduced by RITONAVIR— manufacturer of atovaquone advises avoid concomitant use; atovaquone increases plasma concentration of ZIDOVUDINE (increased risk of toxicity)

▶ Cytotoxics: atovaquone possibly increases plasma concentration of ETOPOSIDE

▶ Histamine: avoidance of atovaquone advised by manufacturer of HISTAMINE

▶ Metoclopramide: plasma concentration of atovaquone reduced by METOCLOPRAMIDE—avoid concomitant use

Atracurium *see* Muscle Relaxants Atropine *see* Antimuscarinics Avanafil

▶ ACE Inhibitors: avanafil possibly enhances hypotensive effect

Interactions | Appendix 1

of ENALAPRIL

▶ Alcohol: possible enhanced hypotensive effect when avanafil given with ALCOHOL

l Alpha-blockers: enhanced hypotensive effect when avanafil given with l ALPHA-BLOCKERS—when patient is stable on the alpha blocker initiate avanafil at the lowest possible dose

l Antibacterials: plasma concentration of avanafil possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN— manufacturer of avanafil advises avoid concomitant use; plasma concentration of avanafil increased by

l ERYTHROMYCIN—see under Avanafil, p. 698; plasma concentration of avanafil possibly reduced by RIFAMPICIN— manufacturer of avanafil advises avoid concomitant use

▶ Antiepileptics: plasma concentration of avanafil possibly reduced by CARBAMAZEPINE, PHENOBARBITAL and PRIMIDONE—

manufacturer of avanafil advises avoid concomitant use

l Antifungals: plasma concentration of avanafil increased by l KETOCONAZOLE—avoid concomitant use; plasma concentration of avanafil possibly increased by

l FLUCONAZOLE—see under Avanafil, p. 698; plasma concentration of avanafil possibly increased by

l ITRACONAZOLE and l VORICONAZOLE—manufacturer of avanafil advises avoid concomitant use

l Antivirals: plasma concentration of avanafil possibly increased by l ATAZANAVIR, l INDINAVIR and l SAQUINAVIR—manufacturer of avanafil advises avoid concomitant use; plasma concentration of avanafil possibly reduced by EFAVIRENZ— manufacturer of avanafil advises avoid concomitant use; plasma concentration of avanafil possibly increased by

l FOSAMPRENAVIR—see under Avanafil, p. 698; plasma concentration of avanafil significantly increased by

l RITONAVIR—avoid concomitant use

l Aprepitant: plasma concentration of avanafil possibly increased by l APREPITANT—see under Avanafil, p. 698

▶ Bosentan: plasma concentration of avanafil possibly reduced by BOSENTAN—manufacturer of avanafil advises avoid concomitant use

l Calcium-channel Blockers: plasma concentration of avanafil possibly increased by l DILTIAZEM and l VERAPAMIL—see under Avanafil, p. 698

▶ Fosaprepitant: plasma concentration of avanafil possibly increased by FOSAPREPITANT

▶ Grapefruit Juice: plasma concentration of avanafil possibly increased by GRAPEFRUIT JUICE— manufacturer of avanafil advises avoid grapefruit juice for 24 hours before avanafil

l Nicorandil: avanafil significantly enhances hypotensive effect of l NICORANDIL (avoid concomitant use)

l Nitrates: avanafil significantly enhances hypotensive effect of

l NITRATES (avoid concomitant use)

l Riociguat: possible enhanced hypotensive effect when avanafil given with l RIOCIGUAT—avoid concomitant use

Axitinib

▶ Antibacterials: plasma concentration of axitinib possibly increased by CLARITHROMYCIN, ERYTHROMYCIN and TELITHROMYCIN (reduce dose of axitinib—consult axitinib product literature); plasma concentration of axitinib possibly decreased by RIFABUTIN (increase dose of axitinib—consult axitinib product literature); plasma concentration of axitinib decreased by RIFAMPICIN (increase dose of axitinib—consult axitinib product literature)

▶ Antidepressants: plasma concentration of axitinib possibly reduced by ST JOHN’S WORT—consider increasing dose of axitinib

▶ Antiepileptics: plasma concentration of axitinib possibly decreased by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL,

PHENYTOIN and PRIMIDONE (increase dose of axitinib—consult axitinib product literature)

▶ Antifungals: plasma concentration of axitinib increased by KETOCONAZOLE (reduce dose of axitinib—consult axitinib product literature); plasma concentration of axitinib possibly

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Axitinib

Antifungals (continued)

increased by ITRACONAZOLE (reduce dose of axitinib—consult axitinib product literature)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Antivirals: plasma concentration of axitinib possibly increased by ATAZANAVIR, INDINAVIR, RITONAVIR and SAQUINAVIR (reduce

dose of axitinib—consult axitinib product literature)

▶ Corticosteroids: plasma concentration of axitinib possibly decreased by DEXAMETHASONE (increase dose of axitinib— consult axitinib product literature)

▶ Grapefruit Juice: plasma concentration of axitinib possibly increased by GRAPEFRUIT JUICE

Azathioprine

▶ ACE Inhibitors: increased risk of anaemia or leucopenia when azathioprine given with CAPTOPRIL especially in renal impairment; increased risk of anaemia when azathioprine given with ENALAPRIL especially in renal impairment

l Allopurinol: enhanced effects and increased toxicity of azathioprine when given with l ALLOPURINOL (reduce dose of azathioprine to one quarter of usual dose)

l Antibacterials: increased risk of haematological toxicity when azathioprine given with l SULFAMETHOXAZOLE (as co- trimoxazole); increased risk of haematological toxicity when azathioprine given with l TRIMETHOPRIM (also with co- trimoxazole)

l Anticoagulants: azathioprine possibly reduces anticoagulant effect of l COUMARINS

l Antivirals: myelosuppressive effects of azathioprine possibly enhanced by l RIBAVIRIN

l Febuxostat: avoidance of azathioprine advised by manufacturer of l FEBUXOSTAT

Azelastine *see* Antihistamines

Azilsartan *see* Angiotensin-II Receptor Antagonists

Azithromycin *see* Macrolides

Aztreonam

l Anticoagulants: aztreonam possibly enhances anticoagulant effect of l COUMARINS

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Baclofen *see* Muscle Relaxants Bambuterol *see* Sympathomimetics, Beta2 Basiliximab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

BCG Vaccine *see* Vaccines Beclometasone *see* Corticosteroids Bedaquiline

l Antibacterials: plasma concentration of bedaquiline possibly

increased by CIPROFLOXACIN, CLARITHROMYCIN and ERYTHROMYCIN—avoid concomitant use if ciprofloxacin, clarithromycin and erythromycin given for more than 14 days; manufacturer of bedaquiline advises avoid concomitant use with MOXIFLOXACIN; plasma concentration of bedaquiline possibly reduced by RIFABUTIN—manufacturer of bedaquiline advises avoid concomitant use; plasma concentration of bedaquiline reduced by l RIFAMPICIN—manufacturer of bedaquiline advises avoid concomitant use; possible increased risk of ventricular arrhythmias when bedaquiline given with l CLOFAZIMINE

▶ Antidepressants: plasma concentration of bedaquiline possibly reduced by ST JOHN’S WORT—manufacturer of bedaquiline advises avoid concomitant use

l Antiepileptics: plasma concentration of bedaquiline possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN and

l PHENYTOIN—manufacturer of bedaquiline advises avoid concomitant use

▶ Antifungals: plasma concentration of bedaquiline increased by KETOCONAZOLE—avoid concomitant use if ketoconazole given for more than 14 days; plasma concentration of bedaquiline possibly increased by FLUCONAZOLE—avoid concomitant use if fluconazole given for more than 14 days

Bedaquiline (continued)

▶ Antivirals: plasma concentration of bedaquiline possibly reduced by EFAVIRENZ and ETRAVIRINE—manufacturer of bedaquiline advises avoid concomitant use; plasma concentration of bedaquiline possibly increased by RITONAVIR—avoid concomitant use if ritonavir given for more than 14 days

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Bee Venom Extracts

l ACE Inhibitors: possible severe anaphylactoid reaction when bee venom extracts given with l ACE INHIBITORS

Belimumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Bendamustine

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Bendroflumethiazide *see* Diuretics

Benperidol *see* Antipsychotics

Benzodiazepines *see* Anxiolytics and Hypnotics

Benzthiazide *see* Diuretics Benzylpenicillin *see* Penicillins Beta-blockers

NOTE Since systemic absorption may follow topical application of beta-blockers to the eye the possibility of interactions, in particular, with drugs such as verapamil should be borne in mind

▶ ACE Inhibitors: enhanced hypotensive effect when beta- blockers given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when beta-blockers given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when beta-blockers given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when beta-blockers given with ALDESLEUKIN

l Alpha-blockers: enhanced hypotensive effect when beta- blockers given with l ALPHA-BLOCKERS, also increased risk of first-dose hypotension with post-synaptic alpha-blockers such as prazosin

▶ Anaesthetics, General: enhanced hypotensive effect when beta- blockers given with GENERAL ANAESTHETICS

l Anaesthetics, Local: propranolol increases risk of l BUPIVACAINE

toxicity

▶ Analgesics: hypotensive effect of beta-blockers antagonised by NSAIDS; plasma concentration of esmolol possibly increased by MORPHINE

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when beta-blockers given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Anti-arrhythmics: increased myocardial depression when beta-

blockers given with l ANTI-ARRHYTHMICS; increased risk of ventricular arrhythmias when sotalol given with

l AMIODARONE, l DISOPYRAMIDE or l DRONEDARONE—avoid

concomitant use; increased risk of bradycardia, AV block and myocardial depression when beta-blockers given with

l AMIODARONE; plasma concentration of metoprolol and propranolol possibly increased by DRONEDARONE; increased risk of myocardial depression and bradycardia when beta- blockers given with l FLECAINIDE; propranolol increases risk of l LIDOCAINE toxicity; nadolol possibly increases risk of LIDOCAINE toxicity; plasma concentration of metoprolol and propranolol increased by PROPAFENONE

l Antibacterials: increased risk of ventricular arrhythmias when sotalol given with l MOXIFLOXACIN—avoid concomitant use; metabolism of bisoprolol and propranolol accelerated by RIFAMPICIN (plasma concentration significantly reduced); plasma concentration of carvedilol, celiprolol and metoprolol reduced by RIFAMPICIN; plasma concentration of *oral* timolol possibly reduced by RIFAMPICIN; increased risk of ventricular arrhythmias when sotalol given with l DELAMANID

l Antidepressants: plasma concentration of metoprolol

increased by CITALOPRAM and ESCITALOPRAM; increased risk of

Beta-blockers

l Antidepressants (continued)

ventricular arrhythmias when sotalol given with

l CITALOPRAM—avoid concomitant use; avoidance of sotalol advised by manufacturer of l ESCITALOPRAM (risk of ventricular arrhythmias); plasma concentration of propranolol increased by FLUVOXAMINE; plasma concentration of metoprolol possibly increased by l PAROXETINE—increased risk of AV block (manufacturer of paroxetine advises avoid concomitant use in cardiac insufficiency); labetalol and propranolol increase plasma concentration of IMIPRAMINE; enhanced hypotensive effect when beta-blockers given with MAOIS; increased risk of ventricular arrhythmias when sotalol given with l TRICYCLICS

▶ Antidiabetics: beta-blockers may mask warning signs of hypoglycaemia (such as tremor) with ANTIDIABETICS; beta- blockers enhance hypoglycaemic effect of INSULIN

▶ Antiepileptics: plasma concentration of propranolol possibly reduced by PHENOBARBITAL and PRIMIDONE

▶ Antifungals: plasma concentration of nadolol possibly increased by KETOCONAZOLE

l Antihistamines: increased risk of ventricular arrhythmias when sotalol given with l MIZOLASTINE—avoid concomitant use

l Antimalarials: avoidance of metoprolol and sotalol advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; avoidance of sotalol advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias); increased risk of bradycardia when beta-blockers given with MEFLOQUINE

l Antimuscarinics: increased risk of ventricular arrhythmias when sotalol given with l TOLTERODINE

l Antipsychotics: increased risk of ventricular arrhythmias when sotalol given with l DROPERIDOL or l ZUCLOPENTHIXOL—avoid concomitant use; possible increased risk of ventricular arrhythmias when sotalol given with l HALOPERIDOL—avoid concomitant use; plasma concentration of both drugs may increase when propranolol given with l CHLORPROMAZINE; increased risk of ventricular arrhythmias when sotalol given with l AMISULPRIDE, l PHENOTHIAZINES, l PIMOZIDE or

l SULPIRIDE; enhanced hypotensive effect when beta-blockers given with PHENOTHIAZINES; possible increased risk of ventricular arrhythmias when sotalol given with

l RISPERIDONE

l Antivirals: increased risk of ventricular arrhythmias when sotalol given with l SAQUINAVIR—avoid concomitant use; avoidance of sotalol advised by manufacturer of l TELAPREVIR (risk of ventricular arrhythmias); avoidance of metoprolol for heart failure advised by manufacturer of l TIPRANAVIR

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when beta-blockers given with ANXIOLYTICS AND HYPNOTICS

l Atomoxetine: increased risk of ventricular arrhythmias when sotalol given with l ATOMOXETINE

l Calcium-channel Blockers: enhanced hypotensive effect when beta-blockers given with CALCIUM-CHANNEL BLOCKERS; possible severe hypotension and heart failure when beta-blockers given with l NIFEDIPINE; increased risk of AV block and bradycardia when beta-blockers given with l DILTIAZEM; asystole, severe hypotension and heart failure when beta- blockers given with l VERAPAMIL (see under Verapamil,

p. 156)

▶ Cardiac Glycosides: increased risk of AV block and bradycardia when beta-blockers given with CARDIAC GLYCOSIDES

l Ciclosporin: carvedilol increases plasma concentration of

l CICLOSPORIN

l Clonidine: increased risk of withdrawal hypertension when beta-blockers given with l CLONIDINE (withdraw beta-blockers several days before slowly withdrawing clonidine)

▶ Corticosteroids: hypotensive effect of beta-blockers antagonised by CORTICOSTEROIDS

l Cytotoxics: possible increased risk of ventricular arrhythmias when sotalol given with l BOSUTINIB; possible increased risk of bradycardia when beta-blockers given with CRIZOTINIB; possible increased risk of ventricular arrhythmias when sotalol given with l VANDETANIB—avoid concomitant use; increased risk of ventricular arrhythmias when sotalol given with l ARSENIC TRIOXIDE

Beta-blockers (continued)

▶ Diazoxide: enhanced hypotensive effect when beta-blockers given with DIAZOXIDE

Interactions | Appendix 1

l Diuretics: enhanced hypotensive effect when beta-blockers given with DIURETICS; risk of ventricular arrhythmias with sotalol increased by hypokalaemia caused by l LOOP DIURETICS or l THIAZIDES AND RELATED DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when beta- blockers given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Ergot Alkaloids: increased peripheral vasoconstriction when beta-blockers given with ERGOTAMINE

l Fingolimod: possible increased risk of bradycardia when beta- blockers given with l FINGOLIMOD

▶ Hormone Antagonists: possible increased risk of bradycardia when carteolol, metoprolol, propranolol or sotalol given with PASIREOTIDE

▶ 5HT1-receptor Agonists: propranolol increases plasma concentration of RIZATRIPTAN (manufacturer of rizatriptan advises halve dose and avoid within 2 hours of propranolol)

l Ivabradine: increased risk of ventricular arrhythmias when sotalol given with l IVABRADINE

▶ Methyldopa: enhanced hypotensive effect when beta-blockers given with METHYLDOPA

▶ Mirabegron: plasma concentration of metoprolol increased by

MIRABEGRON

l Moxisylyte: possible severe postural hypotension when beta- blockers given with l MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when beta-blockers given with MOXONIDINE

▶ Muscle Relaxants: propranolol enhances effects of MUSCLE RELAXANTS; enhanced hypotensive effect when beta-blockers given with BACLOFEN; possible enhanced hypotensive effect and bradycardia when beta-blockers given with TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when beta-blockers given with NITRATES

▶ Oestrogens: hypotensive effect of beta-blockers antagonised by OESTROGENS

▶ Parasympathomimetics: propranolol antagonises effects of NEOSTIGMINE and PYRIDOSTIGMINE; increased risk of arrhythmias when beta-blockers given with PILOCARPINE

▶ Prostaglandins: enhanced hypotensive effect when beta- blockers given with ALPROSTADIL

l Ranolazine: avoidance of sotalol advised by manufacturer of

l RANOLAZINE

l Sympathomimetics: increased risk of severe hypertension and bradycardia when non-cardioselective beta-blockers given with l ADRENALINE (EPINEPHRINE), also reponse to adrenaline (epinephrine) may be reduced; increased risk of severe hypertension and bradycardia when non-cardioselective beta-blockers given with l DOBUTAMINE; possible increased risk of severe hypertension and bradycardia when non- cardioselective beta-blockers given with l NORADRENALINE (NOREPINEPHRINE)

▶ Thyroid Hormones: metabolism of propranolol accelerated by

LEVOTHYROXINE

▶ Ulcer-healing Drugs: plasma concentration of labetalol, metoprolol and propranolol increased by CIMETIDINE; plasma concentration of *oral* timolol possibly increased by CIMETIDINE

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when beta-blockers given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Betahistine

▶ Antihistamines: effect of betahistine theoretically antagonised by ANTIHISTAMINES

Betamethasone *see* Corticosteroids Betaxolol *see* Beta-blockers Bethanechol *see* Parasympathomimetics Bevacizumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Bexarotene

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Interactions | Appendix 1

Bexarotene (continued)

l Lipid-regulating Drugs: plasma concentration of bexarotene increased by l GEMFIBROZIL—avoid concomitant use

Bezafibrate *see* Fibrates

Bicalutamide

▶ Anticoagulants: bicalutamide possibly enhances anticoagulant effect of COUMARINS

▶ Lipid-regulating Drugs: separating administration from bicalutamide by 12 hours advised by manufacturer of LOMITAPIDE

Biguanides *see* Antidiabetics

Bilastine *see* Antihistamines

Bile Acid Sequestrants *see* Colesevelam, Colestipol, and Colestyramine

Bile Acids

▶ Antacids: absorption of bile acids possibly reduced by

ANTACIDS

l Ciclosporin: ursodeoxycholic acid increases absorption of

l CICLOSPORIN

▶ Lipid-regulating Drugs: absorption of bile acids possibly reduced by COLESTIPOL and COLESTYRAMINE

Bisoprolol *see* Beta-blockers

Bisphosphonates

▶ Antacids: absorption of bisphosphonates reduced by ANTACIDS

▶ Antibacterials: increased risk of hypocalcaemia when bisphosphonates given with AMINOGLYCOSIDES

▶ Calcium Salts: absorption of bisphosphonates reduced by

CALCIUM SALTS

l Cytotoxics: sodium clodronate increases plasma concentration of l ESTRAMUSTINE

▶ Iron Salts: absorption of bisphosphonates reduced by *oral* IRON SALTS

Bivalirudin

l Analgesics: increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins)

l Anticoagulants: increased risk of haemorrhage when other anticoagulants given with l APIXABAN, l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

Bleomycin

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: bleomycin possibly reduces absorption of

DIGOXIN *tablets*

l Cytotoxics: increased risk of pulmonary toxicity when bleomycin given with l BRENTUXIMAB VEDOTIN—avoid concomitant use; increased pulmonary toxicity when bleomycin given with l CISPLATIN

Boceprevir

▶ Alpha-blockers: boceprevir possibly increases plasma concentration of DOXAZOSIN and TAMSULOSIN—manufacturer of boceprevir advises avoid concomitant use

▶ Analgesics: possible increased risk of prolonged sedation and respiratory depression when boceprevir given with BUPRENORPHINE; boceprevir possibly affects plasma concentration of METHADONE

l Antibacterials: manufacturer of boceprevir advises avoid concomitant use with l RIFAMPICIN (plasma concentration of boceprevir possibly reduced)

▶ Anticoagulants: avoidance of boceprevir advised by manufacturer of APIXABAN

l Antiepileptics: manufacturer of boceprevir advises avoid concomitant use with l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE (plasma

concentration of boceprevir possibly reduced)

l Antifungals: plasma concentration of boceprevir increased by

l KETOCONAZOLE

l Antimalarials: manufacturer of boceprevir advises avoid concomitant use with l ARTEMETHER WITH LUMEFANTRINE

Boceprevir (continued)

l Antipsychotics: boceprevir possibly increases plasma concentration of l LURASIDONE—avoid concomitant use; manufacturer of boceprevir advises avoid concomitant use with l PIMOZIDE; boceprevir possibly increases plasma concentration of l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: boceprevir reduces plasma concentration of

l ATAZANAVIR; boceprevir possibly increases the plasma concentration of l DACLATASVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); avoid concomitant use of boceprevir with l DARUNAVIR; effects of both drugs possibly reduced when boceprevir given with ETRAVIRINE; avoidance of boceprevir advised by manufacturer of l FOSAMPRENAVIR, NEVIRAPINE and TIPRANAVIR; manufacturers advise avoid concomitant use of boceprevir with l LOPINAVIR; boceprevir increases plasma concentration of MARAVIROC (consider reducing dose of maraviroc); plasma concentration of both drugs reduced when boceprevir given with l RITONAVIR

l Anxiolytics and Hypnotics: boceprevir increases plasma concentration of *oral* l MIDAZOLAM—manufacturer of boceprevir advises avoid concomitant use

▶ Cardiac Glycosides: boceprevir possibly increases side-effects of DIGOXIN

l Ciclosporin: boceprevir increases plasma concentration of

l CICLOSPORIN

l Cilostazol: boceprevir possibly increases plasma concentration of l CILOSTAZOL (see under Cilostazol, p. 206)

▶ Cobicistat: avoidance of boceprevir advised by manufacturer of

COBICISTAT

l Cytotoxics: boceprevir possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; manufacturer of boceprevir advises avoid concomitant use with l DASATINIB, l ERLOTINIB, l GEFITINIB, l IMATINIB,

l LAPATINIB, l NILOTINIB, l PAZOPANIB, l SORAFENIB and

l SUNITINIB; manufacturer of ruxolitinib advises dose reduction when boceprevir given with l RUXOLITINIB—consult ruxolitinib product literature

l Domperidone: possible increased risk of ventricular arrhythmias when boceprevir given with l DOMPERIDONE— avoid concomitant use

l Ergot Alkaloids: manufacturer of boceprevir advises avoid concomitant use with l ERGOT ALKALOIDS

l Lipid-regulating Drugs: boceprevir increases plasma concentration of ATORVASTATIN (reduce dose of atorvastatin); boceprevir increases plasma concentration of PRAVASTATIN; manufacturers advise avoid concomitant use of boceprevir with l SIMVASTATIN

▶ Progestogens: boceprevir increases plasma concentration of

DROSPIRENONE (increased risk of toxicity)

l Sirolimus: boceprevir increases plasma concentration of l SIROLIMUS (increased risk of toxicity—reduce sirolimus dose)

l Tacrolimus: boceprevir increases plasma concentration of

l TACROLIMUS (reduce dose of tacrolimus)

Bortezomib

l Antibacterials: plasma concentration of bortezomib reduced by l RIFAMPICIN—manufacturer of bortezomib advises avoid concomitant use

▶ Antidepressants: plasma concentration of bortezomib possibly reduced by ST JOHN’S WORT—manufacturer of bortezomib advises avoid concomitant use

▶ Antiepileptics: plasma concentration of bortezomib possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL,

PHENYTOIN and PRIMIDONE—manufacturer of bortezomib advises avoid concomitant use

▶ Antifungals: plasma concentration of bortezomib increased by

KETOCONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Bosentan

l Antibacterials: plasma concentration of bosentan reduced by

l RIFAMPICIN—avoid concomitant use

▶ Anticoagulants: manufacturer of bosentan recommends monitoring anticoagulant effect of COUMARINS

Bosentan (continued)

l Antidiabetics: increased risk of hepatotoxicity when bosentan given with l GLIBENCLAMIDE—avoid concomitant use

l Antifungals: plasma concentration of bosentan increased by KETOCONAZOLE; plasma concentration of bosentan possibly increased by l FLUCONAZOLE—avoid concomitant use; plasma concentration of bosentan possibly increased by ITRACONAZOLE

l Antivirals: avoidance of bosentan advised by manufacturer of ELVITEGRAVIR and TIPRANAVIR; bosentan possibly reduces plasma concentration of INDINAVIR; plasma concentration of bosentan increased by l LOPINAVIR and l RITONAVIR (consider reducing dose of bosentan); bosentan possibly reduces plasma concentration of TELAPREVIR, also plasma concentration of bosentan possibly increased

▶ Avanafil: bosentan possibly reduces plasma concentration of AVANAFIL—manufacturer of avanafil advises avoid concomitant use

l Ciclosporin: plasma concentration of bosentan increased by l CICLOSPORIN (also plasma concentration of ciclosporin reduced—avoid concomitant use)

▶ Cobicistat: avoidance of bosentan advised by manufacturer of

COBICISTAT

l Cytotoxics: bosentan possibly reduces plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid concomitant use

▶ Lipid-regulating Drugs: bosentan reduces plasma concentration of SIMVASTATIN

l Oestrogens: bosentan possibly causes contraceptive failure of hormonal contraceptives containing l OESTROGENS (alternative contraception recommended)

l Progestogens: bosentan possibly causes contraceptive failure of hormonal contraceptives containing l PROGESTOGENS (alternative contraception recommended)

▶ Riociguat: bosentan reduces plasma concentration of

RIOCIGUAT

▶ Sildenafil: bosentan reduces plasma concentration of

SILDENAFIL, also plasma concentration of bosentan increased

▶ Tadalafil: bosentan reduces plasma concentration of TADALAFIL

Bosutinib

l Analgesics: possible increased risk of ventricular arrhythmias when bosutinib given with l METHADONE

▶ Antacids: manufacturer of bosutinib advises separating administration with ANTACIDS by about 12 hours

l Anti-arrhythmics: possible increased risk of ventricular arrhythmias when bosutinib given with l AMIODARONE and

l DISOPYRAMIDE; plasma concentration of bosutinib possibly increased by l DRONEDARONE—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib

l Antibacterials: plasma concentration of bosutinib possibly increased by l CIPROFLOXACIN, l CLARITHROMYCIN,

l ERYTHROMYCIN and l TELITHROMYCIN—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; possible increased risk of ventricular arrhythmias when bosutinib given with l MOXIFLOXACIN; plasma concentration of bosutinib possibly reduced by l RIFABUTIN— manufacturer of bosutinib advises avoid concomitant use; plasma concentration of bosutinib reduced by l RIFAMPICIN— manufacturer of bosutinib advises avoid concomitant use

l Antidepressants: plasma concentration of bosutinib possibly reduced by l ST JOHN’S WORT—manufacturer of bosutinib advises avoid concomitant use

l Antiepileptics: plasma concentration of bosutinib possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—

manufacturer of bosutinib advises avoid concomitant use

l Antifungals: plasma concentration of bosutinib increased by

l KETOCONAZOLE—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; plasma concentration of bosutinib possibly increased by l FLUCONAZOLE,

l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE—

manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib

l Antimalarials: possible increased risk of ventricular arrhythmias when bosutinib given with l CHLOROQUINE and l HYDROXYCHLOROQUINE

Bosutinib (continued)

l Antipsychotics: possible increased risk of ventricular arrhythmias when bosutinib given with l HALOPERIDOL; avoid concomitant use of cytotoxics with l CLOZAPINE (increased risk of agranulocytosis)

Interactions | Appendix 1

l Antivirals: plasma concentration of bosutinib possibly increased by l ATAZANAVIR, l BOCEPREVIR, l DARUNAVIR,

l FOSAMPRENAVIR, l INDINAVIR, l RITONAVIR, l SAQUINAVIR and

l TELAPREVIR—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; plasma concentration of bosutinib possibly reduced by l EFAVIRENZ and l ETRAVIRINE— manufacturer of bosutinib advises avoid concomitant use

l Aprepitant: plasma concentration of bosutinib possibly increased by l APREPITANT—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib

l Beta-blockers: possible increased risk of ventricular arrhythmias when bosutinib given with l SOTALOL

l Bosentan: plasma concentration of bosutinib possibly reduced by l BOSENTAN—manufacturer of bosutinib advises avoid concomitant use

l Calcium-channel Blockers: plasma concentration of bosutinib possibly increased by l DILTIAZEM and l VERAPAMIL— manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib

l Cytotoxics: plasma concentration of bosutinib possibly increased by l IMATINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib

l Domperidone: manufacturer of bosutinib advises avoid

concomitant use with l DOMPERIDONE (risk of ventricular arrhythmias)

l Fosaprepitant: plasma concentration of bosutinib possibly increased by l FOSAPREPITANT—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib

l Grapefruit Juice: plasma concentration of bosutinib possibly increased by l GRAPEFRUIT JUICE—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib

l Modafinil: plasma concentration of bosutinib possibly reduced by l MODAFINIL—manufacturer of bosutinib advises avoid concomitant use

▶ Ulcer-healing Drugs: plasma concentration of bosutinib reduced by LANSOPRAZOLE

Brentuximab vedotin

▶ Antibacterials: effects of brentuximab vedotin possibly reduced by RIFAMPICIN

l Antifungals: possible increased risk of neutropenia when brentuximab vedotin given with l KETOCONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Cytotoxics: increased risk of pulmonary toxicity when brentuximab vedotin given with l BLEOMYCIN—avoid concomitant use

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Brimonidine

▶ Antidepressants: manufacturer of brimonidine advises avoid concomitant use with MAOIS, TRICYCLIC-RELATED ANTIDEPRESSANTS and TRICYCLICS

Brinzolamide *see* Diuretics

Bromocriptine

▶ Alcohol: tolerance of bromocriptine reduced by ALCOHOL

▶ Antibacterials: plasma concentration of bromocriptine increased by ERYTHROMYCIN (increased risk of toxicity); plasma concentration of bromocriptine possibly increased by MACROLIDES (increased risk of toxicity)

▶ Antipsychotics: hypoprolactinaemic and antiparkinsonian effects of bromocriptine antagonised by ANTIPSYCHOTICS

▶ Domperidone: hypoprolactinaemic effect of bromocriptine possibly antagonised by DOMPERIDONE

▶ Hormone Antagonists: plasma concentration of bromocriptine increased by OCTREOTIDE

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Metoclopramide: hypoprolactinaemic effect of bromocriptine antagonised by METOCLOPRAMIDE

Interactions | Appendix 1

Bromocriptine (continued)

l Sympathomimetics: risk of toxicity when bromocriptine given with l ISOMETHEPTENE

Buclizine *see* Antihistamines Budesonide *see* Corticosteroids Bumetanide *see* Diuretics Bupivacaine

▶ Anti-arrhythmics: increased myocardial depression when bupivacaine given with ANTI-ARRHYTHMICS

l Beta-blockers: increased risk of bupivacaine toxicity when given with l PROPRANOLOL

Buprenorphine *see* Opioid Analgesics

Bupropion

l Antidepressants: bupropion possibly increases plasma concentration of CITALOPRAM; manufacturer of bupropion advises avoid for 2 weeks after stopping l MAOIS; manufacturer of bupropion advises avoid concomitant use with l MOCLOBEMIDE; bupropion possibly increases plasma concentration of TRICYCLICS (possible increased risk of convulsions)

▶ Antiepileptics: plasma concentration of bupropion reduced by

CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN; metabolism of

bupropion inhibited by SODIUM VALPROATE and VALPROIC ACID

▶ Antivirals: metabolism of bupropion accelerated by EFAVIRENZ (reduced plasma concentration); plasma concentration of bupropion reduced by RITONAVIR

▶ Atomoxetine: possible increased risk of convulsions when bupropion given with ATOMOXETINE

▶ Dopaminergics: increased risk of side-effects when bupropion given with AMANTADINE, CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

l Hormone Antagonists: bupropion possibly inhibits metabolism

of l TAMOXIFEN to active metabolite (avoid concomitant use)

l Methylthioninium: possible risk of CNS toxicity when bupropion given with l METHYLTHIONINIUM—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

Buspirone *see* Anxiolytics and Hypnotics

Busulfan

▶ Analgesics: metabolism of *intravenous* busulfan possibly inhibited by PARACETAMOL (manufacturer of *intravenous* busulfan advises caution within 72 hours of paracetamol)

l Antibacterials: plasma concentration of busulfan increased by

l METRONIDAZOLE (increased risk of toxicity)

▶ Antiepileptics: plasma concentration of busulfan possibly reduced by FOSPHENYTOIN and PHENYTOIN

▶ Antifungals: metabolism of busulfan inhibited by

ITRACONAZOLE (increased risk of toxicity)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cytotoxics: increased risk of hepatotoxicity when busulfan given with TIOGUANINE

Butyrophenones *see* Antipsychotics

Cabazitaxel

l Antibacterials: plasma concentration of cabazitaxel possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN— manufacturer of cabazitaxel advises avoid or consider reducing dose of cabazitaxel; manufacturer of cabazitaxel advises avoid concomitant use with l RIFABUTIN; plasma concentration of cabazitaxel reduced by l RIFAMPICIN— manufacturer of cabazitaxel advises avoid concomitant use

l Antidepressants: manufacturer of cabazitaxel advises avoid concomitant use with l ST JOHN’S WORT

l Antiepileptics: manufacturer of cabazitaxel advises avoid concomitant use with l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE

l Antifungals: manufacturer of cabazitaxel advises avoid concomitant use with l KETOCONAZOLE; plasma concentration of cabazitaxel possibly increased by l ITRACONAZOLE and

l VORICONAZOLE—manufacturer of cabazitaxel advises avoid or consider reducing dose of cabazitaxel

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Cabazitaxel (continued)

l Antivirals: manufacturer of cabazitaxel advises avoid concomitant use with l ATAZANAVIR; plasma concentration of cabazitaxel possibly increased by l INDINAVIR, l RITONAVIR and l SAQUINAVIR—manufacturer of cabazitaxel advises avoid or consider reducing dose of cabazitaxel

Cabergoline

▶ Antibacterials: plasma concentration of cabergoline increased by ERYTHROMYCIN (increased risk of toxicity); plasma concentration of cabergoline possibly increased by MACROLIDES (increased risk of toxicity)

▶ Antipsychotics: hypoprolactinaemic and antiparkinsonian effects of cabergoline antagonised by ANTIPSYCHOTICS

▶ Domperidone: hypoprolactinaemic effect of cabergoline possibly antagonised by DOMPERIDONE

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Metoclopramide: hypoprolactinaemic effect of cabergoline antagonised by METOCLOPRAMIDE

Cabozantinib

l Antibacterials: plasma concentration of cabozantinib possibly increased by CLARITHROMYCIN and ERYTHROMYCIN; plasma concentration of cabozantinib reduced by l RIFAMPICIN— avoid concomitant use

▶ Antidepressants: plasma concentration of cabozantinib possibly reduced by ST JOHN’S WORT—manufacturer of cabozantinib advises avoid concomitant use

l Antiepileptics: plasma concentration of cabozantinib possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—avoid

concomitant use

▶ Antifungals: plasma concentration of cabozantinib increased by KETOCONAZOLE; plasma concentration of cabozantinib possibly increased by ITRACONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Antivirals: plasma concentration of cabozantinib possibly increased by RITONAVIR

▶ Corticosteroids: plasma concentration of cabozantinib possibly reduced by DEXAMETHASONE—manufacturer of cabozantinib advises avoid concomitant use

▶ Grapefruit Juice: plasma concentration of cabozantinib possibly increased by GRAPEFRUIT JUICE

Caffeine citrate

▶ Aminophylline: manufacturer of caffeine citrate advises avoid concomitant use with AMINOPHYLLINE

▶ Anti-arrhythmics: caffeine citrate antagonises anti-arrhythmic effect of ADENOSINE—manufacturer of adenosine advises avoid caffeine citrate for at least 12 hours before adenosine

▶ Antiepileptics: plasma concentration of caffeine citrate reduced by FOSPHENYTOIN and PHENYTOIN; caffeine citrate possibly antagonises effects of PHENOBARBITAL and PRIMIDONE

▶ Theophylline: manufacturer of caffeine citrate advises avoid concomitant use with THEOPHYLLINE

▶ Ulcer-healing Drugs: plasma concentration of caffeine citrate increased by CIMETIDINE

Calcitriol *see* Vitamins

Calcium Salts

NOTE *see also* Antacids

▶ Antibacterials: calcium salts reduce absorption of

CIPROFLOXACIN and TETRACYCLINE

▶ Antivirals: calcium salts reduce absorption of DOLUTEGRAVIR— manufacturer of dolutegravir advises give at least 2 hours before or 6 hours after calcium salts; manufacturer of rilpivirine advises give calcium salts 2 hours before or 4 hours after RILPIVIRINE

▶ Bisphosphonates: calcium salts reduce absorption of

BISPHOSPHONATES

▶ Cardiac Glycosides: large *intravenous* doses of calcium salts can precipitate arrhythmias when given with CARDIAC GLYCOSIDES

▶ Corticosteroids: absorption of calcium salts reduced by

CORTICOSTEROIDS

Calcium Salts (continued)

▶ Cytotoxics: calcium salts reduce absorption of ESTRAMUSTINE (manufacturer of estramustine advises avoid concomitant administration)

▶ Diuretics: increased risk of hypercalcaemia when calcium salts given with THIAZIDES AND RELATED DIURETICS

▶ Eltrombopag: calcium salts possibly reduce absorption of

ELTROMBOPAG (give at least 4 hours apart)

▶ Fluorides: calcium salts reduce absorption of FLUORIDES

▶ Iron Salts: calcium salts reduce absorption of *oral* IRON SALTS

▶ Thyroid Hormones: calcium salts reduce absorption of

LEVOTHYROXINE

▶ Zinc: calcium salts reduce absorption of ZINC

Calcium-channel Blockers

NOTE Dihydropyridine calcium-channel blockers include amlodipine, felodipine, isradipine, lacidipine, lercanidipine, nicardipine, nifedipine, and nimodipine

▶ ACE Inhibitors: enhanced hypotensive effect when calcium- channel blockers given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when calcium-channel blockers given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when calcium-channel blockers given with ALCOHOL; verapamil possibly increases plasma concentration of ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when calcium- channel blockers given with ALDESLEUKIN

▶ Aliskiren: verapamil increases plasma concentration of

ALISKIREN

l Alpha-blockers: verapamil increases plasma concentration of TAMSULOSIN; enhanced hypotensive effect when calcium- channel blockers given with l ALPHA-BLOCKERS, also increased risk of first-dose hypotension with post-synaptic alpha- blockers such as prazosin

l Aminophylline: calcium-channel blockers possibly increase plasma concentration of l AMINOPHYLLINE (enhanced effect); diltiazem increases plasma concentration of AMINOPHYLLINE; verapamil increases plasma concentration of

l AMINOPHYLLINE (enhanced effect)

l Anaesthetics, General: enhanced hypotensive effect when calcium-channel blockers given with GENERAL ANAESTHETICS or ISOFLURANE; hypotensive effect of verapamil enhanced by l GENERAL ANAESTHETICS (also AV delay)

▶ Analgesics: hypotensive effect of calcium-channel blockers antagonised by NSAIDS; diltiazem inhibits metabolism of ALFENTANIL (risk of prolonged or delayed respiratory depression)

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when calcium-channel blockers given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Anti-arrhythmics: increased risk of bradycardia, AV block and

myocardial depression when diltiazem or verapamil given with l AMIODARONE; increased risk of myocardial depression and asystole when verapamil given with l DISOPYRAMIDE or l FLECAINIDE; increased risk of bradycardia and myocardial depression when diltiazem and verapamil given with

l DRONEDARONE; nifedipine increases plasma concentration of

l DRONEDARONE

l Antibacterials: metabolism of calcium-channel blockers possibly inhibited by l CLARITHROMYCIN, l ERYTHROMYCIN and l TELITHROMYCIN (increased risk of side-effects); manufacturer of lercanidipine advises avoid concomitant use with ERYTHROMYCIN; metabolism of diltiazem, nifedipine, nimodipine and verapamil accelerated by l RIFAMPICIN (plasma concentration significantly reduced); metabolism of isradipine and nicardipine possibly accelerated by

l RIFAMPICIN (possible significantly reduced plasma concentration); plasma concentration of felodipine possibly reduced by RIFAMPICIN; avoidance of verapamil advised by manufacturer of FIDAXOMICIN

l Anticoagulants: verapamil possibly increases plasma concentration of l DABIGATRAN (see under Dabigatran Etexilate, p. 117)

l Antidepressants: metabolism of nifedipine possibly inhibited by FLUOXETINE (increased plasma concentration); diltiazem and verapamil increase plasma concentration of IMIPRAMINE;

Calcium-channel Blockers

l Antidepressants (continued)

Interactions | Appendix 1

enhanced hypotensive effect when calcium-channel blockers given with MAOIS; plasma concentration of nifedipine reduced by ST JOHN’S WORT; plasma concentration of amlodipine and felodipine possibly reduced by ST JOHN’S WORT; plasma concentration of verapamil significantly reduced by l ST JOHN’S WORT; diltiazem and verapamil possibly increase plasma concentration of TRICYCLICS

▶ Antidiabetics: glucose tolerance occasionally impaired when nifedipine given with INSULIN

l Antiepileptics: effects of dihydropyridines, nicardipine and nifedipine probably reduced by CARBAMAZEPINE; effects of felodipine and isradipine reduced by CARBAMAZEPINE; diltiazem and verapamil enhance effects of l CARBAMAZEPINE; manufacturer of nimodipine advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN (plasma

concentration of nimodipine possibly reduced); effects of felodipine and verapamil reduced by FOSPHENYTOIN; manufacturer of isradipine advises avoid concomitant use with FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and

PRIMIDONE; diltiazem increases plasma concentration of

l FOSPHENYTOIN and l PHENYTOIN but also effect of diltiazem reduced; effects of calcium-channel blockers probably reduced by l PHENOBARBITAL and l PRIMIDONE; manufacturer of nimodipine advises avoid concomitant use with

l PHENOBARBITAL and l PRIMIDONE (plasma concentration of nimodipine reduced); effects of felodipine and verapamil reduced by PHENYTOIN

l Antifungals: metabolism of dihydropyridines possibly inhibited by ITRACONAZOLE and KETOCONAZOLE (increased plasma concentration); metabolism of felodipine is inhibited by l KETOCONAZOLE (increased plasma concentration)— manufacturer of ketoconazole advises avoid concomitant use; manufacturer of lercanidipine advises avoid concomitant use with ITRACONAZOLE and KETOCONAZOLE; negative inotropic effect possibly increased when calcium-channel blockers given with ITRACONAZOLE; metabolism of felodipine inhibited by l ITRACONAZOLE (increased plasma concentration); plasma concentration of nifedipine increased by MICAFUNGIN

▶ Antimalarials: possible increased risk of bradycardia when calcium-channel blockers given with MEFLOQUINE

▶ Antimuscarinics: avoidance of verapamil advised by manufacturer of DARIFENACIN; verapamil increases plasma concentration of SOLIFENACIN

l Antipsychotics: enhanced hypotensive effect when calcium- channel blockers given with ANTIPSYCHOTICS; diltiazem increases the plasma concentration of l LURASIDONE (see under Lurasidone, p. 315); verapamil possibly increases the plasma concentration of l LURASIDONE (see under Lurasidone, p. 315)

l Antivirals: plasma concentration of verapamil possibly increased by ATAZANAVIR; plasma concentration of diltiazem increased by l ATAZANAVIR (reduce dose of diltiazem); plasma concentration of diltiazem reduced by EFAVIRENZ; manufacturer of lercanidipine advises avoid concomitant use with RITONAVIR; plasma concentration of calcium-channel blockers possibly increased by l RITONAVIR; caution with diltiazem, felodipine, nicardipine, nifedipine and verapamil advised by manufacturer of TELAPREVIR; plasma concentration of amlodipine increased by TELAPREVIR (consider reducing dose of amlodipine)

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when calcium-channel blockers given with ANXIOLYTICS AND HYPNOTICS; diltiazem and verapamil inhibit metabolism of MIDAZOLAM (increased plasma concentration with increased sedation); absorption of lercanidipine increased by MIDAZOLAM; diltiazem and verapamil increase plasma concentration of BUSPIRONE (reduce dose of buspirone)

▶ Aprepitant: plasma concentration of both drugs may increase when diltiazem given with APREPITANT

l Avanafil: diltiazem and verapamil possibly increase plasma concentration of l AVANAFIL—see under Avanafil, p. 698

l Beta-blockers: enhanced hypotensive effect when calcium- channel blockers given with BETA-BLOCKERS; increased risk of

Interactions | Appendix 1

Calcium-channel Blockers

l Beta-blockers (continued)

AV block and bradycardia when diltiazem given with l BETA- BLOCKERS; asystole, severe hypotension and heart failure when verapamil given with l BETA-BLOCKERS (see under Verapamil, p. 156); possible severe hypotension and heart failure when nifedipine given with l BETA-BLOCKERS

▶ Calcium-channel Blockers: plasma concentration of both drugs may increase when diltiazem given with NIFEDIPINE

l Cardiac Glycosides: diltiazem, lercanidipine and nicardipine increase plasma concentration of l DIGOXIN; verapamil increases plasma concentration of l DIGOXIN, also increased risk of AV block and bradycardia; nifedipine possibly increases plasma concentration of l DIGOXIN

l Ciclosporin: diltiazem, nicardipine and verapamil increase plasma concentration of l CICLOSPORIN; combination of lercanidipine with l CICLOSPORIN may increase plasma concentration of either drug (or both)—avoid concomitant use; plasma concentration of nifedipine possibly increased by CICLOSPORIN (increased risk of toxicity including gingival hyperplasia)

▶ Cilostazol: diltiazem increases plasma concentration of

CILOSTAZOL (consider reducing dose of cilostazol)

▶ Clonidine: enhanced hypotensive effect when calcium-channel blockers given with CLONIDINE

l Colchicine: diltiazem and verapamil possibly increase risk of l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

▶ Corticosteroids: hypotensive effect of calcium-channel blockers antagonised by CORTICOSTEROIDS; diltiazem increases plasma concentration of METHYLPREDNISOLONE

l Cytotoxics: verapamil possibly increases plasma concentration of DOXORUBICIN; verapamil possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of verapamil by 6 to 12 hours; diltiazem and verapamil possibly increase the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; possible increased risk of bradycardia when diltiazem or verapamil given with CRIZOTINIB; plasma concentration of both drugs may increase when verapamil given with l EVEROLIMUS (consider reducing the dose of everolimus —consult everolimus product literature); diltiazem and verapamil possibly increase the plasma concentration of l IBRUTINIB— reduce dose of ibrutinib (see under Ibrutinib, p. 809); nifedipine possibly inhibits metabolism of VINCRISTINE

▶ Dapoxetine: manufacturer of dapoxetine advises dose

reduction when diltiazem and verapamil given with

DAPOXETINE (see under Dapoxetine, p. 703)

▶ Diazoxide: enhanced hypotensive effect when calcium- channel blockers given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when calcium-channel blockers given with DIURETICS; diltiazem and verapamil increase plasma concentration of EPLERENONE (reduce dose of eplerenone)

▶ Dopaminergics: enhanced hypotensive effect when calcium- channel blockers given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

l Fingolimod: possible increased risk of bradycardia when

diltiazem or verapamil given with l FINGOLIMOD

▶ Fosaprepitant: plasma concentration of both drugs may increase when diltiazem given with FOSAPREPITANT

▶ Grapefruit Juice: plasma concentration of felodipine, isradipine, lacidipine, lercanidipine, nicardipine, nifedipine, nimodipine and verapamil increased by GRAPEFRUIT JUICE; plasma concentration of amlodipine possibly increased by GRAPEFRUIT JUICE

▶ Hormone Antagonists: diltiazem and verapamil increase plasma concentration of DUTASTERIDE; possible increased risk of bradycardia when diltiazem or verapamil given with PASIREOTIDE

l Ivabradine: diltiazem and verapamil increase plasma concentration of l IVABRADINE—avoid concomitant use

l Lenalidomide: verapamil possibly increases plasma concentration of l LENALIDOMIDE (increased risk of toxicity)

Calcium-channel Blockers (continued)

l Lipid-regulating Drugs: diltiazem increases plasma concentration of ATORVASTATIN—possible increased risk of myopathy; plasma concentration of verapamil increased by l ATORVASTATIN, also possible increased risk of myopathy (consider reducing dose of atorvastatin); possible increased risk of myopathy when amlodipine and diltiazem given with l SIMVASTATIN (see under Simvastatin, p. 181); increased risk of myopathy when verapamil given with l SIMVASTATIN (see under Simvastatin, p. 181); separating administration from amlodipine and lacidipine by 12 hours advised by manufacturer of LOMITAPIDE; avoidance of diltiazem and verapamil advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

▶ Lithium: neurotoxicity may occur when diltiazem or verapamil given with LITHIUM without increased plasma concentration of lithium

l Magnesium (parenteral): profound hypotension reported with concomitant use of nifedipine and l PARENTERAL MAGNESIUM in pre-eclampsia

▶ Methyldopa: enhanced hypotensive effect when calcium- channel blockers given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when calcium- channel blockers given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when calcium- channel blockers given with MOXONIDINE

▶ Muscle Relaxants: verapamil enhances effects of NON- DEPOLARISING MUSCLE RELAXANTS and SUXAMETHONIUM;

enhanced hypotensive effect when calcium-channel blockers given with BACLOFEN or TIZANIDINE; manufacturer of verapamil advises avoid concomitant use of *intravenous* DANTROLENE; possible increased risk of ventricular arrhythmias when diltiazem given with *intravenous* DANTROLENE—manufacturer of diltiazem advises avoid concomitant use; calcium-channel blockers possibly enhance effects of NON-DEPOLARISING MUSCLE RELAXANTS

▶ Nitrates: enhanced hypotensive effect when calcium-channel blockers given with NITRATES

▶ Oestrogens: hypotensive effect of calcium-channel blockers antagonised by OESTROGENS

▶ Prostaglandins: enhanced hypotensive effect when calcium- channel blockers given with ALPROSTADIL

▶ Ranolazine: diltiazem and verapamil increase plasma concentration of RANOLAZINE (consider reducing dose of ranolazine)

▶ Sildenafil: enhanced hypotensive effect when amlodipine given with SILDENAFIL

l Sirolimus: diltiazem increases plasma concentration of

l SIROLIMUS; plasma concentration of both drugs increased when verapamil given with l SIROLIMUS; nicardipine possibly increases plasma concentration of SIROLIMUS

▶ Sulfinpyrazone: plasma concentration of verapamil reduced by

SULFINPYRAZONE

l Tacrolimus: diltiazem, nicardipine and nifedipine increase plasma concentration of l TACROLIMUS; felodipine and verapamil possibly increase plasma concentration of TACROLIMUS

l Theophylline: calcium-channel blockers possibly increase plasma concentration of l THEOPHYLLINE (enhanced effect); diltiazem increases plasma concentration of THEOPHYLLINE; verapamil increases plasma concentration of l THEOPHYLLINE (enhanced effect)

▶ Ticagrelor: diltiazem increases plasma concentration of

TICAGRELOR

▶ Ulcer-healing Drugs: metabolism of calcium-channel blockers possibly inhibited by CIMETIDINE (increased plasma concentration); plasma concentration of isradipine increased by CIMETIDINE (halve dose of isradipine)

▶ Ulipristal: avoidance of verapamil advised by manufacturer of

*low-dose* ULIPRISTAL

▶ Vardenafil: enhanced hypotensive effect when nifedipine given with VARDENAFIL

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when calcium-channel blockers given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Calcium-channel Blockers (dihydropyridines) *see* Calcium- channel Blockers

Canagliflozin *see* Antidiabetics

Canakinumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Candesartan *see* Angiotensin-II Receptor Antagonists

Cannabis Extract

l Antibacterials: plasma concentration of cannabis extract reduced by l RIFAMPICIN—manufacturer of cannabis extract advises avoid concomitant use

l Antidepressants: plasma concentration of cannabis extract possibly reduced by l ST JOHN’S WORT—manufacturer of cannabis extract advises avoid concomitant use; possible increased risk of hypertension and tachycardia when cannabis extract given with TRICYCLICS

l Antiepileptics: plasma concentration of cannabis extract possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—

manufacturer of cannabis extract advises avoid concomitant use

▶ Antifungals: plasma concentration of cannabis extract increased by KETOCONAZOLE

Capecitabine

l Allopurinol: manufacturer of capecitabine advises avoid concomitant use with l ALLOPURINOL

▶ Antibacterials: metabolism of capecitabine inhibited by

METRONIDAZOLE (increased toxicity)

l Anticoagulants: capecitabine enhances anticoagulant effect of

l COUMARINS

▶ Antiepileptics: capecitabine possibly inhibits metabolism of

FOSPHENYTOIN and PHENYTOIN (increased risk of toxicity)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cytotoxics: capecitabine possibly increases plasma concentration of ERLOTINIB

▶ Filgrastim: neutropenia possibly exacerbated when capecitabine given with FILGRASTIM

l Folates: toxicity of capecitabine increased by l FOLIC ACID—

avoid concomitant use

▶ Lipegfilgrastim: neutropenia possibly exacerbated when capecitabine given with LIPEGFILGRASTIM

▶ Pegfilgrastim: neutropenia possibly exacerbated when capecitabine given with PEGFILGRASTIM

▶ Ulcer-healing Drugs: metabolism of capecitabine inhibited by

CIMETIDINE (increased plasma concentration)

Capreomycin

▶ Antibacterials: increased risk of nephrotoxicity when capreomycin given with COLISTIMETHATE SODIUM or POLYMYXINS; increased risk of nephrotoxicity and ototoxicity when capreomycin given with AMINOGLYCOSIDES or VANCOMYCIN

▶ Cytotoxics: increased risk of nephrotoxicity and ototoxicity when capreomycin given with PLATINUM COMPOUNDS

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Captopril *see* ACE Inhibitors

Carbamazepine

▶ Alcohol: CNS side-effects of carbamazepine possibly increased by ALCOHOL

▶ Aminophylline: carbamazepine accelerates metabolism of

AMINOPHYLLINE (reduced effect)

l Analgesics: effects of carbamazepine enhanced by

l DEXTROPROPOXYPHENE; carbamazepine possibly accelerates metabolism of FENTANYL (reduced effect); carbamazepine reduces plasma concentration of METHADONE; carbamazepine reduces effects of TRAMADOL; carbamazepine possibly accelerates metabolism of PARACETAMOL (also isolated reports of hepatotoxicity)

l Anthelmintics: carbamazepine reduces plasma concentration of l ALBENDAZOLE and l PRAZIQUANTEL—consider increasing albendazole and praziquantel dose when given for systemic infections

Carbamazepine (continued)

l Anti-arrhythmics: carbamazepine possibly reduces plasma concentration of l DRONEDARONE—avoid concomitant use

Interactions | Appendix 1

l Antibacterials: plasma concentration of carbamazepine increased by l CLARITHROMYCIN (consider reducing dose of carbamazepine); plasma concentration of carbamazepine increased by l ERYTHROMYCIN; plasma concentration of carbamazepine reduced by l RIFABUTIN; carbamazepine accelerates metabolism of DOXYCYCLINE (reduced effect); carbamazepine possibly reduces plasma concentration of l BEDAQUILINE—manufacturer of bedaquiline advises avoid concomitant use; avoidance of carbamazepine advised by manufacturer of DELAMANID; plasma concentration of carbamazepine increased by l ISONIAZID (also possibly

increased isoniazid hepatotoxicity); carbamazepine reduces plasma concentration of l TELITHROMYCIN (avoid during and for 2 weeks after carbamazepine)

l Anticoagulants: carbamazepine possibly reduces plasma concentration of l APIXABAN—manufacturer of apixaban advises avoid concomitant use when given for treatment of deep-vein thrombosis or pulmonary embolism; carbamazepine accelerates metabolism of l COUMARINS (reduced anticoagulant effect); carbamazepine possibly reduces plasma concentration of DABIGATRAN—manufacturer of dabigatran advises avoid concomitant use; carbamazepine possibly reduces plasma concentration of l RIVAROXABAN— manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antidepressants: carbamazepine possibly reduces plasma

concentration of REBOXETINE; plasma concentration of carbamazepine increased by l FLUOXETINE and l FLUVOXAMINE; carbamazepine reduces plasma concentration of l MIANSERIN, MIRTAZAPINE and TRAZODONE; anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC- RELATED ANTIDEPRESSANTS (convulsive threshold lowered); manufacturer of carbamazepine advises avoid for 2 weeks after stopping l MAOIS, also antagonism of anticonvulsant effect; anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered); plasma concentration of carbamazepine possibly reduced by ST JOHN’S WORT; carbamazepine accelerates metabolism of

l TRICYCLICS (reduced plasma concentration and reduced effect)

l Antiepileptics: carbamazepine possibly reduces plasma concentration of ESLICARBAZEPINE but risk of side-effects increased; carbamazepine possibly reduces plasma concentration of ETHOSUXIMIDE and RETIGABINE; plasma concentration of both drugs often reduced when carbamazepine given with FOSPHENYTOIN or PHENYTOIN, also plasma concentration of fosphenytoin or phenytoin may be increased; carbamazepine often reduces plasma concentration of LAMOTRIGINE, also plasma concentration of an active metabolite of carbamazepine sometimes raised (but evidence is conflicting); possible increased risk of carbamazepine toxicity when given with LEVETIRACETAM; plasma concentration of carbamazepine sometimes reduced by OXCARBAZEPINE (but concentration of an active metabolite of carbamazepine may be increased), also plasma concentration of an active metabolite of oxcarbazepine often reduced; carbamazepine reduces plasma concentration of

l PERAMPANEL (see under Perampanel, p. 398); carbamazepine possibly increases plasma concentration of PHENOBARBITAL and PRIMIDONE; plasma concentration of both drugs possibly reduced when carbamazepine given with RUFINAMIDE; carbamazepine reduces plasma concentration of SODIUM VALPROATE and VALPROIC ACID, also plasma concentration of active metabolite of carbamazepine increased; plasma concentration of carbamazepine increased by l STIRIPENTOL; carbamazepine reduces plasma concentration of TIAGABINE and ZONISAMIDE; carbamazepine often reduces plasma concentration of TOPIRAMATE

l Antifungals: plasma concentration of carbamazepine possibly increased by KETOCONAZOLE, also plasma concentration of ketoconazole possibly reduced; plasma concentration of carbamazepine possibly increased by FLUCONAZOLE and

Interactions | Appendix 1

Carbamazepine

l Antifungals (continued)

MICONAZOLE; carbamazepine possibly reduces plasma concentration of ITRACONAZOLE and l POSACONAZOLE; carbamazepine possibly reduces plasma concentration of l VORICONAZOLE—avoid concomitant use; carbamazepine possibly reduces plasma concentration of CASPOFUNGIN— consider increasing dose of caspofungin

l Antimalarials: avoidance of carbamazepine advised by manufacturer of ARTENIMOL WITH PIPERAQUINE; anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered); carbamazepine accelerates metabolism of HALOPERIDOL, OLANZAPINE, QUETIAPINE and RISPERIDONE

(reduced plasma concentration); carbamazepine reduces plasma concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole —consult aripiprazole product literature); carbamazepine accelerates metabolism of l CLOZAPINE (reduced plasma concentration), also avoid concomitant use of drugs with substantial potential for causing agranulocytosis; carbamazepine possibly reduces plasma concentration of l LURASIDONE— avoid concomitant use; carbamazepine reduces plasma concentration of PALIPERIDONE

l Antivirals: avoidance of carbamazepine advised by

manufacturer of l BOCEPREVIR and l RILPIVIRINE (plasma concentration of boceprevir and rilpivirine possibly reduced); carbamazepine possibly reduces plasma concentration of

l DACLATASVIR and l SIMEPREVIR—manufacturer of daclatasvir and simeprevir advises avoid concomitant use; carbamazepine possibly reduces plasma concentration of DARUNAVIR, FOSAMPRENAVIR, LOPINAVIR, SAQUINAVIR and

TIPRANAVIR; avoidance of carbamazepine advised by manufacturer of DOLUTEGRAVIR, l ELVITEGRAVIR, ETRAVIRINE,

SOFOSBUVIR and l TELAPREVIR; plasma concentration of both drugs reduced when carbamazepine given with EFAVIRENZ; carbamazepine possibly reduces plasma concentration of

l INDINAVIR, also plasma concentration of carbamazepine possibly increased; carbamazepine reduces plasma concentration of NEVIRAPINE; plasma concentration of carbamazepine possibly increased by l RITONAVIR

▶ Anxiolytics and Hypnotics: carbamazepine often reduces plasma concentration of CLONAZEPAM; carbamazepine reduces plasma concentration of MIDAZOLAM

▶ Aprepitant: carbamazepine possibly reduces plasma concentration of APREPITANT

▶ Avanafil: carbamazepine possibly reduces plasma concentration of AVANAFIL—manufacturer of avanafil advises avoid concomitant use

▶ Bupropion: carbamazepine reduces plasma concentration of

BUPROPION

l Calcium-channel Blockers: carbamazepine reduces effects of FELODIPINE and ISRADIPINE; carbamazepine probably reduces effects of DIHYDROPYRIDINES, NICARDIPINE and NIFEDIPINE;

avoidance of carbamazepine advised by manufacturer of NIMODIPINE (plasma concentration of nimodipine possibly reduced); effects of carbamazepine enhanced by l DILTIAZEM and l VERAPAMIL

l Cannabis Extract: carbamazepine possibly reduces plasma concentration of l CANNABIS EXTRACT—manufacturer of cannabis extract advises avoid concomitant use

l Ciclosporin: carbamazepine accelerates metabolism of

l CICLOSPORIN (reduced plasma concentration)

l Clopidogrel: carbamazepine possibly reduces antiplatelet effect of l CLOPIDOGREL

l Cobicistat: carbamazepine possibly reduces plasma concentration of l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Corticosteroids: carbamazepine accelerates metabolism of

l CORTICOSTEROIDS (reduced effect)

l Cytotoxics: carbamazepine possibly decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); carbamazepine possibly reduces plasma concentration of BORTEZOMIB, l BOSUTINIB, CRIZOTINIB, l IBRUTINIB, l IDELALISIB and PONATINIB—manufacturer of

Carbamazepine

l Cytotoxics (continued)

bortezomib, bosutinib, crizotinib, ibrutinib, idelalisib and ponatinib advises avoid concomitant use; carbamazepine possibly reduces plasma concentration of l CABOZANTINIB— avoid concomitant use; avoidance of carbamazepine advised by manufacturer of l CABAZITAXEL, DABRAFENIB, GEFITINIB and VEMURAFENIB; avoidance of carbamazepine advised by manufacturer of DASATINIB, VANDETANIB and l VISMODEGIB (plasma concentration of dasatinib, vandetanib and vismodegib possibly reduced); carbamazepine reduces plasma concentration of l IMATINIB and l LAPATINIB—avoid concomitant use; carbamazepine possibly reduces plasma concentration of ERIBULIN; carbamazepine reduces plasma concentration of IRINOTECAN and its active metabolite; manufacturer of procarbazine advises possible increased risk of hypersensitivity reactions when carbamazepine given with PROCARBAZINE

l Diuretics: increased risk of hyponatraemia when carbamazepine given with DIURETICS; plasma concentration of carbamazepine increased by l ACETAZOLAMIDE; carbamazepine reduces plasma concentration of

l EPLERENONE—avoid concomitant use

▶ Fingolimod: carbamazepine reduces plasma concentration of

FINGOLIMOD

▶ Fosaprepitant: carbamazepine possibly reduces plasma concentration of FOSAPREPITANT

l Hormone Antagonists: carbamazepine possibly reduces plasma concentration of l ABIRATERONE—manufacturer of abiraterone advises avoid concomitant use; metabolism of carbamazepine inhibited by l DANAZOL (increased risk of toxicity); carbamazepine possibly accelerates metabolism of TOREMIFENE (reduced plasma concentration)

▶ 5HT3-receptor Antagonists: carbamazepine accelerates metabolism of ONDANSETRON (reduced effect)

l Ivacaftor: carbamazepine possibly reduces plasma concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

l Lipid-regulating Drugs: carbamazepine reduces plasma concentration of l SIMVASTATIN—consider increasing dose of simvastatin

▶ Lithium: neurotoxicity may occur when carbamazepine given with LITHIUM without increased plasma concentration of lithium

▶ Macitentan: avoidance of carbamazepine advised by manufacturer of MACITENTAN

▶ Muscle Relaxants: carbamazepine antagonises muscle relaxant effect of NON-DEPOLARISING MUSCLE RELAXANTS (accelerated recovery from neuromuscular blockade)

l Oestrogens: carbamazepine accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: carbamazepine accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

▶ Retinoids: plasma concentration of carbamazepine possibly reduced by ISOTRETINOIN

▶ Roflumilast: carbamazepine possibly inhibits effects of ROFLUMILAST (manufacturer of roflumilast advises avoid concomitant use)

▶ Theophylline: carbamazepine accelerates metabolism of

THEOPHYLLINE (reduced effect)

▶ Thyroid Hormones: carbamazepine accelerates metabolism of THYROID HORMONES (may increase requirements for thyroid hormones in hypothyroidism)

▶ Tibolone: carbamazepine accelerates metabolism of TIBOLONE

(reduced plasma concentration)

▶ Ticagrelor: carbamazepine possibly reduces plasma concentration of TICAGRELOR

Carbamazepine (continued)

l Ulcer-healing Drugs: metabolism of carbamazepine inhibited by l CIMETIDINE (increased plasma concentration)

l Ulipristal: avoidance of carbamazepine advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

▶ Vitamins: carbamazepine possibly increases requirements for ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL or VITAMIN D

Carbapenems *see* Ertapenem, Imipenem with Cilastatin, and Meropenem

Carbonic Anhydrase Inhibitors *see* Diuretics Carboplatin *see* Platinum Compounds Carboprost *see* Prostaglandins

Cardiac Glycosides

▶ ACE Inhibitors: plasma concentration of digoxin possibly increased by CAPTOPRIL

▶ Alpha-blockers: plasma concentration of digoxin increased by

PRAZOSIN

▶ Aminosalicylates: absorption of digoxin possibly reduced by

SULFASALAZINE

▶ Analgesics: plasma concentration of cardiac glycosides possibly increased by NSAIDS, also possible exacerbation of heart failure and reduction of renal function

▶ Antacids: absorption of digoxin possibly reduced by ANTACIDS

l Anti-arrhythmics: plasma concentration of digoxin increased by l AMIODARONE, l DRONEDARONE and l PROPAFENONE (halve

dose of digoxin)

▶ Antibacterials: plasma concentration of digoxin possibly increased by GENTAMICIN, TELITHROMYCIN and TRIMETHOPRIM;

absorption of digoxin reduced by NEOMYCIN; plasma concentration of digoxin possibly reduced by RIFAMPICIN; plasma concentration of digoxin increased by MACROLIDES (increased risk of toxicity)

l Antidepressants: plasma concentration of digoxin reduced by

l ST JOHN’S WORT—avoid concomitant use

▶ Antidiabetics: plasma concentration of digoxin possibly reduced by ACARBOSE; plasma concentration of digoxin increased by CANAGLIFLOZIN and SITAGLIPTIN

▶ Antiepileptics: plasma concentration of digoxin possibly reduced by FOSPHENYTOIN and PHENYTOIN

l Antifungals: increased cardiac toxicity with cardiac glycosides if hypokalaemia occurs with l AMPHOTERICIN; plasma concentration of digoxin increased by l ITRACONAZOLE

l Antimalarials: plasma concentration of digoxin possibly increased by l CHLOROQUINE and l HYDROXYCHLOROQUINE; possible increased risk of bradycardia when digoxin given with MEFLOQUINE; plasma concentration of digoxin increased by l QUININE

▶ Antimuscarinics: plasma concentration of digoxin possibly increased by DARIFENACIN

l Antivirals: side-effects of digoxin possibly increased by BOCEPREVIR; plasma concentration of digoxin increased by l DACLATASVIR, ETRAVIRINE, SIMEPREVIR and TELAPREVIR;

plasma concentration of digoxin possibly increased by

RITONAVIR

▶ Anxiolytics and Hypnotics: plasma concentration of digoxin increased by ALPRAZOLAM (increased risk of toxicity)

▶ Beta-blockers: increased risk of AV block and bradycardia when cardiac glycosides given with BETA-BLOCKERS

▶ Calcium Salts: arrhythmias can be precipitated when cardiac glycosides given with large *intravenous* doses of CALCIUM SALTS

l Calcium-channel Blockers: plasma concentration of digoxin

increased by l DILTIAZEM, l LERCANIDIPINE and l NICARDIPINE; plasma concentration of digoxin possibly increased by

l NIFEDIPINE; plasma concentration of digoxin increased by

l VERAPAMIL, also increased risk of AV block and bradycardia

l Ciclosporin: plasma concentration of digoxin increased by

l CICLOSPORIN (increased risk of toxicity)

▶ Cobicistat: plasma concentration of digoxin possibly increased by COBICISTAT—reduce initial dose of digoxin

l Colchicine: possible increased risk of myopathy when digoxin given with l COLCHICINE

Cardiac Glycosides (continued)

▶ Corticosteroids: increased risk of hypokalaemia when cardiac glycosides given with CORTICOSTEROIDS

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▶ Cytotoxics: absorption of digoxin *tablets* possibly reduced by BLEOMYCIN, CARMUSTINE, CYCLOPHOSPHAMIDE, CYTARABINE, DOXORUBICIN, MELPHALAN, METHOTREXATE, PROCARBAZINE and

VINCRISTINE; possible increased risk of bradycardia when digoxin given with CRIZOTINIB; manufacturer of digoxin advises give IBRUTINIB at least 6 hours before or after ibrutinib; plasma concentration of digoxin increased by VANDETANIB—possible increased risk of bradycardia

l Diuretics: increased cardiac toxicity with cardiac glycosides if hypokalaemia occurs with l ACETAZOLAMIDE, l LOOP DIURETICS or l THIAZIDES AND RELATED DIURETICS; plasma concentration of digoxin possibly increased by POTASSIUM CANRENOATE; plasma concentration of digoxin increased by

l SPIRONOLACTONE

▶ Ivacaftor: plasma concentration of digoxin increased by

IVACAFTOR

▶ Lenalidomide: plasma concentration of digoxin possibly increased by LENALIDOMIDE

▶ Lipid-regulating Drugs: absorption of cardiac glycosides possibly reduced by COLESTIPOL and COLESTYRAMINE; plasma concentration of digoxin possibly increased by ATORVASTATIN

▶ Mirabegron: plasma concentration of digoxin increased by

MIRABEGRON—reduce initial dose of digoxin

▶ Muscle Relaxants: risk of ventricular arrhythmias when cardiac glycosides given with SUXAMETHONIUM; possible increased risk of bradycardia when cardiac glycosides given with TIZANIDINE

▶ Penicillamine: plasma concentration of digoxin possibly reduced by PENICILLAMINE

▶ Ranolazine: plasma concentration of digoxin increased by

RANOLAZINE

▶ Sympathomimetics, Beta2: plasma concentration of digoxin possibly reduced by SALBUTAMOL

l Ticagrelor: plasma concentration of digoxin increased by

l TICAGRELOR

▶ Tolvaptan: plasma concentration of digoxin increased by

TOLVAPTAN (increased risk of toxicity)

▶ Ulcer-healing Drugs: plasma concentration of digoxin possibly slightly increased by PROTON PUMP INHIBITORS; absorption of cardiac glycosides possibly reduced by SUCRALFATE

▶ Ulipristal: manufacturer of ulipristal advises give digoxin at least 1.5 hours before or after ULIPRISTAL

Carmustine

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: carmustine possibly reduces absorption of

DIGOXIN *tablets*

▶ Ulcer-healing Drugs: myelosuppressive effects of carmustine possibly enhanced by CIMETIDINE

Carteolol *see* Beta-blockers Carvedilol *see* Beta-blockers Caspofungin

▶ Antibacterials: plasma concentration of caspofungin initially

increased and then reduced by RIFAMPICIN (consider increasing dose of caspofungin)

▶ Antiepileptics: plasma concentration of caspofungin possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN—

consider increasing dose of caspofungin

▶ Antivirals: plasma concentration of caspofungin possibly reduced by EFAVIRENZ and NEVIRAPINE—consider increasing dose of caspofungin

l Ciclosporin: plasma concentration of caspofungin increased by l CICLOSPORIN (manufacturer of caspofungin recommends monitoring liver enzymes)

▶ Corticosteroids: plasma concentration of caspofungin possibly reduced by DEXAMETHASONE—consider increasing dose of caspofungin

l Tacrolimus: caspofungin reduces plasma concentration of

l TACROLIMUS

Catumaxomab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Interactions | Appendix 1

Catumaxomab (continued)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Cefaclor *see* Cephalosporins Cefadroxil *see* Cephalosporins Cefalexin *see* Cephalosporins Cefixime *see* Cephalosporins Cefotaxime *see* Cephalosporins Cefradine *see* Cephalosporins Ceftaroline *see* Cephalosporins Ceftazidime *see* Cephalosporins Ceftriaxone *see* Cephalosporins Cefuroxime *see* Cephalosporins Celecoxib *see* NSAIDs

Celiprolol *see* Beta-blockers

Cephalosporins

▶ Antacids: absorption of cefaclor reduced by ANTACIDS

▶ Antibacterials: possible increased risk of nephrotoxicity when cephalosporins given with AMINOGLYCOSIDES

l Anticoagulants: cephalosporins possibly enhance anticoagulant effect of l COUMARINS

▶ Teriflunomide: plasma concentration of cefaclor increased by

TERIFLUNOMIDE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Certolizumab pegol

l Abatacept: avoid concomitant use of certolizumab pegol with

l ABATACEPT

l Anakinra: avoid concomitant use of certolizumab pegol with

l ANAKINRA

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Cetirizine *see* Antihistamines

Cetuximab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Chenodeoxycholic Acid *see* Bile Acids Chloral *see* Anxiolytics and Hypnotics Chloramphenicol

▶ Antibacterials: metabolism of chloramphenicol accelerated by

RIFAMPICIN (reduced plasma concentration)

l Anticoagulants: chloramphenicol enhances anticoagulant effect of l COUMARINS

l Antidiabetics: chloramphenicol enhances effects of

l SULFONYLUREAS

l Antiepileptics: chloramphenicol increases plasma concentration of l FOSPHENYTOIN and l PHENYTOIN (increased risk of toxicity); metabolism of chloramphenicol possibly accelerated by l PHENOBARBITAL and l PRIMIDONE (reduced plasma concentration)

l Antipsychotics: avoid concomitant use of chloramphenicol with l CLOZAPINE (increased risk of agranulocytosis)

l Ciclosporin: chloramphenicol possibly increases plasma concentration of l CICLOSPORIN

l Clopidogrel: chloramphenicol possibly reduces antiplatelet effect of l CLOPIDOGREL

▶ Hydroxocobalamin: chloramphenicol reduces response to

HYDROXOCOBALAMIN

l Tacrolimus: chloramphenicol possibly increases plasma concentration of l TACROLIMUS

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Chlordiazepoxide *see* Anxiolytics and Hypnotics

Chloroprocaine

l Antibacterials: chloroprocaine possibly inhibits effects of l SULFONAMIDES (manufacturer of chloroprocaine advises avoid concomitant use)

Chloroquine

▶ Adsorbents: absorption of chloroquine reduced by KAOLIN

Chloroquine (continued)

▶ Agalsidase Alfa and Beta: chloroquine possibly inhibits effects of AGALSIDASE ALFA AND BETA (manufacturers of agalsidase alfa and beta advise avoid concomitant use)

▶ Antacids: absorption of chloroquine reduced by ANTACIDS

l Anthelmintics: chloroquine reduces plasma concentration of

l PRAZIQUANTEL—consider increasing praziquantel dose when given for systemic infections

l Anti-arrhythmics: increased risk of ventricular arrhythmias when chloroquine given with l AMIODARONE—avoid concomitant use

l Antibacterials: increased risk of ventricular arrhythmias when chloroquine given with l MOXIFLOXACIN—avoid concomitant use

l Antidepressants: possible increased risk of ventricular arrhythmias when chloroquine given with l CITALOPRAM and l ESCITALOPRAM

l Antimalarials: avoidance of antimalarials advised by

manufacturer of l ARTEMETHER WITH LUMEFANTRINE; increased risk of convulsions when chloroquine given with

l MEFLOQUINE

l Antipsychotics: increased risk of ventricular arrhythmias when chloroquine given with l DROPERIDOL—avoid concomitant use

l Cardiac Glycosides: chloroquine possibly increases plasma concentration of l DIGOXIN

l Ciclosporin: chloroquine increases plasma concentration of

l CICLOSPORIN (increased risk of toxicity)

l Cytotoxics: possible increased risk of ventricular arrhythmias when chloroquine given with l BOSUTINIB

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

▶ Lanthanum: absorption of chloroquine possibly reduced by

LANTHANUM (give at least 2 hours apart)

▶ Laronidase: chloroquine possibly inhibits effects of LARONIDASE (manufacturer of laronidase advises avoid concomitant use)

▶ Parasympathomimetics: chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of NEOSTIGMINE and PYRIDOSTIGMINE

▶ Ulcer-healing Drugs: metabolism of chloroquine inhibited by

CIMETIDINE (increased plasma concentration)

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Chlorothiazide *see* Diuretics Chlorphenamine *see* Antihistamines Chlorpromazine *see* Antipsychotics Chlortalidone *see* Diuretics

Cholera Vaccine *see* Vaccines Ciclesonide *see* Corticosteroids Ciclosporin

l ACE Inhibitors: increased risk of hyperkalaemia when

ciclosporin given with l ACE INHIBITORS

l Aliskiren: ciclosporin increases plasma concentration of

l ALISKIREN—avoid concomitant use

▶ Allopurinol: plasma concentration of ciclosporin possibly increased by ALLOPURINOL (risk of nephrotoxicity)

l Ambrisentan: ciclosporin increases plasma concentration of

l AMBRISENTAN (see under Ambrisentan, p. 162)

l Analgesics: increased risk of nephrotoxicity when ciclosporin given with l NSAIDS; ciclosporin increases plasma concentration of l DICLOFENAC (halve dose of diclofenac)

l Angiotensin-II Receptor Antagonists: increased risk of hyperkalaemia when ciclosporin given with l ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Anti-arrhythmics: plasma concentration of ciclosporin possibly increased by AMIODARONE and PROPAFENONE

l Antibacterials: metabolism of ciclosporin inhibited by

l CLARITHROMYCIN and l ERYTHROMYCIN (increased plasma concentration); metabolism of ciclosporin accelerated by l RIFAMPICIN (reduced plasma concentration); plasma concentration of ciclosporin possibly reduced by

l SULFADIAZINE; increased risk of nephrotoxicity when ciclosporin given with l AMINOGLYCOSIDES, l POLYMYXINS, l QUINOLONES, l SULFONAMIDES or l VANCOMYCIN; plasma

concentration of ciclosporin possibly increased by

Ciclosporin

l Antibacterials (continued)

l CHLORAMPHENICOL and l TELITHROMYCIN; increased risk of myopathy when ciclosporin given with l DAPTOMYCIN (preferably avoid concomitant use); avoidance of ciclosporin advised by manufacturer of FIDAXOMICIN; metabolism of ciclosporin possibly inhibited by l MACROLIDES (increased plasma concentration); increased risk of nephrotoxicity when ciclosporin given with l TRIMETHOPRIM, also plasma concentration of ciclosporin reduced by *intravenous* trimethoprim

l Anticoagulants: ciclosporin possibly increases plasma concentration of l DABIGATRAN—manufacturer of dabigatran advises avoid concomitant use

l Antidepressants: plasma concentration of ciclosporin reduced by l ST JOHN’S WORT—avoid concomitant use

▶ Antidiabetics: ciclosporin possibly enhances hypoglycaemic effect of REPAGLINIDE

l Antiepileptics: metabolism of ciclosporin accelerated by

l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE (reduced plasma concentration); plasma concentration of ciclosporin possibly reduced by OXCARBAZEPINE

l Antifungals: metabolism of ciclosporin inhibited by

l FLUCONAZOLE, l ITRACONAZOLE, l KETOCONAZOLE,

l POSACONAZOLE and l VORICONAZOLE (increased plasma concentration); metabolism of ciclosporin possibly inhibited by l MICONAZOLE (increased plasma concentration); increased risk of nephrotoxicity when ciclosporin given with

l AMPHOTERICIN; ciclosporin increases plasma concentration of l CASPOFUNGIN (manufacturer of caspofungin recommends monitoring liver enzymes); plasma concentration of ciclosporin possibly reduced by GRISEOFULVIN and TERBINAFINE; plasma concentration of ciclosporin possibly increased by MICAFUNGIN

l Antimalarials: plasma concentration of ciclosporin increased by l CHLOROQUINE and l HYDROXYCHLOROQUINE (increased risk of toxicity)

▶ Antimuscarinics: avoidance of ciclosporin advised by manufacturer of DARIFENACIN

l Antivirals: increased risk of nephrotoxicity when ciclosporin given with ACICLOVIR or VALACICLOVIR; plasma concentration of ciclosporin possibly increased by l ATAZANAVIR and

l RITONAVIR; plasma concentration of ciclosporin increased by

l BOCEPREVIR, l FOSAMPRENAVIR and l INDINAVIR; plasma

concentration of ciclosporin possibly reduced by l EFAVIRENZ; plasma concentration of both drugs increased when ciclosporin given with l SAQUINAVIR; plasma concentration of both drugs increased when ciclosporin given with

l TELAPREVIR (reduce dose of ciclosporin)

l Beta-blockers: plasma concentration of ciclosporin increased by l CARVEDILOL

l Bile Acids: absorption of ciclosporin increased by

l URSODEOXYCHOLIC ACID

l Bosentan: ciclosporin increases plasma concentration of l BOSENTAN (also plasma concentration of ciclosporin reduced—avoid concomitant use)

l Calcium-channel Blockers: combination of ciclosporin with

l LERCANIDIPINE may increase plasma concentration of either drug (or both)—avoid concomitant use; plasma concentration of ciclosporin increased by l DILTIAZEM, l NICARDIPINE and

l VERAPAMIL; ciclosporin possibly increases plasma concentration of NIFEDIPINE (increased risk of toxicity including gingival hyperplasia)

l Cardiac Glycosides: ciclosporin increases plasma concentration of l DIGOXIN (increased risk of toxicity)

l Colchicine: possible increased risk of nephrotoxicity and myotoxicity when ciclosporin given with l COLCHICINE— suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

▶ Colestilan: manufacturer of colestilan advises give ciclosporin at least 1 hour before or 3 hours after COLESTILAN

l Corticosteroids: plasma concentration of ciclosporin increased by high-dose l METHYLPREDNISOLONE (risk of convulsions); ciclosporin increases plasma concentration of PREDNISOLONE

Ciclosporin (continued)

l Cytotoxics: increased risk of nephrotoxicity when ciclosporin given with l MELPHALAN; increased risk of neurotoxicity when ciclosporin given with l DOXORUBICIN; ciclosporin increases plasma concentration of l EPIRUBICIN and l IDARUBICIN; ciclosporin reduces excretion of MITOXANTRONE (increased plasma concentration); risk of toxicity when ciclosporin given with l METHOTREXATE; ciclosporin possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of ciclosporin by 6 to 12 hours; caution with ciclosporin advised by manufacturer of

Interactions | Appendix 1

l CRIZOTINIB; ciclosporin increases plasma concentration of

l EVEROLIMUS (consider reducing the dose of everolimus — consult everolimus product literature); plasma concentration of ciclosporin possibly increased by IMATINIB; *in vitro* studies suggest a possible interaction between ciclosporin and DOCETAXEL (consult docetaxel product literature); ciclosporin possibly increases plasma concentration of ETOPOSIDE (increased risk of toxicity)

▶ Dexrazoxane: increased risk of immunosupression with ciclosporin advised by manufacturer of DEXRAZOXANE

l Diuretics: plasma concentration of ciclosporin possibly increased by l ACETAZOLAMIDE; increased risk of hyperkalaemia when ciclosporin given with l POTASSIUM- SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS; increased

risk of nephrotoxicity and possibly hypermagnesaemia when ciclosporin given with THIAZIDES AND RELATED DIURETICS

l Grapefruit Juice: plasma concentration of ciclosporin increased by l GRAPEFRUIT JUICE (increased risk of toxicity)

l Hormone Antagonists: metabolism of ciclosporin inhibited by l DANAZOL (increased plasma concentration); plasma concentration of ciclosporin reduced by LANREOTIDE and

l OCTREOTIDE; plasma concentration of ciclosporin possibly reduced by l PASIREOTIDE

l Lenalidomide: ciclosporin possibly increases plasma concentration of l LENALIDOMIDE (increased risk of toxicity)

l Lipid-regulating Drugs: absorption of ciclosporin reduced by

l COLESEVELAM; increased risk of renal impairment when ciclosporin given with BEZAFIBRATE or FENOFIBRATE; increased risk of myopathy when ciclosporin given with l ATORVASTATIN (see under Atorvastatin, p. 179); increased risk of myopathy when ciclosporin given with l FLUVASTATIN or l PRAVASTATIN; increased risk of myopathy when ciclosporin given with

l ROSUVASTATIN or l SIMVASTATIN (avoid concomitant use); plasma concentration of both drugs may increase when ciclosporin given with l EZETIMIBE; separating administration from ciclosporin by 12 hours advised by manufacturer of LOMITAPIDE

▶ Mannitol: possible increased risk of nephrotoxicity when

ciclosporin given with MANNITOL

l Metoclopramide: plasma concentration of ciclosporin increased by l METOCLOPRAMIDE

▶ Mifamurtide: avoidance of ciclosporin advised by manufacturer of MIFAMURTIDE

l Modafinil: plasma concentration of ciclosporin reduced by

l MODAFINIL

▶ Oestrogens: plasma concentration of ciclosporin possibly increased by OESTROGENS

l Orlistat: absorption of ciclosporin possibly reduced by

l ORLISTAT

l Potassium Salts: increased risk of hyperkalaemia when ciclosporin given with l POTASSIUM SALTS

▶ Progestogens: plasma concentration of ciclosporin possibly increased by PROGESTOGENS

▶ Ranolazine: plasma concentration of both drugs may increase when ciclosporin given with RANOLAZINE

▶ Sevelamer: plasma concentration of ciclosporin possibly reduced by SEVELAMER

▶ Sirolimus: ciclosporin increases plasma concentration of

SIROLIMUS

l Sulfinpyrazone: plasma concentration of ciclosporin reduced by l SULFINPYRAZONE

l Tacrolimus: plasma concentration of ciclosporin increased by l TACROLIMUS (increased risk of nephrotoxicity)—avoid concomitant use

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Ciclosporin (continued)

▶ Ticagrelor: ciclosporin increases plasma concentration of

TICAGRELOR

l Ulcer-healing Drugs: plasma concentration of ciclosporin possibly increased by l CIMETIDINE; plasma concentration of ciclosporin possibly affected by OMEPRAZOLE

▶ Vitamins: plasma concentration of ciclosporin possibly affected by VITAMIN E

Cilostazol

l Anagrelide: avoidance of cilostazol advised by manufacturer of

l ANAGRELIDE

l Antibacterials: plasma concentration of cilostazol possibly increased by l CLARITHROMYCIN (see under Cilostazol, p. 206); plasma concentration of cilostazol increased by

l ERYTHROMYCIN (see under Cilostazol, p. 206)

l Antifungals: plasma concentration of cilostazol increased by l KETOCONAZOLE (see under Cilostazol, p. 206); plasma concentration of cilostazol possibly increased by

l ITRACONAZOLE (see under Cilostazol, p. 206)

l Antivirals: plasma concentration of cilostazol possibly increased by l BOCEPREVIR, l RITONAVIR and l TELAPREVIR (see under Cilostazol, p. 206)

▶ Calcium-channel Blockers: plasma concentration of cilostazol increased by DILTIAZEM (consider reducing dose of cilostazol)

▶ Lipid-regulating Drugs: separating administration from cilostazol by 12 hours advised by manufacturer of LOMITAPIDE

l Ulcer-healing Drugs: plasma concentration of cilostazol increased by l OMEPRAZOLE (see under Cilostazol, p. 206)

Cimetidine *see* Histamine H2-antagonists

Cinacalcet

▶ Antifungals: metabolism of cinacalcet inhibited by

KETOCONAZOLE (increased plasma concentration)

l Hormone Antagonists: cinacalcet possibly inhibits metabolism of l TAMOXIFEN to active metabolite (avoid concomitant use)

Cinnarizine *see* Antihistamines Ciprofibrate *see* Fibrates Ciprofloxacin *see* Quinolones Cisatracurium *see* Muscle Relaxants Cisplatin *see* Platinum Compounds Citalopram *see* Antidepressants, SSRI Cladribine

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of cladribine advised by manufacturer of

l LAMIVUDINE

Clarithromycin *see* Macrolides Clemastine *see* Antihistamines Clindamycin

l Muscle Relaxants: clindamycin enhances effects of l NON-

DEPOLARISING MUSCLE RELAXANTS and l SUXAMETHONIUM

▶ Parasympathomimetics: clindamycin antagonises effects of

NEOSTIGMINE and PYRIDOSTIGMINE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Clobazam *see* Anxiolytics and Hypnotics

Clofazimine

l Antibacterials: possible increased risk of ventricular arrhythmias when clofazimine given with l BEDAQUILINE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Clomethiazole *see* Anxiolytics and Hypnotics Clomipramine *see* Antidepressants, Tricyclic Clonazepam *see* Anxiolytics and Hypnotics Clonidine

▶ ACE Inhibitors: enhanced hypotensive effect when clonidine

given with ACE INHIBITORS; previous treatment with clonidine possibly delays antihypertensive effect of CAPTOPRIL

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when clonidine given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when clonidine given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when clonidine given with ALDESLEUKIN

▶ Alpha-blockers: enhanced hypotensive effect when clonidine given with ALPHA-BLOCKERS

Clonidine (continued)

▶ Anaesthetics, General: enhanced hypotensive effect when clonidine given with GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of clonidine antagonised by

NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when clonidine given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Antidepressants: enhanced hypotensive effect when clonidine

given with MAOIS; hypotensive effect of clonidine possibly antagonised by MIRTAZAPINE; hypotensive effect of clonidine antagonised by l TRICYCLICS, also increased risk of hypertension on clonidine withdrawal

▶ Antipsychotics: enhanced hypotensive effect when clonidine given with PHENOTHIAZINES

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when clonidine given with ANXIOLYTICS AND HYPNOTICS

l Beta-blockers: increased risk of withdrawal hypertension when clonidine given with l BETA-BLOCKERS (withdraw beta- blockers several days before slowly withdrawing clonidine)

▶ Calcium-channel Blockers: enhanced hypotensive effect when clonidine given with CALCIUM-CHANNEL BLOCKERS

▶ Corticosteroids: hypotensive effect of clonidine antagonised by

CORTICOSTEROIDS

▶ Cytotoxics: possible increased risk of bradycardia when clonidine given with CRIZOTINIB

▶ Diazoxide: enhanced hypotensive effect when clonidine given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when clonidine given with DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when clonidine given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Histamine: avoidance of clonidine advised by manufacturer of

HISTAMINE

▶ Methyldopa: enhanced hypotensive effect when clonidine given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when clonidine given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when clonidine given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when clonidine given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when clonidine given with NITRATES

▶ Oestrogens: hypotensive effect of clonidine antagonised by

OESTROGENS

▶ Prostaglandins: enhanced hypotensive effect when clonidine given with ALPROSTADIL

l Sympathomimetics: possible risk of hypertension when clonidine given with ADRENALINE (EPINEPHRINE) or NORADRENALINE (NOREPINEPHRINE); serious adverse events reported with concomitant use of clonidine and

l METHYLPHENIDATE (causality not established)

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when clonidine given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Clopamide *see* Diuretics

Clopidogrel

▶ Analgesics: increased risk of bleeding when clopidogrel given with NSAIDS or ASPIRIN

l Antibacterials: antiplatelet effect of clopidogrel possibly reduced by l CHLORAMPHENICOL, l CIPROFLOXACIN and

l ERYTHROMYCIN

l Anticoagulants: manufacturer of clopidogrel advises avoid concomitant use with l WARFARIN; antiplatelet action of clopidogrel enhances anticoagulant effect of l COUMARINS and l PHENINDIONE; increased risk of bleeding when clopidogrel given with HEPARINS

l Antidepressants: antiplatelet effect of clopidogrel possibly reduced by l FLUOXETINE, l FLUVOXAMINE and l MOCLOBEMIDE

l Antiepileptics: antiplatelet effect of clopidogrel possibly reduced by l CARBAMAZEPINE and l OXCARBAZEPINE

l Antifungals: antiplatelet effect of clopidogrel possibly reduced by l FLUCONAZOLE, l ITRACONAZOLE, l KETOCONAZOLE and

l VORICONAZOLE

Clopidogrel (continued)

l Antivirals: antiplatelet effect of clopidogrel possibly reduced by l ETRAVIRINE

▶ Dipyridamole: increased risk of bleeding when clopidogrel given with DIPYRIDAMOLE

▶ Iloprost: increased risk of bleeding when clopidogrel given with ILOPROST

l Lipid-regulating Drugs: clopidogrel increases plasma concentration of l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature)

▶ Prasugrel: possible increased risk of bleeding when clopidogrel given with PRASUGREL

l Ulcer-healing Drugs: antiplatelet effect of clopidogrel possibly reduced by l CIMETIDINE, LANSOPRAZOLE, PANTOPRAZOLE and

RABEPRAZOLE; antiplatelet effect of clopidogrel reduced by

l ESOMEPRAZOLE and l OMEPRAZOLE

Clozapine *see* Antipsychotics Co-amoxiclav *see* Penicillins Co-beneldopa

▶ ACE Inhibitors: enhanced hypotensive effect when co-

beneldopa given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when co-beneldopa given with ADRENERGIC NEURONE BLOCKERS

▶ Alpha-blockers: enhanced hypotensive effect when co- beneldopa given with ALPHA-BLOCKERS

l Anaesthetics, General: increased risk of arrhythmias when co- beneldopa given with l VOLATILE LIQUID GENERAL ANAESTHETICS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when co-beneldopa given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antibacterials: effects of co-beneldopa possibly reduced by

ISONIAZID

l Antidepressants: risk of hypertensive crisis when co-beneldopa given with l MAOIS, avoid co-beneldopa for at least 2 weeks after stopping MAOIs; increased risk of side-effects when co- beneldopa given with MOCLOBEMIDE

▶ Antiepileptics: effects of co-beneldopa possibly reduced by

FOSPHENYTOIN and PHENYTOIN

▶ Antimuscarinics: absorption of co-beneldopa possibly reduced by ANTIMUSCARINICS

▶ Antipsychotics: effects of co-beneldopa antagonised by ANTIPSYCHOTICS; avoidance of co-beneldopa advised by manufacturer of AMISULPRIDE (antagonism of effect)

▶ Anxiolytics and Hypnotics: effects of co-beneldopa possibly antagonised by BENZODIAZEPINES

▶ Beta-blockers: enhanced hypotensive effect when co- beneldopa given with BETA-BLOCKERS

▶ Bupropion: increased risk of side-effects when co-beneldopa given with BUPROPION

▶ Calcium-channel Blockers: enhanced hypotensive effect when co-beneldopa given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when co-beneldopa given with CLONIDINE

▶ Diazoxide: enhanced hypotensive effect when co-beneldopa given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when co-beneldopa given with DIURETICS

▶ Dopaminergics: enhanced effects and increased toxicity of co- beneldopa when given with SELEGILINE (reduce dose of co- beneldopa)

▶ Iron Salts: absorption of co-beneldopa possibly reduced by

*oral* IRON SALTS

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: enhanced hypotensive effect when co-beneldopa given with METHYLDOPA; antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Moxonidine: enhanced hypotensive effect when co-beneldopa given with MOXONIDINE

▶ Muscle Relaxants: possible agitation, confusion and hallucinations when co-beneldopa given with BACLOFEN

▶ Nitrates: enhanced hypotensive effect when co-beneldopa given with NITRATES

Co-beneldopa (continued)

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when co-beneldopa given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Interactions | Appendix 1

Cobicistat

l Alpha-blockers: cobicistat possibly increases plasma concentration of l ALFUZOSIN—manufacturer of cobicistat advises avoid concomitant use

l Anti-arrhythmics: cobicistat possibly increases plasma

concentration of l AMIODARONE—manufacturer of cobicistat advises avoid concomitant use

l Antibacterials: plasma concentration of cobicistat reduced by l RIFABUTIN (adjust dose—consult product literature); plasma concentration of cobicistat possibly reduced by

l RIFAMPICIN—manufacturer of cobicistat advises avoid concomitant use

l Anticoagulants: avoidance of cobicistat advised by manufacturer of APIXABAN; cobicistat possibly enhances anticoagulant effect of l RIVAROXABAN—avoid concomitant use

l Antidepressants: plasma concentration of cobicistat possibly reduced by l ST JOHN’S WORT—manufacturer of cobicistat advises avoid concomitant use

l Antiepileptics: plasma concentration of cobicistat possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—

manufacturer of cobicistat advises avoid concomitant use

▶ Antifungals: cobicistat possibly increases plasma concentration of ITRACONAZOLE and KETOCONAZOLE— manufacturer of cobicistat advises reduce dose of itraconazole and ketoconazole

l Antipsychotics: cobicistat possibly increases plasma concentration of l LURASIDONE—avoid concomitant use; cobicistat possibly increases plasma concentration of

l PIMOZIDE—manufacturer of cobicistat advises avoid concomitant use

l Antivirals: manufacturer of cobicistat advises avoid concomitant use with BOCEPREVIR; cobicistat possibly increases the plasma concentration of l DACLATASVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); cobicistat possibly increases plasma concentration of

l MARAVIROC (reduce dose of maraviroc); avoidance of cobicistat advised by manufacturer of NEVIRAPINE; cobicistat possibly increases plasma concentration of l SIMEPREVIR— manufacturer of simeprevir advises avoid concomitant use; plasma concentration of both drugs reduced when cobicistat given with l TIPRANAVIR (avoid concomitant use)

l Anxiolytics and Hypnotics: manufacturer of cobicistat advises avoid concomitant use with *oral* l MIDAZOLAM

▶ Bosentan: manufacturer of cobicistat advises avoid concomitant use with BOSENTAN

▶ Cardiac Glycosides: cobicistat possibly increases plasma concentration of DIGOXIN—reduce initial dose of digoxin

l Cytotoxics: cobicistat possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Domperidone: possible increased risk of ventricular arrhythmias when cobicistat given with l DOMPERIDONE— avoid concomitant use

l Ergot Alkaloids: cobicistat possibly increases plasma concentration of l ERGOT ALKALOIDS—manufacturer of cobicistat advises avoid concomitant use

l Lipid-regulating Drugs: cobicistat possibly increases plasma concentration of ATORVASTATIN—manufacturer of cobicistat advises reduce dose of atorvastatin; manufacturer of cobicistat advises avoid concomitant use with l SIMVASTATIN

l Oestrogens: cobicistat accelerates metabolism of l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

▶ Progestogens: cobicistat increases plasma concentration of

NORGESTIMATE

l Sildenafil: cobicistat possibly increases plasma concentration of l SILDENAFIL—manufacturer of cobicistat advises avoid concomitant use of sildenafil for pulmonary arterial

Interactions | Appendix 1

Cobicistat

l Sildenafil (continued)

hypertension or reduce dose of sildenafil for erectile dysfunction—consult cobicistat product literature

▶ Sympathomimetics, Beta2: manufacturer of cobicistat advises avoid concomitant use with SALMETEROL

l Tadalafil: cobicistat possibly increases plasma concentration of l TADALAFIL—manufacturer of cobicistat advises reduce dose of tadalafil (consult cobicistat product literature)

l Vardenafil: cobicistat possibly increases plasma concentration of l VARDENAFIL—manufacturer of cobicistat advises reduce dose of vardenafil (consult cobicistat product literature)

Co-careldopa

▶ ACE Inhibitors: enhanced hypotensive effect when co- careldopa given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when co-careldopa given with ADRENERGIC NEURONE BLOCKERS

▶ Alpha-blockers: enhanced hypotensive effect when co- careldopa given with ALPHA-BLOCKERS

l Anaesthetics, General: increased risk of arrhythmias when co- careldopa given with l VOLATILE LIQUID GENERAL ANAESTHETICS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when co-careldopa given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antibacterials: effects of co-careldopa possibly reduced by

ISONIAZID

l Antidepressants: risk of hypertensive crisis when co-careldopa given with l MAOIS, avoid co-careldopa for at least 2 weeks after stopping MAOIs; increased risk of side-effects when co- careldopa given with MOCLOBEMIDE

▶ Antiepileptics: effects of co-careldopa possibly reduced by

FOSPHENYTOIN and PHENYTOIN

▶ Antimuscarinics: absorption of co-careldopa possibly reduced by ANTIMUSCARINICS

▶ Antipsychotics: effects of co-careldopa antagonised by ANTIPSYCHOTICS; avoidance of co-careldopa advised by manufacturer of AMISULPRIDE (antagonism of effect)

▶ Anxiolytics and Hypnotics: effects of co-careldopa possibly antagonised by BENZODIAZEPINES

▶ Beta-blockers: enhanced hypotensive effect when co- careldopa given with BETA-BLOCKERS

▶ Bupropion: increased risk of side-effects when co-careldopa given with BUPROPION

▶ Calcium-channel Blockers: enhanced hypotensive effect when co-careldopa given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when co-careldopa given with CLONIDINE

▶ Diazoxide: enhanced hypotensive effect when co-careldopa given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when co-careldopa given with DIURETICS

▶ Dopaminergics: enhanced effects and increased toxicity of co- careldopa when given with SELEGILINE (reduce dose of co- careldopa)

▶ Iron Salts: absorption of co-careldopa possibly reduced by *oral*

IRON SALTS

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: enhanced hypotensive effect when co-careldopa given with METHYLDOPA; antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Moxonidine: enhanced hypotensive effect when co-careldopa given with MOXONIDINE

▶ Muscle Relaxants: possible agitation, confusion and hallucinations when co-careldopa given with BACLOFEN

▶ Nitrates: enhanced hypotensive effect when co-careldopa given with NITRATES

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when co-careldopa given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Codeine *see* Opioid Analgesics Co-fluampicil *see* Penicillins Colchicine

l Anti-arrhythmics: possible increased risk of colchicine toxicity

when given with l AMIODARONE

Colchicine (continued)

l Antibacterials: possible increased risk of colchicine toxicity when given with l AZITHROMYCIN, l CLARITHROMYCIN,

l ERYTHROMYCIN and l TELITHROMYCIN—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Antifungals: possible increased risk of colchicine toxicity when given with l ITRACONAZOLE and l KETOCONAZOLE—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Antivirals: possible increased risk of colchicine toxicity when given with l ATAZANAVIR, l INDINAVIR, l RITONAVIR and

l TELAPREVIR—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Calcium-channel Blockers: possible increased risk of colchicine toxicity when given with l DILTIAZEM and l VERAPAMIL— suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Cardiac Glycosides: possible increased risk of myopathy when colchicine given with l DIGOXIN

l Ciclosporin: possible increased risk of nephrotoxicity and myotoxicity when colchicine given with l CICLOSPORIN— suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Grapefruit Juice: possible increased risk of colchicine toxicity when given with l GRAPEFRUIT JUICE

l Lipid-regulating Drugs: possible increased risk of myopathy when colchicine given with l FIBRATES or l STATINS

Colecalciferol *see* Vitamins

Colesevelam

NOTE Other drugs should be taken at least 4 hours before or after colesevelam to reduce possible interference with absorption

▶ Antidiabetics: colesevelam reduces absorption of GLIBENCLAMIDE and GLIPIZIDE; colesevelam reduces absorption of GLIMEPIRIDE—manufacturer of glimepiride advises give at least 4 hours before colesevelam; manufacturer of canagliflozin advises give bile acid sequestrants at least 1 hour after or 4–6 before CANAGLIFLOZIN

▶ Antiepileptics: colesevelam possibly reduces absorption of

FOSPHENYTOIN and PHENYTOIN

l Ciclosporin: colesevelam reduces absorption of l CICLOSPORIN

▶ Lipid-regulating Drugs: bile acid sequestrants possibly reduce absorption of LOMITAPIDE (give at least 4 hours apart)

▶ Oestrogens: colesevelam reduces absorption of

ETHINYLESTRADIOL

▶ Thyroid Hormones: colesevelam reduces absorption of

LEVOTHYROXINE

Colestilan

NOTE Other drugs should be taken at least 1 hour before or 3 hours after colestilan to reduce possible interference with absorption

▶ Ciclosporin: manufacturer of colestilan advises give

CICLOSPORIN at least 1 hour before or 3 hours after colestilan

▶ Mycophenolate: manufacturer of colestilan advises give MYCOPHENOLATE at least 1 hour before or 3 hours after colestilan

▶ Tacrolimus: manufacturer of colestilan advises give

TACROLIMUS at least 1 hour before or 3 hours after colestilan

▶ Thyroid Hormones: manufacturer of colestilan advises give LEVOTHYROXINE at least 1 hour before or 3 hours after colestilan

Colestipol

NOTE Other drugs should be taken at least 1 hour before or 4–6 hours after colestipol to reduce possible interference with absorption

▶ Antibacterials: colestipol possibly reduces absorption of

TETRACYCLINE

▶ Antidiabetics: manufacturer of canagliflozin advises give bile acid sequestrants at least 1 hour after or 4–6 before CANAGLIFLOZIN

▶ Bile Acids: colestipol possibly reduces absorption of BILE ACIDS

▶ Cardiac Glycosides: colestipol possibly reduces absorption of

CARDIAC GLYCOSIDES

▶ Diuretics: colestipol reduces absorption of THIAZIDES AND RELATED DIURETICS (give at least 2 hours apart)

Colestipol (continued)

▶ Lipid-regulating Drugs: bile acid sequestrants possibly reduce absorption of LOMITAPIDE (give at least 4 hours apart)

▶ Thyroid Hormones: colestipol reduces absorption of THYROID HORMONES

Colestyramine

NOTE Other drugs should be taken at least 1 hour before or 4–6 hours after colestyramine to reduce possible interference with absorption

▶ Analgesics: colestyramine increases the excretion of MELOXICAM; colestyramine reduces absorption of PARACETAMOL

▶ Antibacterials: colestyramine possibly reduces absorption of TETRACYCLINE; colestyramine antagonises effects of *oral* VANCOMYCIN

l Anticoagulants: colestyramine may enhance or reduce

anticoagulant effect of l COUMARINS and l PHENINDIONE

▶ Antidiabetics: colestyramine possibly enhances hypoglycaemic effect of ACARBOSE; manufacturer of canagliflozin advises give bile acid sequestrants at least 1 hour after or 4–6 before CANAGLIFLOZIN

▶ Antiepileptics: colestyramine possibly reduces absorption of

SODIUM VALPROATE and VALPROIC ACID

▶ Bile Acids: colestyramine possibly reduces absorption of BILE ACIDS

▶ Cardiac Glycosides: colestyramine possibly reduces absorption

of CARDIAC GLYCOSIDES

▶ Diuretics: colestyramine reduces absorption of THIAZIDES AND RELATED DIURETICS (give at least 2 hours apart)

▶ Leflunomide: colestyramine significantly decreases effect of LEFLUNOMIDE (enhanced elimination)—avoid unless drug elimination desired

▶ Lipid-regulating Drugs: bile acid sequestrants possibly reduce absorption of LOMITAPIDE (give at least 4 hours apart)

▶ Mycophenolate: colestyramine reduces absorption of

MYCOPHENOLATE

▶ Raloxifene: colestyramine reduces absorption of RALOXIFENE (manufacturer of raloxifene advises avoid concomitant administration)

▶ Teriflunomide: colestyramine significantly decreases effect of TERIFLUNOMIDE (enhanced elimination)—avoid unless drug elimination desired

▶ Thyroid Hormones: colestyramine reduces absorption of

THYROID HORMONES

▶ Vitamins: colestyramine possibly reduces absorption of CALCITRIOL (give at least 1 hour before or 4 to 6 hours after colestyramine)

Colistimethate Sodium *see* Polymyxins Contraceptives, oral *see* Oestrogens and Progestogens Corticosteroids

NOTE Interactions do not generally apply to corticosteroids used for topical action (including inhalation) unless specified

▶ ACE Inhibitors: corticosteroids antagonise hypotensive effect of ACE INHIBITORS

▶ Adrenergic Neurone Blockers: corticosteroids antagonise hypotensive effect of ADRENERGIC NEURONE BLOCKERS

l Aldesleukin: avoidance of corticosteroids advised by manufacturer of l ALDESLEUKIN

▶ Alpha-blockers: corticosteroids antagonise hypotensive effect of ALPHA-BLOCKERS

▶ Aminophylline: increased risk of hypokalaemia when corticosteroids given with AMINOPHYLLINE

▶ Analgesics: increased risk of gastro-intestinal bleeding and ulceration when corticosteroids given with NSAIDS; increased risk of gastro-intestinal bleeding and ulceration when corticosteroids given with ASPIRIN, also corticosteroids reduce plasma concentration of salicylate

▶ Angiotensin-II Receptor Antagonists: corticosteroids antagonise hypotensive effect of ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antacids: absorption of deflazacort reduced by ANTACIDS

▶ Anthelmintics: dexamethasone increases plasma concentration of active metabolite of ALBENDAZOLE; continuous use of dexamethasone possibly reduces plasma concentration of PRAZIQUANTEL

l Antibacterials: plasma concentration of methylprednisolone possibly increased by CLARITHROMYCIN; metabolism of

Corticosteroids

l Antibacterials (continued)

Interactions | Appendix 1

corticosteroids possibly inhibited by ERYTHROMYCIN; metabolism of methylprednisolone inhibited by ERYTHROMYCIN; corticosteroids possibly reduce plasma concentration of ISONIAZID; metabolism of corticosteroids accelerated by l RIFAMYCINS (reduced effect)

l Anticoagulants: corticosteroids may enhance or reduce anticoagulant effect of l COUMARINS (high-dose corticosteroids enhance anticoagulant effect); corticosteroids may enhance or reduce anticoagulant effect of PHENINDIONE

▶ Antidiabetics: corticosteroids antagonise hypoglycaemic effect of ANTIDIABETICS

l Antiepileptics: metabolism of corticosteroids accelerated by

l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE (reduced effect)

l Antifungals: metabolism of corticosteroids possibly inhibited by ITRACONAZOLE and KETOCONAZOLE; plasma concentration of active metabolite of ciclesonide increased by

l KETOCONAZOLE; plasma concentration of *inhaled* mometasone increased by KETOCONAZOLE; plasma concentration of *inhaled* and *oral* (and possibly also *intranasal* and *rectal*) budesonide increased by

l ITRACONAZOLE and l KETOCONAZOLE; *inhaled* fluticasone plasma concentration is possibly increased by KETOCONAZOLE; metabolism of methylprednisolone inhibited by KETOCONAZOLE; increased risk of hypokalaemia when corticosteroids given with l AMPHOTERICIN—avoid concomitant use unless corticosteroids needed to control reactions; plasma concentration of *inhaled* fluticasone increased by ITRACONAZOLE; metabolism of methylprednisolone possibly inhibited by ITRACONAZOLE; dexamethasone possibly reduces plasma concentration of CASPOFUNGIN—consider increasing dose of caspofungin

l Antivirals: dexamethasone possibly reduces plasma concentration of DACLATASVIR and SIMEPREVIR—manufacturer of daclatasvir and simeprevir advises avoid concomitant use; dexamethasone possibly reduces plasma concentration of INDINAVIR, LOPINAVIR, SAQUINAVIR and TELAPREVIR; avoidance

of dexamethasone (except when given as a single dose) advised by manufacturer of l RILPIVIRINE; plasma concentration of *inhaled* and *intranasal* fluticasone increased by l RITONAVIR—increased risk of adrenal suppression; plasma concentration of budesonide (including *inhaled*, *intranasal*, and *rectal* budesonide) possibly increased by

l RITONAVIR—increased risk of adrenal suppresion; plasma concentration of corticosteroids possibly increased by

l RITONAVIR—increased risk of adrenal suppresision; plasma concentration of *inhaled* and *intranasal* budesonide and fluticasone possibly increased by TELAPREVIR

▶ Aprepitant: metabolism of dexamethasone and methylprednisolone inhibited by APREPITANT (reduce dose of dexamethasone and methylprednisolone)

▶ Beta-blockers: corticosteroids antagonise hypotensive effect of

BETA-BLOCKERS

▶ Calcium Salts: corticosteroids reduce absorption of CALCIUM SALTS

▶ Calcium-channel Blockers: corticosteroids antagonise

hypotensive effect of CALCIUM-CHANNEL BLOCKERS; plasma concentration of methylprednisolone increased by DILTIAZEM

▶ Cardiac Glycosides: increased risk of hypokalaemia when corticosteroids given with CARDIAC GLYCOSIDES

l Ciclosporin: high-dose methylprednisolone increases plasma concentration of l CICLOSPORIN (risk of convulsions); plasma concentration of prednisolone increased by CICLOSPORIN

▶ Clonidine: corticosteroids antagonise hypotensive effect of

CLONIDINE

▶ Cytotoxics: possible increased risk of hepatoxicity when dexamethasone given with *high-dose* METHOTREXATE; dexamethasone possibly decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); dexamethasone possibly reduces plasma concentration of CABOZANTINIB—manufacturer of cabozantinib advises avoid concomitant use

▶ Diazoxide: corticosteroids antagonise hypotensive effect of

DIAZOXIDE

Interactions | Appendix 1

Corticosteroids (continued)

▶ Diuretics: corticosteroids antagonise diuretic effect of DIURETICS; increased risk of hypokalaemia when corticosteroids given with ACETAZOLAMIDE, LOOP DIURETICS or THIAZIDES AND RELATED DIURETICS

▶ Fosaprepitant: metabolism of dexamethasone and methylprednisolone inhibited by FOSAPREPITANT (reduce dose of dexamethasone and methylprednisolone)

l Grapefruit Juice: plasma concentration of *oral* budesonide increased by l GRAPEFRUIT JUICE—avoid concurrent use or separate administration by as much as possible and consider reducing *oral* budesonide dose

▶ Histamine: avoidance of corticosteroids advised by manufacturer of HISTAMINE

▶ Methyldopa: corticosteroids antagonise hypotensive effect of

METHYLDOPA

▶ Mifamurtide: avoidance of corticosteroids advised by manufacturer of MIFAMURTIDE

▶ Mifepristone: effect of corticosteroids (including *inhaled* corticosteroids) may be reduced for 3–4 days after MIFEPRISTONE

▶ Moxonidine: corticosteroids antagonise hypotensive effect of

MOXONIDINE

▶ Muscle Relaxants: corticosteroids possibly antagonise effects of PANCURONIUM and VECURONIUM

▶ Nitrates: corticosteroids antagonise hypotensive effect of

NITRATES

▶ Oestrogens: plasma concentration of corticosteroids increased by oral contraceptives containing OESTROGENS

▶ Sodium Benzoate: corticosteroids possibly reduce effects of

SODIUM BENZOATE

▶ Sodium Phenylbutyrate: corticosteroids possibly reduce effects of SODIUM PHENYLBUTYRATE

▶ Somatropin: corticosteroids may inhibit growth-promoting effect of SOMATROPIN

▶ Sympathomimetics: metabolism of dexamethasone accelerated by EPHEDRINE

▶ Sympathomimetics, Beta2: increased risk of hypokalaemia when corticosteroids given with high doses of BETA2 SYMPATHOMIMETICS

▶ Theophylline: increased risk of hypokalaemia when corticosteroids given with THEOPHYLLINE

l Vaccines: high doses of corticosteroids impair immune response to l VACCINES—avoid concomitant use with live vaccines

▶ Vasodilator Antihypertensives: corticosteroids antagonise hypotensive effect of HYDRALAZINE, MINOXIDIL and SODIUM NITROPRUSSIDE

Co-trimoxazole *see* Trimethoprim and Sulfamethoxazole

Coumarins

NOTE Change in patient’s clinical condition, particularly associated with liver disease, intercurrent illness, or drug administration, necessitates more frequent testing. Major changes in diet (especially involving salads and vegetables) and in alcohol consumption may also affect anticoagulant control

l Alcohol: anticoagulant control with coumarins may be

affected by major changes in consumption of l ALCOHOL

▶ Allopurinol: anticoagulant effect of coumarins possibly enhanced by ALLOPURINOL

l Anabolic Steroids: anticoagulant effect of coumarins enhanced by l ANABOLIC STEROIDS

l Analgesics: anticoagulant effect of coumarins possibly enhanced by l NSAIDS; increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins); anticoagulant effect of coumarins enhanced by

l TRAMADOL; increased risk of bleeding when coumarins given with l ASPIRIN (due to antiplatelet effect); anticoagulant effect of coumarins possibly enhanced by prolonged regular use of PARACETAMOL

l Anthelmintics: anticoagulant effect of coumarins possibly enhanced by IVERMECTIN; anticoagulant effect of warfarin possibly enhanced by l LEVAMISOLE

Coumarins (continued)

l Anti-arrhythmics: metabolism of coumarins inhibited by

l AMIODARONE (enhanced anticoagulant effect); anticoagulant effect of warfarin may be enhanced or reduced by DISOPYRAMIDE; anticoagulant effect of coumarins possibly enhanced by l DRONEDARONE; anticoagulant effect of coumarins enhanced by l PROPAFENONE

l Antibacterials: experience in anticoagulant clinics suggests that INR possibly altered when coumarins are given with l NEOMYCIN (given for local action on gut); anticoagulant effect of coumarins possibly enhanced by l AZITHROMYCIN, l AZTREONAM, l CEPHALOSPORINS, CIPROFLOXACIN, LEVOFLOXACIN, l TETRACYCLINES, TIGECYCLINE and

TRIMETHOPRIM; anticoagulant effect of coumarins enhanced by l CHLORAMPHENICOL, l CLARITHROMYCIN, l ERYTHROMYCIN, l METRONIDAZOLE, l NALIDIXIC ACID, l NORFLOXACIN,

l OFLOXACIN and l SULFONAMIDES; plasma concentration of warfarin possibly increased by ORITAVANCIN; an interaction between coumarins and broad-spectrum PENICILLINS has not been demonstrated in studies, but common experience in anticoagulant clinics is that INR can be altered; metabolism of coumarins accelerated by l RIFAMYCINS (reduced anticoagulant effect)

l Anticoagulants: increased risk of haemorrhage when other anticoagulants given with l APIXABAN, l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

l Antidepressants: anticoagulant effect of warfarin possibly enhanced by l VENLAFAXINE; anticoagulant effect of warfarin may be enhanced or reduced by TRAZODONE; anticoagulant effect of coumarins possibly enhanced by l SSRIS; anticoagulant effect of coumarins reduced by l ST JOHN’S WORT (avoid concomitant use); anticoagulant effect of warfarin enhanced by MIRTAZAPINE; anticoagulant effect of coumarins may be enhanced or reduced by l TRICYCLICS

l Antidiabetics: anticoagulant effect of warfarin possibly enhanced by EXENATIDE; coumarins possibly enhance hypoglycaemic effect of l SULFONYLUREAS, also possible changes to anticoagulant effect

l Antiepileptics: metabolism of coumarins accelerated by

l CARBAMAZEPINE, l PHENOBARBITAL and l PRIMIDONE (reduced

anticoagulant effect); plasma concentration of warfarin reduced by ESLICARBAZEPINE; metabolism of coumarins accelerated by l FOSPHENYTOIN and l PHENYTOIN (possibility of reduced anticoagulant effect, but enhancement also reported); anticoagulant effect of coumarins possibly enhanced by SODIUM VALPROATE and VALPROIC ACID

l Antifungals: anticoagulant effect of coumarins enhanced by

l FLUCONAZOLE, l ITRACONAZOLE, l KETOCONAZOLE and

l VORICONAZOLE; anticoagulant effect of coumarins enhanced by l MICONAZOLE (miconazole oral gel and possibly vaginal and topical formulations absorbed); anticoagulant effect of coumarins reduced by l GRISEOFULVIN

▶ Antimalarials: isolated reports that anticoagulant effect of warfarin may be enhanced by PROGUANIL; plasma concentration of both drugs increased when warfarin given with QUININE

l Antivirals: anticoagulant effect of warfarin may be enhanced or reduced by ATAZANAVIR, l NEVIRAPINE and l RITONAVIR; plasma concentration of coumarins possibly affected by

l EFAVIRENZ; anticoagulant effect of coumarins may be enhanced or reduced by FOSAMPRENAVIR; anticoagulant effect of coumarins possibly enhanced by l RITONAVIR; anticoagulant effect of warfarin possibly enhanced by SAQUINAVIR; plasma concentration of warfarin possibly affected by l TELAPREVIR

▶ Anxiolytics and Hypnotics: anticoagulant effect of coumarins may transiently be enhanced by CHLORAL

▶ Aprepitant: anticoagulant effect of warfarin possibly reduced by APREPITANT

l Azathioprine: anticoagulant effect of coumarins possibly reduced by l AZATHIOPRINE

▶ Bosentan: monitoring anticoagulant effect of coumarins recommended by manufacturer of BOSENTAN

Coumarins (continued)

l Clopidogrel: anticoagulant effect of coumarins enhanced due to antiplatelet action of l CLOPIDOGREL; avoidance of warfarin advised by manufacturer of l CLOPIDOGREL

l Corticosteroids: anticoagulant effect of coumarins may be enhanced or reduced by l CORTICOSTEROIDS (high-dose corticosteroids enhance anticoagulant effect)

l Cranberry Juice: anticoagulant effect of coumarins possibly enhanced by l CRANBERRY JUICE—avoid concomitant use

l Cytotoxics: anticoagulant effect of coumarins possibly enhanced by l ETOPOSIDE, l IFOSFAMIDE and l SORAFENIB; anticoagulant effect of coumarins enhanced by

l CAPECITABINE, l FLUOROURACIL and l TEGAFUR; anticoagulant effect of warfarin possibly enhanced by l GEFITINIB, GEMCITABINE and l VEMURAFENIB; anticoagulant effect of coumarins possibly reduced by l MERCAPTOPURINE and

l MITOTANE; plasma concentration of warfarin reduced by DABRAFENIB; increased risk of bleeding when coumarins given with l ERLOTINIB; avoidance of coumarins advised by manufacturer of IBRUTINIB; replacement of warfarin with a heparin advised by manufacturer of IMATINIB (possibility of enhanced warfarin effect); increased risk of bleeding when warfarin given with l REGORAFENIB

l Dipyridamole: anticoagulant effect of coumarins enhanced due to antiplatelet action of l DIPYRIDAMOLE

l Disulfiram: anticoagulant effect of coumarins enhanced by

l DISULFIRAM

l Dopaminergics: anticoagulant effect of warfarin enhanced by

l ENTACAPONE

l Enteral Foods: anticoagulant effect of coumarins antagonised by vitamin K (present in some l ENTERAL FEEDS )

▶ Fosaprepitant: anticoagulant effect of warfarin possibly reduced by FOSAPREPITANT

l Glucosamine: anticoagulant effect of warfarin enhanced by

l GLUCOSAMINE (avoid concomitant use)

l Hormone Antagonists: anticoagulant effect of coumarins possibly enhanced by BICALUTAMIDE and l TOREMIFENE; metabolism of coumarins inhibited by l DANAZOL (enhanced anticoagulant effect); plasma concentration of coumarins possibly reduced by l ENZALUTAMIDE; anticoagulant effect of coumarins enhanced by l FLUTAMIDE and l TAMOXIFEN

▶ Iloprost: anticoagulant effect of coumarins possibly enhanced by ILOPROST

▶ Lactulose: anticoagulant effect of coumarins possibly enhanced by LACTULOSE

▶ Leflunomide: anticoagulant effect of warfarin possibly enhanced by LEFLUNOMIDE

▶ Leukotriene Receptor Antagonists: anticoagulant effect of warfarin enhanced by ZAFIRLUKAST

▶ Levocarnitine: anticoagulant effect of coumarins possibly enhanced by LEVOCARNITINE

l Lipid-regulating Drugs: anticoagulant effect of coumarins may be enhanced or reduced by l COLESTYRAMINE; anticoagulant effect of warfarin may be transiently reduced by ATORVASTATIN; anticoagulant effect of coumarins enhanced by l FIBRATES and l FLUVASTATIN; anticoagulant effect of coumarins possibly enhanced by EZETIMIBE and

l ROSUVASTATIN; anticoagulant effect of coumarins can be enhanced by SIMVASTATIN; anticoagulant effect of warfarin possibly enhanced by LOMITAPIDE

▶ Memantine: anticoagulant effect of warfarin possibly enhanced by MEMANTINE

▶ Oestrogens: anticoagulant effect of coumarins may be enhanced or reduced by OESTROGENS

▶ Orlistat: monitoring anticoagulant effect of coumarins recommended by manufacturer of ORLISTAT

▶ Prasugrel: possible increased risk of bleeding when coumarins given with PRASUGREL

▶ Progestogens: anticoagulant effect of coumarins may be enhanced or reduced by PROGESTOGENS

▶ Raloxifene: anticoagulant effect of coumarins antagonised by

RALOXIFENE

l Retinoids: anticoagulant effect of coumarins possibly reduced by l ACITRETIN

l Sulfinpyrazone: anticoagulant effect of coumarins enhanced by l SULFINPYRAZONE

Coumarins (continued)

l Sympathomimetics: anticoagulant effect of coumarins possibly enhanced by l METHYLPHENIDATE

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l Testolactone: anticoagulant effect of coumarins enhanced by

l TESTOLACTONE

l Testosterone: anticoagulant effect of coumarins enhanced by

l TESTOSTERONE

l Thyroid Hormones: anticoagulant effect of coumarins enhanced by l THYROID HORMONES

▶ Ubidecarenone: anticoagulant effect of warfarin may be enhanced or reduced by UBIDECARENONE

l Ulcer-healing Drugs: metabolism of coumarins inhibited by

l CIMETIDINE (enhanced anticoagulant effect); anticoagulant effect of coumarins possibly enhanced by l ESOMEPRAZOLE and l OMEPRAZOLE; anticoagulant effect of coumarins might be enhanced by PANTOPRAZOLE; absorption of coumarins possibly reduced by l SUCRALFATE (reduced anticoagulant effect)

▶ Vaccines: anticoagulant effect of warfarin possibly enhanced by INFLUENZA VACCINE

l Vitamins: anticoagulant effect of coumarins possibly enhanced by l VITAMIN E; anticoagulant effect of coumarins antagonised by l VITAMIN K

Cranberry Juice

l Anticoagulants: cranberry juice possibly enhances anticoagulant effect of l COUMARINS—avoid concomitant use

Crizotinib

l Analgesics: manufacturer of crizotinib advises caution with

l ALFENTANIL and l FENTANYL

l Antibacterials: plasma concentration of crizotinib possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN— manufacturer of crizotinib advises avoid concomitant use; plasma concentration of crizotinib possibly reduced by RIFABUTIN—manufacturer of crizotinib advises avoid concomitant use; plasma concentration of crizotinib reduced by l RIFAMPICIN—manufacturer of crizotinib advises avoid concomitant use

▶ Antidepressants: plasma concentration of crizotinib possibly reduced by ST JOHN’S WORT—manufacturer of crizotinib advises avoid concomitant use

▶ Antiepileptics: plasma concentration of crizotinib possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL,

PHENYTOIN and PRIMIDONE—manufacturer of crizotinib advises avoid concomitant use

l Antifungals: plasma concentration of crizotinib increased by l KETOCONAZOLE—avoid concomitant use; plasma concentration of crizotinib possibly increased by

l ITRACONAZOLE and l VORICONAZOLE—manufacturer of crizotinib advises avoid concomitant use

▶ Antimalarials: possible increased risk of bradycardia when crizotinib given with MEFLOQUINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis); manufacturer of crizotinib advises caution with l PIMOZIDE

l Antivirals: plasma concentration of crizotinib possibly increased by l ATAZANAVIR, l INDINAVIR, l RITONAVIR and l SAQUINAVIR—manufacturer of crizotinib advises avoid concomitant use

l Anxiolytics and Hypnotics: crizotinib increases plasma concentration of l MIDAZOLAM

▶ Beta-blockers: possible increased risk of bradycardia when crizotinib given with BETA-BLOCKERS

▶ Calcium-channel Blockers: possible increased risk of bradycardia when crizotinib given with DILTIAZEM or VERAPAMIL

▶ Cardiac Glycosides: possible increased risk of bradycardia when crizotinib given with DIGOXIN

l Ciclosporin: manufacturer of crizotinib advises caution with

l CICLOSPORIN

▶ Clonidine: possible increased risk of bradycardia when crizotinib given with CLONIDINE

l Cytotoxics: crizotinib possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Ergot Alkaloids: manufacturer of crizotinib advises caution with l ERGOT ALKALOIDS

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Crizotinib (continued)

l Grapefruit Juice: plasma concentration of crizotinib possibly increased by l GRAPEFRUIT JUICE—manufacturer of crizotinib advises avoid concomitant use

l Oestrogens: manufacturer of crizotinib advises contraceptive effect of l OESTROGENS possibly reduced

▶ Parasympathomimetics: possible increased risk of bradycardia when crizotinib given with PILOCARPINE

l Progestogens: manufacturer of crizotinib advises contraceptive effect of l PROGESTOGENS possibly reduced

l Sirolimus: manufacturer of crizotinib advises caution with

l SIROLIMUS

l Tacrolimus: manufacturer of crizotinib advises caution with

l TACROLIMUS

Cyclizine *see* Antihistamines Cyclopenthiazide *see* Diuretics Cyclopentolate *see* Antimuscarinics Cyclophosphamide

▶ Antifungals: side-effects of cyclophosphamide possibly increased by FLUCONAZOLE and ITRACONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: cyclophosphamide possibly reduces absorption of DIGOXIN *tablets*

l Cytotoxics: increased toxicity when high-dose cyclophosphamide given with l PENTOSTATIN—avoid concomitant use

▶ Muscle Relaxants: cyclophosphamide enhances effects of

SUXAMETHONIUM

Cycloserine

l Alcohol: increased risk of convulsions when cycloserine given with l ALCOHOL

▶ Antibacterials: increased risk of CNS toxicity when cycloserine given with ISONIAZID

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Cyproheptadine *see* Antihistamines

Cytarabine

▶ Antifungals: cytarabine possibly reduces plasma concentration of FLUCYTOSINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: cytarabine possibly reduces absorption of

DIGOXIN *tablets*

▶ Cytotoxics: intracellular concentration of cytarabine increased by FLUDARABINE

Cytotoxics *see* individual drugs

Dabigatran

l Analgesics: possible increased risk of bleeding when dabigatran given with l NSAIDS; increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with l KETOROLAC (avoid concomitant use, including low-dose heparins)

l Anti-arrhythmics: plasma concentration of dabigatran

increased by l AMIODARONE (see under Dabigatran Etexilate,

p. 117); plasma concentration of dabigatran increased by

l DRONEDARONE—avoid concomitant use

l Antibacterials: possible increased risk of bleeding when dabigatran given with CLARITHROMYCIN; plasma concentration of dabigatran reduced by l RIFAMPICIN—manufacturer of dabigatran advises avoid concomitant use

l Anticoagulants: increased risk of haemorrhage when dabigatran given with other l ANTICOAGULANTS (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency); increased risk of haemorrhage when other anticoagulants given with l APIXABAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

l Antidepressants: possible increased risk of bleeding when dabigatran given with l SSRI-RELATED ANTIDEPRESSANTS or

l SSRIS; plasma concentration of dabigatran possibly reduced

Dabigatran

l Antidepressants (continued)

by ST JOHN’S WORT—manufacturer of dabigatran advises avoid concomitant use

▶ Antiepileptics: plasma concentration of dabigatran possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN—

manufacturer of dabigatran advises avoid concomitant use

l Antifungals: plasma concentration of dabigatran increased by l KETOCONAZOLE—avoid concomitant use; manufacturer of dabigatran advises avoid concomitant use with ITRACONAZOLE

▶ Antivirals: plasma concentration of dabigatran possibly increased by RILPIVIRINE and TELAPREVIR

l Calcium-channel Blockers: plasma concentration of dabigatran possibly increased by l VERAPAMIL (see under Dabigatran Etexilate, p. 117)

l Ciclosporin: plasma concentration of dabigatran possibly increased by l CICLOSPORIN—manufacturer of dabigatran advises avoid concomitant use

l Sulfinpyrazone: possible increased risk of bleeding when dabigatran given with l SULFINPYRAZONE

l Tacrolimus: plasma concentration of dabigatran possibly increased by l TACROLIMUS—manufacturer of dabigatran advises avoid concomitant use

l Ticagrelor: plasma concentration of dabigatran increased by

l TICAGRELOR

▶ Ulipristal: manufacturer of ulipristal advises give dabigatran at least 1.5 hours before or after ULIPRISTAL

Dabrafenib

▶ Antibacterials: manufacturer of dabrafenib advises avoid concomitant use with RIFAMPICIN

▶ Anticoagulants: dabrafenib reduces plasma concentration of

WARFARIN

▶ Antidepressants: manufacturer of dabrafenib advises avoid concomitant use with ST JOHN’S WORT

▶ Antiepileptics: manufacturer of dabrafenib advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

▶ Antifungals: plasma concentration of dabrafenib increased by

KETOCONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Lipid-regulating Drugs: plasma concentration of dabrafenib increased by GEMFIBROZIL

l Oestrogens: manufacturer of dabrafenib advises contraceptive effect of hormonal contraceptives containing l OESTROGENS possibly reduced (alternative contraceptive recommended)

l Progestogens: manufacturer of dabrafenib advises contraceptive effect of hormonal contraceptives containing l PROGESTOGENS possibly reduced (alternative contraceptive recommended)

▶ Ulcer-healing Drugs: manufacturer of dabrafenib advises avoid concomitant use with PROTON PUMP INHIBITORS (plasma concentration of dabrafenib possibly reduced)

Dacarbazine

l Aldesleukin: avoidance of dacarbazine advised by manufacturer of l ALDESLEUKIN

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Daclatasvir

l Anti-arrhythmics: possible increased risk of bradycardia when daclatasvir (with sofosbuvir) given with l AMIODARONE—see under Amiodarone, p. 88

l Antibacterials: plasma concentration of daclatasvir possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN—reduce dose of daclatasvir (see under Daclatasvir, p. 544); plasma concentration of daclatasvir possibly reduced by

l RIFABUTIN—manufacturer of daclatasvir advises avoid concomitant use; plasma concentration of daclatasvir reduced by l RIFAMPICIN—avoid concomitant use

▶ Antidepressants: plasma concentration of daclatasvir possibly reduced by ST JOHN’S WORT—manufacturer of daclatasvir advises avoid concomitant use

l Antiepileptics: plasma concentration of daclatasvir possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l OXCARBAZEPINE, l PHENOBARBITAL, l PHENYTOIN and

Daclatasvir

l Antiepileptics (continued)

l PRIMIDONE—manufacturer of daclatasvir advises avoid concomitant use

l Antifungals: plasma concentration of daclatasvir increased by l KETOCONAZOLE—reduce dose of daclatasvir (see under Daclatasvir, p. 544); plasma concentration of daclatasvir possibly increased by l ITRACONAZOLE, l POSACONAZOLE and

l VORICONAZOLE—reduce dose of daclatasvir (see under Daclatasvir, p. 544)

l Antivirals: plasma concentration of daclatasvir increased by l ATAZANAVIR and l TELAPREVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); plasma concentration of daclatasvir possibly increased by l BOCEPREVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); manufacturer

of daclatasvir advises avoid concomitant use with DARUNAVIR and LOPINAVIR (plasma concentration of daclatasvir possibly increased); plasma concentration of daclatasvir reduced by

l EFAVIRENZ—increase dose of daclatasvir (see under Daclatasvir, p. 544); manufacturer of daclatasvir advises avoid concomitant use with ETRAVIRINE and NEVIRAPINE (plasma concentration of daclatasvir possibly reduced)

l Cardiac Glycosides: daclatasvir increases plasma concentration of l DIGOXIN

l Cobicistat: plasma concentration of daclatasvir possibly increased by l COBICISTAT—reduce dose of daclatasvir (see under Daclatasvir, p. 544)

▶ Corticosteroids: plasma concentration of daclatasvir possibly reduced by DEXAMETHASONE—manufacturer of daclatasvir advises avoid concomitant use

▶ Lipid-regulating Drugs: daclatasvir increases plasma concentration of ROSUVASTATIN

Dactinomycin

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Vitamins: dactinomycin possibly reduces effects of ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL and VITAMIN D

Dairy Products

▶ Antibacterials: dairy products reduce absorption of CIPROFLOXACIN and NORFLOXACIN; dairy products reduce absorption of TETRACYCLINES (except doxycycline and minocycline)

▶ Cytotoxics: dairy products possibly reduce plasma concentration of MERCAPTOPURINE—manufacturer of mercaptopurine advises give at least 1 hour before or 2 hours after dairy products

▶ Eltrombopag: dairy products possibly reduce absorption of

ELTROMBOPAG (give at least 4 hours apart)

Dalteparin *see* Heparins

Danaparoid

l Analgesics: increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins)

l Anticoagulants: increased risk of haemorrhage when other anticoagulants given with l APIXABAN, l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

Danazol

l Anticoagulants: danazol inhibits metabolism of l COUMARINS

(enhanced anticoagulant effect)

l Antiepileptics: danazol inhibits metabolism of

l CARBAMAZEPINE (increased risk of toxicity)

l Ciclosporin: danazol inhibits metabolism of l CICLOSPORIN

(increased plasma concentration)

l Lipid-regulating Drugs: possible increased risk of myopathy when danazol given with l SIMVASTATIN—avoid concomitant use

▶ Tacrolimus: danazol possibly increases plasma concentration of TACROLIMUS

Dantrolene *see* Muscle Relaxants Dapagliflozin *see* Antidiabetics Dapoxetine

l Alcohol: increased sedative effect when dapoxetine given with

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l ALCOHOL

l Analgesics: possible increased risk of serotonergic effects when dapoxetine given with l TRAMADOL (manufacturer of dapoxetine advises tramadol should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping tramadol)

l Antibacterials: manufacturer of dapoxetine advises dose reduction when dapoxetine given with CLARITHROMYCIN and ERYTHROMYCIN (see under Dapoxetine, p. 703); manufacturer of dapoxetine advises avoid concomitant use with

l TELITHROMYCIN (increased risk of toxicity)

l Antidepressants: possible increased risk of serotonergic effects when dapoxetine given with l SSRIS, l ST JOHN’S WORT,

l DULOXETINE, l TRICYCLICS and l VENLAFAXINE (manufacturer of dapoxetine advises SSRIs, St John’s wort, duloxetine, tricyclics and venlafaxine should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping SSRIs, St John’s wort, duloxetine, tricyclics and venlafaxine); increased risk of serotonergic effects when dapoxetine given with l MAOIS (MAOIs should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping MAOIs)

l Antifungals: plasma concentration of dapoxetine increased by l KETOCONAZOLE—manufacturer of dapoxetine advises avoid concomitant use; manufacturer of dapoxetine advises dose reduction when dapoxetine given with FLUCONAZOLE (see under Dapoxetine, p. 703); manufacturer of dapoxetine advises avoid concomitant use with l ITRACONAZOLE (increased risk of toxicity)

l Antivirals: manufacturer of dapoxetine advises avoid concomitant use with l ATAZANAVIR, l RITONAVIR and

l SAQUINAVIR (increased risk of toxicity); manufacturer of dapoxetine advises dose reduction when dapoxetine given with FOSAMPRENAVIR (see under Dapoxetine, p. 703)

▶ Aprepitant: manufacturer of dapoxetine advises dose reduction when dapoxetine given with APREPITANT (see under Dapoxetine, p. 703)

▶ Calcium-channel Blockers: manufacturer of dapoxetine advises dose reduction when dapoxetine given with DILTIAZEM and VERAPAMIL (see under Dapoxetine, p. 703)

l 5HT1-receptor Agonists: possible increased risk of serotonergic effects when dapoxetine given with l 5HT1 AGONISTS (manufacturer of dapoxetine advises 5HT1 agonists should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping 5HT1 agonists)

l Lithium: possible increased risk of serotonergic effects when dapoxetine given with l LITHIUM (manufacturer of dapoxetine advises lithium should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping lithium)

▶ Sildenafil: manufacturer of dapoxetine advises avoid concomitant use with SILDENAFIL

▶ Tadalafil: manufacturer of dapoxetine advises avoid concomitant use with TADALAFIL

▶ Vardenafil: manufacturer of dapoxetine advises avoid concomitant use with VARDENAFIL

Dapsone

▶ Antibacterials: plasma concentration of dapsone reduced by RIFAMYCINS; plasma concentration of both drugs may increase when dapsone given with TRIMETHOPRIM

l Antivirals: increased risk of ventricular arrhythmias when dapsone given with l SAQUINAVIR—avoid concomitant use

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Daptomycin

l Ciclosporin: increased risk of myopathy when daptomycin given with l CICLOSPORIN (preferably avoid concomitant use)

l Lipid-regulating Drugs: increased risk of myopathy when daptomycin given with l FIBRATES or l STATINS (preferably avoid concomitant use)

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Daptomycin (continued)

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Darifenacin *see* Antimuscarinics

Darunavir

▶ Anti-arrhythmics: darunavir possibly increases plasma concentration of LIDOCAINE—avoid concomitant use

l Antibacterials: darunavir increases plasma concentration of

l RIFABUTIN (reduce dose of rifabutin); plasma concentration of darunavir significantly reduced by l RIFAMPICIN—avoid concomitant use

▶ Anticoagulants: avoidance of darunavir advised by manufacturer of APIXABAN and RIVAROXABAN

l Antidepressants: darunavir possibly reduces plasma concentration of PAROXETINE and SERTRALINE; plasma concentration of darunavir reduced by l ST JOHN’S WORT— avoid concomitant use

▶ Antiepileptics: plasma concentration of darunavir possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

▶ Antifungals: plasma concentration of both drugs increased when darunavir given with KETOCONAZOLE

l Antimalarials: plasma concentration of lumefantrine increased when darunavir given with ARTEMETHER WITH LUMEFANTRINE; darunavir possibly increases plasma concentration of

l QUININE (increased risk of toxicity)

l Antipsychotics: darunavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); darunavir possibly increases plasma concentration of

l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: avoid concomitant use of darunavir with

l BOCEPREVIR or l TELAPREVIR; avoidance of darunavir advised by manufacturer of DACLATASVIR (plasma concentration of daclatasvir possibly increased); manufacturer of darunavir advises take DIDANOSINE 1 hour before or 2 hours after darunavir; plasma concentration of darunavir reduced by

l EFAVIRENZ (adjust dose—consult product literature); plasma concentration of both drugs increased when darunavir given with INDINAVIR; plasma concentration of darunavir reduced by l LOPINAVIR, also plasma concentration of lopinavir increased (avoid concomitant use); darunavir increases plasma concentration of l MARAVIROC (consider reducing dose of maraviroc); increased risk of rash when darunavir given with RALTEGRAVIR; plasma concentration of darunavir reduced by SAQUINAVIR; plasma concentration of both drugs increased when darunavir given with l SIMEPREVIR— manufacturer of simeprevir advises avoid concomitant use

l Cytotoxics: darunavir possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; darunavir possibly increases plasma concentration of

l EVEROLIMUS—manufacturer of everolimus advises avoid concomitant use; darunavir possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Ergot Alkaloids: increased risk of ergotism when darunavir given with l ERGOT ALKALOIDS—manufacturer of darunavir advises avoid concomitant use

l Lipid-regulating Drugs: possible increased risk of myopathy when darunavir given with ATORVASTATIN; darunavir possibly increases plasma concentration of PRAVASTATIN; darunavir increases plasma concentration of l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature); avoidance of darunavir advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

l Orlistat: absorption of darunavir possibly reduced by

l ORLISTAT

l Ranolazine: darunavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

Dasatinib

l Antibacterials: manufacturer of dasatinib advises avoid concomitant use with CLARITHROMYCIN, ERYTHROMYCIN and

Dasatinib

l Antibacterials (continued)

TELITHROMYCIN (plasma concentration of dasatinib possibly increased); metabolism of dasatinib accelerated by

l RIFAMPICIN (reduced plasma concentration—avoid concomitant use)

▶ Antiepileptics: manufacturer of dasatinib advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE (plasma

concentration of dasatinib possibly reduced)

▶ Antifungals: plasma concentration of dasatinib possibly increased by KETOCONAZOLE; manufacturer of dasatinib advises avoid concomitant use with ITRACONAZOLE (plasma concentration of dasatinib possibly increased)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of dasatinib advised by manufacturer of l BOCEPREVIR; manufacturer of dasatinib advises avoid concomitant use with RITONAVIR (plasma concentration of dasatinib possibly increased)

▶ Grapefruit Juice: manufacturer of dasatinib advises avoid concomitant use with GRAPEFRUIT JUICE (plasma concentration of dasatinib possibly increased)

▶ Lipid-regulating Drugs: dasatinib possibly increases plasma concentration of SIMVASTATIN

▶ Ulcer-healing Drugs: plasma concentration of dasatinib possibly reduced by FAMOTIDINE

Decitabine

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Deferasirox

l Aminophylline: deferasirox increases plasma concentration of

l AMINOPHYLLINE (consider reducing dose of aminophylline)

▶ Antacids: absorption of deferasirox possibly reduced by ANTACIDS containing aluminium (manufacturer of deferasirox advises avoid concomitant use)

▶ Antibacterials: plasma concentration of deferasirox reduced by

RIFAMPICIN

▶ Antidiabetics: deferasirox increases plasma concentration of

REPAGLINIDE

▶ Antipsychotics: manufacturer of deferasirox advises avoid concomitant use with CLOZAPINE

▶ Anxiolytics and Hypnotics: deferasirox possibly reduces plasma concentration of MIDAZOLAM

▶ Muscle Relaxants: manufacturer of deferasirox advises avoid concomitant use with TIZANIDINE

l Theophylline: deferasirox increases plasma concentration of

l THEOPHYLLINE (consider reducing dose of theophylline)

Deferiprone

▶ Antacids: absorption of deferiprone possibly reduced by ANTACIDS containing aluminium (manufacturer of deferiprone advises avoid concomitant use)

Deflazacort *see* Corticosteroids

Delamanid

l Analgesics: increased risk of ventricular arrhythmias when delamanid given with l METHADONE

l Anti-arrhythmics: increased risk of ventricular arrhythmias when delamanid given with l AMIODARONE or l DISOPYRAMIDE

l Antibacterials: possible increased risk of ventricular arrhythmias when delamanid given with l CLARITHROMYCIN and l ERYTHROMYCIN; increased risk of ventricular arrhythmias when delamanid given with l MOXIFLOXACIN; plasma concentration of delamanid reduced by l RIFAMPICIN; delamanid increases plasma concentration of ETHAMBUTOL

l Antidepressants: possible increased risk of ventricular arrhythmias when delamanid given with l TRICYCLICS that prolong the QT interval

▶ Antiepileptics: manufacturer of delamanid advises avoid concomitant use with CARBAMAZEPINE

l Antipsychotics: increased risk of ventricular arrhythmias when delamanid given with l DROPERIDOL, l HALOPERIDOL or

l PIMOZIDE; increased risk of ventricular arrhythmias when delamanid given with l PHENOTHIAZINES that prolong the QT interval

Delamanid (continued)

l Antivirals: plasma concentration of delamanid increased by LOPINAVIR and RITONAVIR; increased risk of ventricular arrhythmias when delamanid given with l SAQUINAVIR

l Beta-blockers: increased risk of ventricular arrhythmias when delamanid given with l SOTALOL

l Cytotoxics: increased risk of ventricular arrhythmias when delamanid given with l ARSENIC TRIOXIDE or l VINFLUNINE; possible increased risk of ventricular arrhythmias when delamanid given with l VINBLASTINE, l VINCRISTINE,

l VINDESINE and l VINORELBINE

l Domperidone: possible increased risk of ventricular arrhythmias when delamanid given with l DOMPERIDONE

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when delamanid given with l PENTAMIDINE ISETIONATE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Demeclocycline *see* Tetracyclines

Desferrioxamine

▶ Antipsychotics: avoidance of desferrioxamine advised by manufacturer of LEVOMEPROMAZINE; manufacturer of desferrioxamine advises avoid concomitant use with PROCHLORPERAZINE

Desflurane *see* Anaesthetics, General Desloratadine *see* Antihistamines Desmopressin

▶ Analgesics: effects of desmopressin enhanced by INDOMETACIN

▶ Loperamide: plasma concentration of *oral* desmopressin increased by LOPERAMIDE

Desogestrel *see* Progestogens Dexamethasone *see* Corticosteroids Dexamfetamine *see* Sympathomimetics Dexibuprofen *see* NSAIDs Dexketoprofen *see* NSAIDs Dexrazoxane

l Antiepileptics: dexrazoxane possibly reduces absorption of

l FOSPHENYTOIN and l PHENYTOIN

▶ Ciclosporin: manufacturer of dexrazoxane advises increased risk of immunosuppression with CICLOSPORIN

▶ Tacrolimus: manufacturer of dexrazoxane advises increased risk of immunosuppression with TACROLIMUS

l Vaccines: risk of generalised infections when dexrazoxane given with live l VACCINES—avoid concomitant use

Dextromethorphan *see* Opioid Analgesics Dextropropoxyphene *see* Opioid Analgesics Diamorphine *see* Opioid Analgesics Diazepam *see* Anxiolytics and Hypnotics Diazoxide

▶ ACE Inhibitors: enhanced hypotensive effect when diazoxide given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when diazoxide given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when diazoxide given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when diazoxide given with ALDESLEUKIN

▶ Alpha-blockers: enhanced hypotensive effect when diazoxide given with ALPHA-BLOCKERS

▶ Anaesthetics, General: enhanced hypotensive effect when diazoxide given with GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of diazoxide antagonised by

NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when diazoxide given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antidepressants: enhanced hypotensive effect when diazoxide given with MAOIS or TRICYCLIC-RELATED ANTIDEPRESSANTS

▶ Antidiabetics: diazoxide antagonises hypoglycaemic effect of

ANTIDIABETICS

▶ Antiepileptics: diazoxide reduces plasma concentration of FOSPHENYTOIN and PHENYTOIN, also effect of diazoxide may be reduced

▶ Antipsychotics: enhanced hypotensive effect when diazoxide given with PHENOTHIAZINES

Diazoxide (continued)

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when diazoxide given with ANXIOLYTICS AND HYPNOTICS

Interactions | Appendix 1

▶ Beta-blockers: enhanced hypotensive effect when diazoxide given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when diazoxide given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when diazoxide given with CLONIDINE

▶ Corticosteroids: hypotensive effect of diazoxide antagonised by CORTICOSTEROIDS

▶ Diuretics: enhanced hypotensive and hyperglycaemic effects when diazoxide given with DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when diazoxide given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Methyldopa: enhanced hypotensive effect when diazoxide given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when diazoxide given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when diazoxide given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when diazoxide given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when diazoxide given with NITRATES

▶ Prostaglandins: enhanced hypotensive effect when diazoxide given with ALPROSTADIL

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when diazoxide given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Diclofenac *see* NSAIDs Dicycloverine *see* Antimuscarinics Didanosine

NOTE Antacids in tablet formulation might affect absorption of other drugs—give at least 2 hours apart

l Allopurinol: plasma concentration of didanosine increased by

l ALLOPURINOL (risk of toxicity)—avoid concomitant use

▶ Analgesics: plasma concentration of didanosine possibly reduced by METHADONE

▶ Antibacterials: manufacturer of norfloxacin advises give didanosine at least 2 hours before or after NORFLOXACIN

l Antivirals: didanosine *tablets* reduce absorption of ATAZANAVIR (give at least 2 hours before or 1 hour after didanosine *tablets*); manufacturer of darunavir advises take didanosine 1 hour before or 2 hours after DARUNAVIR; plasma concentration of didanosine possibly increased by GANCICLOVIR and VALGANCICLOVIR; didanosine *tablets* reduce absorption of INDINAVIR (give at least 1 hour apart); increased risk of side-effects when didanosine given with l RIBAVIRIN— avoid concomitant use; manufacturer of rilpivirine advises give didanosine 2 hours before or 4 hours after RILPIVIRINE; manufacturer of ritonavir advises didanosine and RITONAVIR should be taken 2.5 hours apart; increased risk of side-effects when didanosine given with l STAVUDINE; plasma concentration of didanosine increased by l TENOFOVIR (increased risk of toxicity)—avoid concomitant use; plasma concentration of didanosine reduced by TIPRANAVIR— manufacturer of tipranavir advises tipranavir and didanosine *capsules* should be taken at least 2 hours apart

l Cytotoxics: increased risk of toxicity when didanosine given

with l HYDROXYCARBAMIDE—avoid concomitant use

l Orlistat: absorption of didanosine possibly reduced by

l ORLISTAT

Dienogest *see* Progestogens

Diethylcarbamazine

▶ Antacids: excretion of diethylcarbamazine increased by

SODIUM BICARBONATE

Digoxin *see* Cardiac Glycosides Dihydrocodeine *see* Opioid Analgesics Dihydrotachysterol *see* Vitamins Diltiazem *see* Calcium-channel Blockers Dimethyl sulfoxide

l Analgesics: avoid concomitant use of dimethyl sulfoxide with

l SULINDAC

Dinoprostone *see* Prostaglandins

Interactions | Appendix 1

Diphenoxylate *see* Opioid Analgesics Diphtheria Vaccines *see* Vaccines Dipipanone *see* Opioid Analgesics Dipyridamole

▶ Antacids: absorption of dipyridamole possibly reduced by

ANTACIDS

l Anti-arrhythmics: dipyridamole enhances and extends effect of l ADENOSINE (important risk of toxicity)—reduce dose of adenosine, see p. 87

l Anticoagulants: antiplatelet action of dipyridamole enhances anticoagulant effect of l COUMARINS and l PHENINDIONE; dipyridamole enhances anticoagulant effect of HEPARINS

▶ Clopidogrel: increased risk of bleeding when dipyridamole given with CLOPIDOGREL

▶ Cytotoxics: dipyridamole possibly reduces effects of

FLUDARABINE

Disopyramide

▶ Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with BUPIVACAINE, LEVOBUPIVACAINE,

PRILOCAINE or ROPIVACAINE

l Anti-arrhythmics: increased myocardial depression when anti- arrhythmics given with other l ANTI-ARRHYTHMICS; increased risk of ventricular arrhythmias when disopyramide given with l AMIODARONE or l DRONEDARONE—avoid concomitant use

l Antibacterials: plasma concentration of disopyramide possibly increased by l AZITHROMYCIN (increased risk of toxicity); plasma concentration of disopyramide possibly increased by l CLARITHROMYCIN (increased risk of ventricular arrhythmias); plasma concentration of disopyramide increased by

l ERYTHROMYCIN (increased risk of toxicity); increased risk of ventricular arrhythmias when disopyramide given with

l MOXIFLOXACIN—avoid concomitant use; increased risk of ventricular arrhythmias when disopyramide given with

l DELAMANID; metabolism of disopyramide accelerated by

l RIFAMYCINS (reduced plasma concentration); possible increased risk of ventricular arrhythmias when disopyramide given with l TELITHROMYCIN

▶ Anticoagulants: disopyramide may enhance or reduce anticoagulant effect of WARFARIN

l Antidepressants: avoidance of disopyramide advised by manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when disopyramide given with l TRICYCLICS

▶ Antidiabetics: disopyramide possibly enhances hypoglycaemic effect of GLICLAZIDE, INSULIN and METFORMIN

▶ Antiepileptics: plasma concentration of disopyramide reduced by FOSPHENYTOIN and PHENYTOIN; metabolism of disopyramide accelerated by PHENOBARBITAL and PRIMIDONE (reduced plasma concentration)

l Antifungals: increased risk of ventricular arrhythmias when disopyramide given with l KETOCONAZOLE—avoid concomitant use; avoidance of disopyramide advised by manufacturer of

l ITRACONAZOLE

l Antihistamines: increased risk of ventricular arrhythmias when disopyramide given with l MIZOLASTINE—avoid concomitant use

l Antimalarials: avoidance of disopyramide advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE (risk of ventricular arrhythmias); avoidance of disopyramide advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

l Antimuscarinics: increased risk of antimuscarinic side-effects when disopyramide given with ANTIMUSCARINICS; increased risk of ventricular arrhythmias when disopyramide given with l TOLTERODINE

l Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with

l ANTIPSYCHOTICS that prolong the QT interval; increased risk of ventricular arrhythmias when disopyramide given with

l AMISULPRIDE, l DROPERIDOL, l PIMOZIDE or

l ZUCLOPENTHIXOL—avoid concomitant use; possible increased risk of ventricular arrhythmias when disopyramide given with l HALOPERIDOL—avoid concomitant use; increased risk of ventricular arrhythmias when disopyramide given with l PHENOTHIAZINES or l SULPIRIDE

Disopyramide (continued)

l Antivirals: plasma concentration of disopyramide possibly increased by l RITONAVIR (increased risk of toxicity); increased risk of ventricular arrhythmias when disopyramide given with l SAQUINAVIR—avoid concomitant use; avoidance of disopyramide advised by manufacturer of l TELAPREVIR (risk of ventricular arrhythmias)

l Atomoxetine: increased risk of ventricular arrhythmias when disopyramide given with l ATOMOXETINE

l Beta-blockers: increased myocardial depression when anti- arrhythmics given with l BETA-BLOCKERS; increased risk of ventricular arrhythmias when disopyramide given with

l SOTALOL—avoid concomitant use

l Calcium-channel Blockers: increased risk of myocardial depression and asystole when disopyramide given with l VERAPAMIL

l Cytotoxics: possible increased risk of ventricular arrhythmias

when disopyramide given with l BOSUTINIB; possible increased risk of ventricular arrhythmias when disopyramide given with l VANDETANIB—avoid concomitant use; increased risk of ventricular arrhythmias when disopyramide given with l ARSENIC TRIOXIDE

l Diuretics: increased cardiac toxicity with disopyramide if

hypokalaemia occurs with l ACETAZOLAMIDE, l LOOP DIURETICS

or l THIAZIDES AND RELATED DIURETICS

l Fingolimod: possible increased risk of bradycardia when disopyramide given with l FINGOLIMOD

l Ivabradine: increased risk of ventricular arrhythmias when disopyramide given with l IVABRADINE

▶ Nitrates: disopyramide reduces effects of sublingual tablets of NITRATES (failure to dissolve under tongue owing to dry mouth)

l Pentamidine Isetionate: possible increased risk of ventricular arrhythmias when disopyramide given with l PENTAMIDINE ISETIONATE

l Ranolazine: avoidance of disopyramide advised by

manufacturer of l RANOLAZINE

▶ Sildenafil: manufacturer of disopyramide advises avoid concomitant use with SILDENAFIL (risk of ventricular arrhythmias)

▶ Tadalafil: manufacturer of disopyramide advises avoid concomitant use with TADALAFIL (risk of ventricular arrhythmias)

▶ Vardenafil: manufacturer of disopyramide advises avoid concomitant use with VARDENAFIL (risk of ventricular arrhythmias)

Disulfiram

▶ Alcohol: disulfiram reaction when disulfiram given with

ALCOHOL

▶ Aminophylline: disulfiram inhibits metabolism of

AMINOPHYLLINE (increased risk of toxicity)

▶ Antibacterials: psychotic reaction reported when disulfiram given with METRONIDAZOLE; CNS effects of disulfiram possibly increased by ISONIAZID

l Anticoagulants: disulfiram enhances anticoagulant effect of

l COUMARINS

▶ Antidepressants: increased disulfiram reaction with alcohol reported with concomitant AMITRIPTYLINE; disulfiram inhibits metabolism of TRICYCLICS (increased plasma concentration)

l Antiepileptics: disulfiram inhibits metabolism of

l FOSPHENYTOIN and l PHENYTOIN (increased risk of toxicity)

▶ Anxiolytics and Hypnotics: disulfiram increases risk of TEMAZEPAM toxicity; disulfiram inhibits metabolism of BENZODIAZEPINES (increased sedative effects)

l Paraldehyde: risk of toxicity when disulfiram given with

l PARALDEHYDE

▶ Theophylline: disulfiram inhibits metabolism of THEOPHYLLINE

(increased risk of toxicity)

Diuretics

NOTE Since systemic absorption may follow topical application of brinzolamide to the eye, the possibility of interactions should be borne in mind

NOTE Since systemic absorption may follow topical application of dorzolamide to the eye, the possibility of interactions should be borne in mind

Diuretics (continued)

l ACE Inhibitors: enhanced hypotensive effect when diuretics given with l ACE INHIBITORS; increased risk of severe hyperkalaemia when potassium-sparing diuretics and aldosterone antagonists given with l ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when diuretics given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when diuretics given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when diuretics given with ALDESLEUKIN

▶ Aliskiren: plasma concentration of furosemide reduced by ALISKIREN; increased risk of hyperkalaemia when potassium- sparing diuretics and aldosterone antagonists given with ALISKIREN

▶ Allopurinol: increased risk of hypersensitivity when thiazides and related diuretics given with ALLOPURINOL especially in renal impairment

l Alpha-blockers: enhanced hypotensive effect when diuretics given with l ALPHA-BLOCKERS, also increased risk of first-dose hypotension with post-synaptic alpha-blockers such as prazosin

▶ Aminophylline: increased risk of hypokalaemia when acetazolamide, loop diuretics or thiazides and related diuretics given with AMINOPHYLLINE

▶ Anaesthetics, General: enhanced hypotensive effect when diuretics given with GENERAL ANAESTHETICS

l Analgesics: diuretics increase risk of nephrotoxicity of NSAIDS, also antagonism of diuretic effect; diuretic effect of potassium canrenoate possibly antagonised by NSAIDS; possible increased risk of hyperkalaemia when potassium- sparing diuretics and aldosterone antagonists given with NSAIDS; furosemide possibly increases the excretion of ACEMETACIN; effects of diuretics antagonised by INDOMETACIN and KETOROLAC; increased risk of hyperkalaemia when potassium-sparing diuretics and aldosterone antagonists given with INDOMETACIN; occasional reports of reduced renal function when triamterene given with l INDOMETACIN—avoid concomitant use; increased risk of toxicity when acetazolamide given with high-dose l ASPIRIN; diuretic effect of spironolactone antagonised by ASPIRIN; possible increased risk of toxicity when loop diuretics given with high-dose ASPIRIN (also possible reduced effect of loop diuretics)

l Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when diuretics given with l ANGIOTENSIN-II RECEPTOR ANTAGONISTS; increased risk of hyperkalaemia when potassium-sparing diuretics and aldosterone antagonists given with l ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Anti-arrhythmics: hypokalaemia caused by acetazolamide, loop diuretics or thiazides and related diuretics increases cardiac toxicity with AMIODARONE; plasma concentration of eplerenone increased by AMIODARONE (reduce dose of eplerenone); hypokalaemia caused by acetazolamide, loop diuretics or thiazides and related diuretics increases cardiac toxicity with l DISOPYRAMIDE; hypokalaemia caused by acetazolamide, loop diuretics or thiazides and related diuretics increases cardiac toxicity with l FLECAINIDE; hypokalaemia caused by acetazolamide, loop diuretics or thiazides and related diuretics antagonises action of

l LIDOCAINE

l Antibacterials: plasma concentration of eplerenone increased by l CLARITHROMYCIN and l TELITHROMYCIN—avoid concomitant use; plasma concentration of eplerenone increased by ERYTHROMYCIN (reduce dose of eplerenone); plasma concentration of eplerenone reduced by

l RIFAMPICIN—avoid concomitant use; avoidance of diuretics advised by manufacturer of LYMECYCLINE; increased risk of otoxicity when loop diuretics given with l AMINOGLYCOSIDES, l POLYMYXINS or l VANCOMYCIN; acetazolamide antagonises effects of l METHENAMINE; possible increased risk of hyperkalaemia when spironolactone given with TRIMETHOPRIM; increased risk of hyperkalaemia when eplerenone given with TRIMETHOPRIM

l Antidepressants: possible increased risk of hypokalaemia when loop diuretics or thiazides and related diuretics given with REBOXETINE; enhanced hypotensive effect when diuretics

Diuretics

l Antidepressants (continued)

Interactions | Appendix 1

given with MAOIS; plasma concentration of eplerenone reduced by l ST JOHN’S WORT—avoid concomitant use; increased risk of postural hypotension when diuretics given with TRICYCLICS

▶ Antidiabetics: loop diuretics and thiazides and related diuretics antagonise hypoglycaemic effect of ANTIDIABETICS; diuretic effect of diuretics possibly enhanced by CANAGLIFLOZIN; avoidance of loop diuretics advised by manufacturer of CANAGLIFLOZIN; diuretic effect of loop diuretics and thiazides and related diuretics possibly enhanced by DAPAGLIFLOZIN

l Antiepileptics: plasma concentration of eplerenone reduced by

l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE—avoid concomitant use; increased risk of hyponatraemia when diuretics given with CARBAMAZEPINE; acetazolamide increases plasma concentration of l CARBAMAZEPINE; effects of furosemide antagonised by FOSPHENYTOIN and PHENYTOIN; acetazolamide possibly increases plasma concentration of l FOSPHENYTOIN and l PHENYTOIN; increased risk of osteomalacia when carbonic anhydrase inhibitors given with FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN or PRIMIDONE;

hydrochlorothiazide possibly increases plasma concentration of TOPIRAMATE; avoidance of carbonic anhydrase inhibitors in children advised by manufacturer of ZONISAMIDE

l Antifungals: plasma concentration of eplerenone increased by l ITRACONAZOLE and l KETOCONAZOLE—avoid concomitant use; increased risk of hypokalaemia when loop diuretics or thiazides and related diuretics given with AMPHOTERICIN; hydrochlorothiazide increases plasma concentration of FLUCONAZOLE; plasma concentration of eplerenone increased by FLUCONAZOLE (reduce dose of eplerenone)

l Antipsychotics: hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with l AMISULPRIDE; enhanced hypotensive effect when diuretics given with PHENOTHIAZINES; hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with l PIMOZIDE (avoid concomitant use)

l Antivirals: plasma concentration of eplerenone increased by

l RITONAVIR—avoid concomitant use; plasma concentration of eplerenone increased by SAQUINAVIR (reduce dose of eplerenone)

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when diuretics given with ANXIOLYTICS AND HYPNOTICS; administration of *parenteral* furosemide with CHLORAL may displace thyroid hormone from binding sites

l Atomoxetine: hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with l ATOMOXETINE

l Beta-blockers: enhanced hypotensive effect when diuretics given with BETA-BLOCKERS; hypokalaemia caused by loop diuretics or thiazides and related diuretics increases risk of ventricular arrhythmias with l SOTALOL

▶ Calcium Salts: increased risk of hypercalcaemia when thiazides and related diuretics given with CALCIUM SALTS

▶ Calcium-channel Blockers: enhanced hypotensive effect when diuretics given with CALCIUM-CHANNEL BLOCKERS; plasma concentration of eplerenone increased by DILTIAZEM and VERAPAMIL (reduce dose of eplerenone)

l Cardiac Glycosides: hypokalaemia caused by acetazolamide, loop diuretics or thiazides and related diuretics increases cardiac toxicity with l CARDIAC GLYCOSIDES; spironolactone increases plasma concentration of l DIGOXIN; potassium canrenoate possibly increases plasma concentration of DIGOXIN

l Ciclosporin: increased risk of nephrotoxicity and possibly hypermagnesaemia when thiazides and related diuretics given with CICLOSPORIN; increased risk of hyperkalaemia when potassium-sparing diuretics and aldosterone antagonists given with l CICLOSPORIN; acetazolamide possibly increases plasma concentration of l CICLOSPORIN

▶ Clonidine: enhanced hypotensive effect when diuretics given with CLONIDINE

▶ Corticosteroids: diuretic effect of diuretics antagonised by

CORTICOSTEROIDS; increased risk of hypokalaemia when

Interactions | Appendix 1

Diuretics

Corticosteroids (continued)

acetazolamide, loop diuretics or thiazides and related diuretics given with CORTICOSTEROIDS

l Cytotoxics: alkaline urine due to acetazolamide increases exceretion of METHOTREXATE; hypokalaemia caused by acetazolamide, loop diuretics or thiazides and related diuretics increases risk of ventricular arrhythmias with

l ARSENIC TRIOXIDE; avoidance of spironolactone advised by manufacturer of MITOTANE (antagonism of effect); increased risk of nephrotoxicity and ototoxicity when diuretics given with PLATINUM COMPOUNDS

▶ Diazoxide: enhanced hypotensive and hyperglycaemic effects when diuretics given with DIAZOXIDE

▶ Diuretics: increased risk of hypokalaemia when loop diuretics or thiazides and related diuretics given with ACETAZOLAMIDE; profound diuresis possible when metolazone given with FUROSEMIDE; increased risk of hypokalaemia when thiazides and related diuretics given with LOOP DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when diuretics given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Hormone Antagonists: increased risk of hypercalcaemia when thiazides and related diuretics given with TOREMIFENE

▶ Lipid-regulating Drugs: absorption of thiazides and related diuretics reduced by COLESTIPOL and COLESTYRAMINE (give at least 2 hours apart)

l Lithium: loop diuretics and thiazides and related diuretics reduce excretion of l LITHIUM (increased plasma concentration and risk of toxicity)—loop diuretics safer than thiazides; potassium-sparing diuretics and aldosterone antagonists reduce excretion of l LITHIUM (increased plasma concentration and risk of toxicity); acetazolamide increases the excretion of l LITHIUM

▶ Methyldopa: enhanced hypotensive effect when diuretics given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when diuretics given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when diuretics given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when diuretics given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when diuretics given with NITRATES

▶ Oestrogens: diuretic effect of diuretics antagonised by

OESTROGENS

l Potassium Salts: increased risk of hyperkalaemia when potassium-sparing diuretics and aldosterone antagonists given with l POTASSIUM SALTS

▶ Progestogens: risk of hyperkalaemia when potassium-sparing diuretics and aldosterone antagonists given with DROSPIRENONE (monitor serum potassium during first cycle)

▶ Prostaglandins: enhanced hypotensive effect when diuretics given with ALPROSTADIL

▶ Sympathomimetics, Beta2: increased risk of hypokalaemia when acetazolamide, loop diuretics or thiazides and related diuretics given with high doses of BETA2SYMPATHOMIMETICS

l Tacrolimus: increased risk of hyperkalaemia when potassium-

sparing diuretics and aldosterone antagonists given with

l TACROLIMUS

▶ Theophylline: increased risk of hypokalaemia when acetazolamide, loop diuretics or thiazides and related diuretics given with THEOPHYLLINE

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when diuretics given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

▶ Vitamins: increased risk of hypercalcaemia when thiazides and related diuretics given with ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL or VITAMIN D

Diuretics, Loop *see* Diuretics

Diuretics, Potassium-sparing and Aldosterone Antagonists *see*

Diuretics

Diuretics, Thiazide and related *see* Diuretics

Dobutamine *see* Sympathomimetics

Docetaxel

l Antibacterials: plasma concentration of docetaxel possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN— manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose

l Antifungals: *in vitro* studies suggest a possible interaction between docetaxel and KETOCONAZOLE (consult docetaxel product literature); plasma concentration of docetaxel possibly increased by l ITRACONAZOLE and l VORICONAZOLE— manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: plasma concentration of docetaxel possibly increased by l INDINAVIR, l RITONAVIR and l SAQUINAVIR— manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose

▶ Ciclosporin: *in vitro* studies suggest a possible interaction between docetaxel and CICLOSPORIN (consult docetaxel product literature)

▶ Cytotoxics: possible increased risk of neutropenia when docetaxel given with LAPATINIB; plasma concentration of docetaxel increased by SORAFENIB

Dolutegravir

▶ Antacids: absorption of dolutegravir reduced by ALUMINIUM HYDROXIDE and ORAL MAGNESIUM SALTS—manufacturer of dolutegravir advises give at least 2 hours before or 6 hours after aluminium hydroxide and oral magnesium salts

l Antibacterials: plasma concentration of dolutegravir reduced by l RIFAMPICIN (see under Dolutegravir, p. 557)

▶ Antidepressants: manufacturer of dolutegravir advises avoid concomitant use with ST JOHN’S WORT

▶ Antiepileptics: manufacturer of dolutegravir advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN,

OXCARBAZEPINE, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Antivirals: plasma concentration of dolutegravir reduced by l EFAVIRENZ, l ETRAVIRINE and l TIPRANAVIR (see under Dolutegravir, p. 557); plasma concentration of dolutegravir reduced by l FOSAMPRENAVIR; plasma concentration of dolutegravir possibly reduced by l NEVIRAPINE (see under Dolutegravir, p. 557)

▶ Calcium Salts: absorption of dolutegravir reduced by CALCIUM SALTS—manufacturer of dolutegravir advises give at least 2 hours before or 6 hours after calcium salts

▶ Iron Salts: absorption of dolutegravir reduced by *oral* IRON SALTS—manufacturer of dolutegravir advises give at least 2 hours before or 6 hours after *oral* iron salts

Domperidone

▶ Analgesics: effects of domperidone on gastro-intestinal activity antagonised by OPIOID ANALGESICS

l Antibacterials: possible increased risk of ventricular arrhythmias when domperidone given with l CLARITHROMYCIN or l TELITHROMYCIN—avoid concomitant use; plasma concentration of domperidone increased by l ERYTHROMYCIN (increased risk of ventricular arrhythmias—avoid concomitant use); possible increased risk of ventricular arrhythmias when domperidone given with l DELAMANID

l Antifungals: avoidance of domperidone advised by manufacturer of l KETOCONAZOLE (risk of ventricular arrhythmias); possible increased risk of ventricular arrhythmias when domperidone given with l ITRACONAZOLE or l VORICONAZOLE—avoid concomitant use

l Antimalarials: avoidance of domperidone advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

▶ Antimuscarinics: effects of domperidone on gastro-intestinal activity antagonised by ANTIMUSCARINICS

l Antivirals: possible increased risk of ventricular arrhythmias when domperidone given with l BOCEPREVIR, l RITONAVIR,

l SAQUINAVIR or l TELAPREVIR—avoid concomitant use

l Cobicistat: possible increased risk of ventricular arrhythmias when domperidone given with l COBICISTAT—avoid concomitant use

l Cytotoxics: avoidance of domperidone advised by manufacturer of l BOSUTINIB (risk of ventricular arrhythmias)

Domperidone (continued)

▶ Dopaminergics: domperidone possibly antagonises hypoprolactinaemic effects of BROMOCRIPTINE and CABERGOLINE

Donepezil *see* Parasympathomimetics

Dopamine *see* Sympathomimetics

Dopaminergics *see* Amantadine, Apomorphine, Bromocriptine, Cabergoline, Entacapone, Levodopa, Pergolide, Pramipexole, Quinagolide, Rasagiline, Ropinirole, Rotigotine, Selegiline, and Tolcapone

Dopexamine *see* Sympathomimetics

Dorzolamide *see* Diuretics

Dosulepin *see* Antidepressants, Tricyclic

Doxapram

▶ Aminophylline: increased CNS stimulation when doxapram given with AMINOPHYLLINE

l Anaesthetics, General: increased risk of arrhythmias when doxapram given with l VOLATILE LIQUID GENERAL ANAESTHETICS (avoid doxapram for at least 10 minutes after volatile liquid general anaesthetics)

▶ Antidepressants: effects of doxapram enhanced by MAOIS

▶ Sympathomimetics: increased risk of hypertension when doxapram given with SYMPATHOMIMETICS

▶ Theophylline: increased CNS stimulation when doxapram given with THEOPHYLLINE

Doxazosin *see* Alpha-blockers

Doxepin *see* Antidepressants, Tricyclic

Doxorubicin

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Antivirals: doxorubicin possibly inhibits effects of STAVUDINE

▶ Calcium-channel Blockers: plasma concentration of doxorubicin possibly increased by VERAPAMIL

▶ Cardiac Glycosides: doxorubicin possibly reduces absorption of

DIGOXIN *tablets*

l Ciclosporin: increased risk of neurotoxicity when doxorubicin given with l CICLOSPORIN

▶ Cytotoxics: plasma concentration of doxorubicin increased by

SORAFENIB

▶ Ulcer-healing Drugs: plasma concentration of doxorubicin reduced by CIMETIDINE

l Vaccines: risk of generalised infections when doxorubicin given with live l VACCINES—avoid concomitant use

Doxycycline *see* Tetracyclines

Dronedarone

▶ Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with BUPIVACAINE, LEVOBUPIVACAINE,

PRILOCAINE or ROPIVACAINE

l Anti-arrhythmics: increased myocardial depression when anti- arrhythmics given with other l ANTI-ARRHYTHMICS; increased risk of ventricular arrhythmias when dronedarone given with l AMIODARONE or l DISOPYRAMIDE—avoid concomitant use

l Antibacterials: manufacturer of dronedarone advises avoid concomitant use with l CLARITHROMYCIN (risk of ventricular arrhythmias); plasma concentration of dronedarone increased by l ERYTHROMYCIN (increased risk of ventricular arrhythmias—avoid concomitant use); plasma concentration of dronedarone reduced by l RIFAMPICIN—avoid concomitant use; avoidance of dronedarone advised by manufacturer of FIDAXOMICIN; increased risk of ventricular arrhythmias when dronedarone given with l TELITHROMYCIN—avoid concomitant use

l Anticoagulants: dronedarone possibly enhances anticoagulant

effect of l COUMARINS and l PHENINDIONE; dronedarone increases plasma concentration of l DABIGATRAN—avoid concomitant use; avoidance of dronedarone advised by manufacturer of RIVAROXABAN

l Antidepressants: avoidance of dronedarone advised by manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); plasma concentration of dronedarone possibly reduced by l ST JOHN’S WORT—avoid concomitant use; manufacturer of dronedarone advises avoid concomitant use with l TRICYCLICS (risk of ventricular arrhythmias)

Dronedarone (continued)

l Antiepileptics: plasma concentration of dronedarone possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

Interactions | Appendix 1

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—avoid

concomitant use

l Antifungals: plasma concentration of dronedarone increased by l KETOCONAZOLE—avoid concomitant use; manufacturer of dronedarone advises avoid concomitant use with

l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE

l Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with

l ANTIPSYCHOTICS that prolong the QT interval; manufacturer of dronedarone advises avoid concomitant use with

l PHENOTHIAZINES (risk of ventricular arrhythmias)

l Antivirals: manufacturer of dronedarone advises avoid concomitant use with l RITONAVIR; increased risk of ventricular arrhythmias when dronedarone given with l SAQUINAVIR—avoid concomitant use

l Beta-blockers: increased myocardial depression when anti- arrhythmics given with l BETA-BLOCKERS; dronedarone possibly increases plasma concentration of METOPROLOL and PROPRANOLOL; increased risk of ventricular arrhythmias when dronedarone given with l SOTALOL—avoid concomitant use

l Calcium-channel Blockers: plasma concentration of dronedarone increased by l NIFEDIPINE; increased risk of bradycardia and myocardial depression when dronedarone given with l DILTIAZEM and l VERAPAMIL

l Cardiac Glycosides: dronedarone increases plasma concentration of l DIGOXIN (halve dose of digoxin)

l Cytotoxics: dronedarone possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; dronedarone possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Fingolimod: possible increased risk of bradycardia when dronedarone given with l FINGOLIMOD

l Grapefruit Juice: plasma concentration of dronedarone increased by l GRAPEFRUIT JUICE—avoid concomitant use

l Lipid-regulating Drugs: dronedarone possibly increases plasma concentration of ATORVASTATIN; dronedarone increases plasma concentration of l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature); increased risk of myopathy when dronedarone given with l SIMVASTATIN; avoidance of dronedarone advised by manufacturer of

l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

▶ Sirolimus: manufacturer of dronedarone advises caution with

SIROLIMUS

▶ Tacrolimus: manufacturer of dronedarone advises caution with

TACROLIMUS

Droperidol *see* Antipsychotics Drospirenone *see* Progestogens Duloxetine

▶ Analgesics: possible increased serotonergic effects when SSRI-

related antidepressants given with FENTANYL; possible increased serotonergic effects when duloxetine given with PETHIDINE or TRAMADOL

l Antibacterials: metabolism of duloxetine inhibited by

l CIPROFLOXACIN—avoid concomitant use

l Anticoagulants: possible increased risk of bleeding when SSRI- related antidepressants given with l DABIGATRAN

l Antidepressants: metabolism of duloxetine inhibited by

l FLUVOXAMINE—avoid concomitant use; possible increased serotonergic effects when duloxetine given with SSRIS, ST JOHN’S WORT, AMITRIPTYLINE, CLOMIPRAMINE, l MOCLOBEMIDE or

VENLAFAXINE; duloxetine should not be started until 2 weeks after stopping l MAOIS, also MAOIs should not be started until at least 5 days after stopping duloxetine; after stopping SSRI-related antidepressants do not start l MOCLOBEMIDE for at least 1 week

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

Interactions | Appendix 1

Duloxetine (continued)

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

l Dapoxetine: possible increased risk of serotonergic effects when duloxetine given with l DAPOXETINE (manufacturer of dapoxetine advises duloxetine should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping duloxetine)

▶ 5HT1-receptor Agonists: possible increased serotonergic effects when duloxetine given with 5HT1 AGONISTS

▶ 5HT3-receptor Antagonists: possible increased serotonergic

effects when SSRI-related antidepressants given with 5HT3 ANTAGONISTS

l Methylthioninium: risk of CNS toxicity when SSRI-related antidepressants given with l METHYLTHIONINIUM—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

Dutasteride

▶ Calcium-channel Blockers: plasma concentration of dutasteride increased by DILTIAZEM and VERAPAMIL

Dydrogesterone *see* Progestogens

Efavirenz

▶ Analgesics: efavirenz reduces plasma concentration of

METHADONE

▶ Antibacterials: efavirenz reduces plasma concentration of CLARITHROMYCIN, also plasma concentration of active metabolite of clarithromycin increased; efavirenz reduces plasma concentration of RIFABUTIN—increase dose of rifabutin; plasma concentration of efavirenz reduced by RIFAMPICIN—increase dose of efavirenz; efavirenz possibly reduces plasma concentration of BEDAQUILINE—manufacturer of bedaquiline advises avoid concomitant use

l Anticoagulants: efavirenz possibly affects plasma

concentration of l COUMARINS

l Antidepressants: plasma concentration of efavirenz reduced by

l ST JOHN’S WORT—avoid concomitant use

▶ Antiepileptics: plasma concentration of both drugs reduced when efavirenz given with CARBAMAZEPINE

l Antifungals: efavirenz reduces plasma concentration of

ITRACONAZOLE, l KETOCONAZOLE and l POSACONAZOLE;

efavirenz reduces plasma concentration of l VORICONAZOLE, also plasma concentration of efavirenz increased (increase voriconazole dose and reduce efavirenz dose); efavirenz possibly reduces plasma concentration of CASPOFUNGIN— consider increasing dose of caspofungin

l Antimalarials: efavirenz reduces plasma concentration of

l ARTEMETHER WITH LUMEFANTRINE; efavirenz possibly affects plasma concentration of PROGUANIL

l Antipsychotics: efavirenz possibly reduces plasma concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); efavirenz possibly increases plasma concentration of l PIMOZIDE (increased risk of ventricular arrhythmias—avoid concomitant use)

l Antivirals: avoidance of efavirenz advised by manufacturer of l ATAZANAVIR (plasma concentration of atazanavir reduced); efavirenz reduces the plasma concentration of

l DACLATASVIR—increase dose of daclatasvir (see under Daclatasvir, p. 544); efavirenz reduces plasma concentration of l DARUNAVIR (adjust dose—consult product literature); efavirenz reduces the plasma concentration of

l DOLUTEGRAVIR (see under Dolutegravir, p. 557); avoidance of efavirenz advised by manufacturer of ELVITEGRAVIR; efavirenz possibly reduces plasma concentration of

l ETRAVIRINE—avoid concomitant use; efavirenz reduces plasma concentration of INDINAVIR and SIMEPREVIR; efavirenz reduces plasma concentration of l LOPINAVIR—consider increasing dose of lopinavir; efavirenz possibly reduces plasma concentration of l MARAVIROC—consider increasing dose of maraviroc; plasma concentration of efavirenz reduced by l NEVIRAPINE—avoid concomitant use; toxicity of efavirenz increased by l RITONAVIR, monitor liver function tests —manufacturer of *Atripla* ® advises avoid concomitant use with *high-dose* ritonavir; efavirenz significantly reduces

Efavirenz

l Antivirals (continued)

plasma concentration of SAQUINAVIR; efavirenz reduces plasma concentration of l TELAPREVIR—increase dose of telaprevir

l Anxiolytics and Hypnotics: increased risk of prolonged sedation when efavirenz given with l MIDAZOLAM—avoid concomitant use

l Atovaquone: efavirenz reduces plasma concentration of

l ATOVAQUONE—avoid concomitant use

▶ Avanafil: efavirenz possibly reduces plasma concentration of AVANAFIL—manufacturer of avanafil advises avoid concomitant use

▶ Bupropion: efavirenz accelerates metabolism of BUPROPION

(reduced plasma concentration)

▶ Calcium-channel Blockers: efavirenz reduces plasma concentration of DILTIAZEM

l Ciclosporin: efavirenz possibly reduces plasma concentration of l CICLOSPORIN

l Cytotoxics: efavirenz possibly reduces plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid concomitant use

l Ergot Alkaloids: increased risk of ergotism when efavirenz given with l ERGOT ALKALOIDS—avoid concomitant use

▶ Grapefruit Juice: plasma concentration of efavirenz possibly increased by GRAPEFRUIT JUICE

▶ Lipid-regulating Drugs: efavirenz reduces plasma concentration of ATORVASTATIN, PRAVASTATIN and SIMVASTATIN

l Orlistat: absorption of efavirenz possibly reduced by

l ORLISTAT

l Progestogens: efavirenz possibly reduces contraceptive effect of l PROGESTOGENS

l Tacrolimus: efavirenz possibly affects plasma concentration of

l TACROLIMUS

Eletriptan *see* 5HT1-receptor Agonists (under HT)

Eltrombopag

▶ Antacids: absorption of eltrombopag reduced by ANTACIDS

(give at least 4 hours apart)

▶ Antivirals: plasma concentration of eltrombopag possibly reduced by LOPINAVIR

▶ Calcium Salts: absorption of eltrombopag possibly reduced by

CALCIUM SALTS (give at least 4 hours apart)

▶ Dairy Products: absorption of eltrombopag possibly reduced by

DAIRY PRODUCTS (give at least 4 hours apart)

▶ Iron Salts: absorption of eltrombopag possibly reduced by *oral*

IRON SALTS (give at least 4 hours apart)

l Lipid-regulating Drugs: eltrombopag increases plasma concentration of l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature)

▶ Selenium: absorption of eltrombopag possibly reduced by

SELENIUM (give at least 4 hours apart)

▶ Zinc: absorption of eltrombopag possibly reduced by ZINC

(give at least 4 hours apart)

Elvitegravir

▶ Antacids: absorption of elvitegravir reduced by ALUMINIUM HYDROXIDE and ORAL MAGNESIUM SALTS (give at least 4 hours apart)

l Antibacterials: plasma concentration of elvitegravir reduced by l RIFABUTIN also plasma concentration of active metabolite of rifabutin increased—reduce dose of rifabutin; manufacturer of elvitegravir advises avoid concomitant use with

l RIFAMPICIN

l Antidepressants: manufacturer of elvitegravir advises avoid concomitant use with l ST JOHN’S WORT

l Antiepileptics: manufacturer of elvitegravir advises avoid concomitant use with l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE

l Antivirals: plasma concentration of elvitegravir increased by l ATAZANAVIR and l LOPINAVIR boosted with ritonavir (reduce dose of elvitegravir); manufacturer of elvitegravir advises avoid concomitant use with EFAVIRENZ and NEVIRAPINE

▶ Bosentan: manufacturer of elvitegravir advises avoid concomitant use with BOSENTAN

l Orlistat: absorption of elvitegravir possibly reduced by

l ORLISTAT

Elvitegravir (continued)

▶ Progestogens: elvitegravir increases plasma concentration of

NORGESTIMATE

Empagliflozin *see* Antidiabetics

Emtricitabine

▶ Antivirals: manufacturer of emtricitabine advises avoid concomitant use with LAMIVUDINE

l Orlistat: absorption of emtricitabine possibly reduced by

l ORLISTAT

Enalapril *see* ACE Inhibitors

Enfuvirtide

l Orlistat: absorption of enfuvirtide possibly reduced by

l ORLISTAT

Enoxaparin *see* Heparins

Enoximone *see* Phosphodiesterase Inhibitors

Entacapone

l Anticoagulants: entacapone enhances anticoagulant effect of

l WARFARIN

l Antidepressants: manufacturer of entacapone advises caution with MOCLOBEMIDE, TRICYCLICS and VENLAFAXINE; avoid

concomitant use of entacapone with non-selective l MAOIS

▶ Dopaminergics: entacapone possibly enhances effects of APOMORPHINE; entacapone possibly reduces plasma concentration of RASAGILINE; manufacturer of entacapone advises max. dose of 10 mg SELEGILINE if used concomitantly

▶ Iron Salts: absorption of entacapone reduced by *oral* IRON SALTS

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: entacapone possibly enhances effects of METHYLDOPA; antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Sympathomimetics: entacapone possibly enhances effects of ADRENALINE (EPINEPHRINE), DOBUTAMINE, DOPAMINE and NORADRENALINE (NOREPINEPHRINE)

Enteral Foods

l Anticoagulants: the presence of vitamin K in some enteral feeds can antagonise the anticoagulant effect of l COUMARINS and l PHENINDIONE

▶ Antiepileptics: enteral feeds possibly reduce absorption of

FOSPHENYTOIN and PHENYTOIN

Enzalutamide

▶ Antibacterials: manufacturer of enzalutamide advises avoid concomitant use with RIFAMPICIN

l Anticoagulants: enzalutamide possibly reduces plasma concentration of l COUMARINS

l Lipid-regulating Drugs: plasma concentration of enzalutamide increased by l GEMFIBROZIL—manufacturer of enzalutamide advises avoid concomitant use or halve dose of enzalutamide

Ephedrine *see* Sympathomimetics

Epinephrine

NOTE Epinephrine interactions as for adrenaline, see under sympathomimetics

Epirubicin

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Ciclosporin: plasma concentration of epirubicin increased by

l CICLOSPORIN

l Ulcer-healing Drugs: plasma concentration of epirubicin increased by l CIMETIDINE

Eplerenone *see* Diuretics

Eprosartan *see* Angiotensin-II Receptor Antagonists

Eptifibatide

▶ Iloprost: increased risk of bleeding when eptifibatide given with ILOPROST

Ergocalciferol *see* Vitamins Ergometrine *see* Ergot Alkaloids Ergot Alkaloids

l Antibacterials: increased risk of ergotism when ergometrine

given with l CLARITHROMYCIN or l ERYTHROMYCIN—avoid concomitant use; increased risk of ergotism when ergotamine given with l MACROLIDES or l TELITHROMYCIN—avoid concomitant use; increased risk of ergotism when ergotamine given with TETRACYCLINES

Ergot Alkaloids (continued)

▶ Antidepressants: possible risk of hypertension when ergotamine given with REBOXETINE

Interactions | Appendix 1

l Antifungals: avoidance of ergot alkaloids advised by manufacturer of l KETOCONAZOLE; avoidance of ergometrine advised by manufacturer of l ITRACONAZOLE (increased risk of ergotism); increased risk of ergotism when ergometrine given with l VORICONAZOLE—avoid concomitant use; increased risk of ergotism when ergotamine given with l IMIDAZOLES or

l TRIAZOLES—avoid concomitant use

▶ Antipsychotics: plasma concentration of ergot alkaloids possibly increased by LURASIDONE (increased risk of toxicity)

l Antivirals: plasma concentration of ergot alkaloids possibly increased by l ATAZANAVIR—avoid concomitant use; avoidance of ergot alkaloids advised by manufacturer of

l BOCEPREVIR and l TELAPREVIR; increased risk of ergotism when ergot alkaloids given with l DARUNAVIR—manufacturer of darunavir advises avoid concomitant use; increased risk of ergotism when ergot alkaloids given with l EFAVIRENZ—avoid concomitant use; increased risk of ergotism when ergotamine given with l FOSAMPRENAVIR, l INDINAVIR, l RITONAVIR or

l SAQUINAVIR—avoid concomitant use; increased risk of ergotism when ergometrine given with l INDINAVIR or

l RITONAVIR—avoid concomitant use

▶ Beta-blockers: increased peripheral vasoconstriction when ergotamine given with BETA-BLOCKERS

l Cobicistat: plasma concentration of ergot alkaloids possibly increased by l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Cytotoxics: caution with ergot alkaloids advised by manufacturer of l CRIZOTINIB; avoidance of ergotamine advised by manufacturer of IDELALISIB

l 5HT1-receptor Agonists: increased risk of vasospasm when ergotamine given with l ALMOTRIPTAN, l RIZATRIPTAN,

l SUMATRIPTAN or l ZOLMITRIPTAN (avoid ergotamine for 6 hours after almotriptan, rizatriptan, sumatriptan or zolmitriptan, avoid almotriptan, rizatriptan, sumatriptan or zolmitriptan for 24 hours after ergotamine); increased risk of vasospasm when ergotamine given with l ELETRIPTAN,

l FROVATRIPTAN or l NARATRIPTAN (avoid ergotamine for 24 hours after eletriptan, frovatriptan or naratriptan, avoid eletriptan, frovatriptan or naratriptan for 24 hours after ergotamine)

▶ Sympathomimetics: increased risk of ergotism when ergotamine given with SYMPATHOMIMETICS

l Ticagrelor: plasma concentration of ergot alkaloids possibly increased by l TICAGRELOR

l Ulcer-healing Drugs: increased risk of ergotism when ergotamine given with l CIMETIDINE—avoid concomitant use

Ergotamine *see* Ergot Alkaloids

Eribulin

▶ Antibacterials: plasma concentration of eribulin possibly reduced by RIFAMPICIN

▶ Antidepressants: plasma concentration of eribulin possibly reduced by ST JOHN’S WORT

▶ Antiepileptics: plasma concentration of eribulin possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Erlotinib

l Analgesics: increased risk of bleeding when erlotinib given with l NSAIDS

l Antacids: plasma concentration of erlotinib possibly reduced by l ANTACIDS—give antacids at least 4 hours before or 2 hours after erlotinib

▶ Antibacterials: plasma concentration of erlotinib increased by CIPROFLOXACIN; metabolism of erlotinib accelerated by RIFAMPICIN (reduced plasma concentration)

l Anticoagulants: increased risk of bleeding when erlotinib given with l COUMARINS

▶ Antifungals: metabolism of erlotinib inhibited by

KETOCONAZOLE (increased plasma concentration)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of erlotinib advised by manufacturer of

l BOCEPREVIR

Interactions | Appendix 1

Erlotinib (continued)

▶ Cytotoxics: plasma concentration of erlotinib possibly increased by CAPECITABINE

l Ulcer-healing Drugs: manufacturer of erlotinib advises avoid concomitant use with l CIMETIDINE, l ESOMEPRAZOLE,

l FAMOTIDINE, l LANSOPRAZOLE, l NIZATIDINE, l PANTOPRAZOLE

and l RABEPRAZOLE; plasma concentration of erlotinib reduced by l RANITIDINE—manufacturer of erlotinib advises give at least 2 hours before or 10 hours after ranitidine; plasma concentration of erlotinib reduced by l OMEPRAZOLE— manufacturer of erlotinib advises avoid concomitant use

Ertapenem

l Antiepileptics: carbapenems reduce plasma concentration of

l SODIUM VALPROATE and l VALPROIC ACID—avoid concomitant use

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Erythromycin *see* Macrolides Escitalopram *see* Antidepressants, SSRI Eslicarbazepine

▶ Anticoagulants: eslicarbazepine reduces plasma concentration

of WARFARIN

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antiepileptics: plasma concentration of eslicarbazepine possibly reduced by CARBAMAZEPINE but risk of side-effects increased; plasma concentration of eslicarbazepine reduced by FOSPHENYTOIN and PHENYTOIN, also plasma concentration of fosphenytoin and phenytoin increased; manufacturer of eslicarbazepine advises avoid concomitant use with OXCARBAZEPINE

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

▶ Lipid-regulating Drugs: eslicarbazepine reduces plasma concentration of ROSUVASTATIN; eslicarbazepine reduces plasma concentration of SIMVASTATIN—consider increasing dose of simvastatin

l Oestrogens: eslicarbazepine accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: eslicarbazepine accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

Esmolol *see* Beta-blockers

Esomeprazole *see* Proton Pump Inhibitors

Estradiol *see* Oestrogens

Estramustine

▶ Antacids: absorption of estramustine possibly reduced by

ALUMINIUM HYDROXIDE and ORAL MAGNESIUM SALTS—

manufacturer of estramustine advises avoid concomitant administration

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Bisphosphonates: plasma concentration of estramustine increased by l SODIUM CLODRONATE

▶ Calcium Salts: absorption of estramustine reduced by CALCIUM SALTS (manufacturer of estramustine advises avoid concomitant administration)

Estriol *see* Oestrogens Estrone *see* Oestrogens Etanercept

l Abatacept: avoid concomitant use of etanercept with

l ABATACEPT

Etanercept (continued)

l Anakinra: avoid concomitant use of etanercept with

l ANAKINRA

l Vaccines: risk of generalised infections when etanercept given with live l VACCINES—avoid concomitant use

Ethambutol

▶ Antibacterials: plasma concentration of ethambutol increased by DELAMANID

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Ethinylestradiol *see* Oestrogens

Ethosuximide

l Antibacterials: metabolism of ethosuximide inhibited by l ISONIAZID (increased plasma concentration and risk of toxicity)

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antiepileptics: plasma concentration of ethosuximide possibly reduced by CARBAMAZEPINE, PHENOBARBITAL and PRIMIDONE;

plasma concentration of ethosuximide possibly reduced by l FOSPHENYTOIN and l PHENYTOIN, also plasma concentration of fosphenytoin and phenytoin possibly increased; plasma concentration of ethosuximide possibly increased by SODIUM VALPROATE and VALPROIC ACID

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Etodolac *see* NSAIDs

Etomidate *see* Anaesthetics, General Etonogestrel *see* Progestogens Etoposide

l Anticoagulants: etoposide possibly enhances anticoagulant

effect of l COUMARINS

▶ Antiepileptics: plasma concentration of etoposide possibly reduced by FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

▶ Antifungals: plasma concentration of etoposide increased by

KETOCONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Atovaquone: plasma concentration of etoposide possibly increased by ATOVAQUONE

▶ Ciclosporin: plasma concentration of etoposide possibly increased by CICLOSPORIN (increased risk of toxicity)

Etoricoxib *see* NSAIDs

Etravirine

l Antibacterials: etravirine reduces plasma concentration of

l CLARITHROMYCIN (but concentration of an active metabolite increased), also plasma concentration of etravirine increased; plasma concentration of both drugs reduced when etravirine given with l RIFABUTIN; manufacturer of etravirine advises avoid concomitant use with RIFAMPICIN; etravirine possibly reduces plasma concentration of BEDAQUILINE—manufacturer of bedaquiline advises avoid concomitant use

▶ Antidepressants: manufacturer of etravirine advises avoid concomitant use with ST JOHN’S WORT

▶ Antiepileptics: manufacturer of etravirine advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

▶ Antimalarials: etravirine reduces plasma concentration of

ARTEMETHER WITH LUMEFANTRINE

l Antivirals: effects of both drugs possibly reduced when etravirine given with BOCEPREVIR; avoidance of etravirine advised by manufacturer of DACLATASVIR (plasma concentration of daclatasvir possibly reduced); etravirine reduces the plasma concentration of l DOLUTEGRAVIR (see under Dolutegravir, p. 557); plasma concentration of etravirine possibly reduced by l EFAVIRENZ and l NEVIRAPINE—

Etravirine

l Antivirals (continued)

avoid concomitant use; etravirine increases plasma concentration of l FOSAMPRENAVIR (consider reducing dose of fosamprenavir); etravirine possibly reduces plasma concentration of l INDINAVIR—avoid concomitant use; etravirine possibly reduces plasma concentration of MARAVIROC; avoidance of etravirine advised by manufacturer of SIMEPREVIR; plasma concentration of etravirine reduced by l TIPRANAVIR, also plasma concentration of tipranavir increased (avoid concomitant use)

▶ Cardiac Glycosides: etravirine increases plasma concentration of DIGOXIN

l Clopidogrel: etravirine possibly reduces antiplatelet effect of

l CLOPIDOGREL

l Cytotoxics: etravirine possibly reduces plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid concomitant use

▶ Lipid-regulating Drugs: etravirine possibly reduces plasma concentration of ATORVASTATIN

l Orlistat: absorption of etravirine possibly reduced by

l ORLISTAT

▶ Sildenafil: etravirine reduces plasma concentration of

SILDENAFIL

Everolimus

l ACE Inhibitors: increased risk of angioedema when everolimus given with l ACE INHIBITORS

l Antibacterials: plasma concentration of everolimus possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN— manufacturer of everolimus advises avoid concomitant use; plasma concentration of everolimus increased by

l ERYTHROMYCIN (consider reducing the dose of everolimus — consult everolimus product literature); plasma concentration of everolimus reduced by l RIFAMPICIN (avoid concomitant use or consider increasing the dose of everolimus —consult everolimus product literature)

▶ Antidepressants: plasma concentration of everolimus possibly reduced by ST JOHN’S WORT—manufacturer of everolimus advises avoid concomitant use

l Antifungals: plasma concentration of everolimus increased by l KETOCONAZOLE—manufacturer of ketoconazole advises avoid concomitant use; plasma concentration of everolimus possibly increased by l ITRACONAZOLE, l POSACONAZOLE and

l VORICONAZOLE—manufacturer of everolimus advises avoid concomitant use

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: plasma concentration of everolimus possibly increased by l ATAZANAVIR, l DARUNAVIR, l INDINAVIR,

l RITONAVIR and l SAQUINAVIR—manufacturer of everolimus advises avoid concomitant use

l Calcium-channel Blockers: plasma concentration of both drugs may increase when everolimus given with l VERAPAMIL (consider reducing the dose of everolimus —consult everolimus product literature)

l Ciclosporin: plasma concentration of everolimus increased by l CICLOSPORIN (consider reducing the dose of everolimus — consult everolimus product literature)

l Cytotoxics: plasma concentration of everolimus increased by l IMATINIB (consider reducing the dose of everolimus — consult everolimus product literature)

▶ Grapefruit Juice: manufacturer of everolimus advises avoid concomitant use with GRAPEFRUIT JUICE

Exemestane

▶ Antibacterials: plasma concentration of exemestane possibly reduced by RIFAMPICIN

Exenatide *see* Antidiabetics

Ezetimibe

▶ Anticoagulants: ezetimibe possibly enhances anticoagulant effect of COUMARINS

l Ciclosporin: plasma concentration of both drugs may increase when ezetimibe given with l CICLOSPORIN

l Lipid-regulating Drugs: ezetimibe increases plasma concentration of l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature); increased risk of cholelithiasis

Ezetimibe

l Lipid-regulating Drugs (continued)

Interactions | Appendix 1

and gallbladder disease when ezetimibe given with

FIBRATES—discontinue if suspected Famotidine *see* Histamine H2-antagonists Fampridine

l Ulcer-healing Drugs: manufacturer of fampridine advises avoid

concomitant use with l CIMETIDINE

Febuxostat

l Azathioprine: manufacturer of febuxostat advises avoid concomitant use with l AZATHIOPRINE

l Cytotoxics: manufacturer of febuxostat advises avoid concomitant use with l MERCAPTOPURINE

Felodipine *see* Calcium-channel Blockers

Fenofibrate *see* Fibrates Fenoprofen *see* NSAIDs Fentanyl *see* Opioid Analgesics Ferrous Fumarate *see* Iron salts Ferrous Gluconate *see* Iron salts Ferrous Sulfate *see* Iron salts

Fesoterodine *see* Antimuscarinics Fexofenadine *see* Antihistamines Fibrates

l Antibacterials: increased risk of myopathy when fibrates given

with l DAPTOMYCIN (preferably avoid concomitant use)

l Anticoagulants: fibrates enhance anticoagulant effect of

l COUMARINS and l PHENINDIONE

l Antidiabetics: fibrates may improve glucose tolerance and have an additive effect with INSULIN or SULFONYLUREAS; gemfibrozil possibly enhances hypoglycaemic effect of NATEGLINIDE; increased risk of severe hypoglycaemia when gemfibrozil given with l REPAGLINIDE—avoid concomitant use

▶ Ciclosporin: increased risk of renal impairment when bezafibrate or fenofibrate given with CICLOSPORIN

l Colchicine: possible increased risk of myopathy when fibrates given with l COLCHICINE

l Cytotoxics: gemfibrozil increases plasma concentration of DABRAFENIB; gemfibrozil increases plasma concentration of l BEXAROTENE—avoid concomitant use

l Hormone Antagonists: gemfibrozil increases plasma concentration of l ENZALUTAMIDE—manufacturer of enzalutamide advises avoid concomitant use or halve dose of enzalutamide

▶ Leukotriene Receptor Antagonists: gemfibrozil increases plasma concentration of MONTELUKAST

l Lipid-regulating Drugs: increased risk of myopathy when gemfibrozil given with l ATORVASTATIN, l FLUVASTATIN or

l PRAVASTATIN (preferably avoid concomitant use); increased risk of myopathy when fibrates given with l ROSUVASTATIN (see under Rosuvastatin, p. 180); possible increased risk of myopathy when bezafibrate given with l SIMVASTATIN (see under Simvastatin, p. 181); possible increased risk of myopathy when ciprofibrate given with l SIMVASTATIN (see under Simvastatin, p. 181); increased risk of myopathy when gemfibrozil given with l SIMVASTATIN (avoid concomitant use); increased risk of cholelithiasis and gallbladder disease when fibrates given with EZETIMIBE—discontinue if suspected; increased risk of myopathy when fibrates given with l STATINS; reduce maximum dose of fenofibrate when given with STATINS—see under Fenofibrate, p. 175

Fidaxomicin

▶ Anti-arrhythmics: manufacturer of fidaxomicin advises avoid concomitant use with AMIODARONE and DRONEDARONE

▶ Antibacterials: manufacturer of fidaxomicin advises avoid concomitant use with CLARITHROMYCIN and ERYTHROMYCIN

▶ Antifungals: manufacturer of fidaxomicin advises avoid concomitant use with KETOCONAZOLE

▶ Calcium-channel Blockers: manufacturer of fidaxomicin advises avoid concomitant use with VERAPAMIL

▶ Ciclosporin: manufacturer of fidaxomicin advises avoid concomitant use with CICLOSPORIN

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

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Filgrastim

▶ Cytotoxics: neutropenia possibly exacerbated when filgrastim given with CAPECITABINE, FLUOROURACIL or TEGAFUR

Fingolimod

l Anti-arrhythmics: possible increased risk of bradycardia when fingolimod given with l AMIODARONE, l DISOPYRAMIDE or

l DRONEDARONE

▶ Antidepressants: plasma concentration of fingolimod possibly reduced by ST JOHN’S WORT—manufacturer of fingolimod advises avoid concomitant use

▶ Antiepileptics: plasma concentration of fingolimod reduced by

CARBAMAZEPINE

l Antifungals: plasma concentration of fingolimod increased by

l KETOCONAZOLE

l Beta-blockers: possible increased risk of bradycardia when fingolimod given with l BETA-BLOCKERS

l Calcium-channel Blockers: possible increased risk of bradycardia when fingolimod given with l DILTIAZEM or l VERAPAMIL

Flavoxate *see* Antimuscarinics

Flecainide

▶ Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with BUPIVACAINE, LEVOBUPIVACAINE,

PRILOCAINE or ROPIVACAINE

l Anti-arrhythmics: increased myocardial depression when anti- arrhythmics given with other l ANTI-ARRHYTHMICS; plasma concentration of flecainide increased by l AMIODARONE (halve dose of flecainide)

l Antidepressants: plasma concentration of flecainide increased by FLUOXETINE; increased risk of ventricular arrhythmias when flecainide given with l TRICYCLICS

l Antihistamines: increased risk of ventricular arrhythmias when flecainide given with l MIZOLASTINE—avoid concomitant use

l Antimalarials: avoidance of flecainide advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE (risk of ventricular arrhythmias); plasma concentration of flecainide increased by l QUININE

l Antimuscarinics: increased risk of ventricular arrhythmias when flecainide given with l TOLTERODINE

l Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with

l ANTIPSYCHOTICS that prolong the QT interval; increased risk of arrhythmias when flecainide given with l CLOZAPINE

l Antivirals: plasma concentration of flecainide possibly increased by l FOSAMPRENAVIR, l INDINAVIR, l LOPINAVIR and l RITONAVIR (increased risk of ventricular arrhythmias—avoid concomitant use); increased risk of ventricular arrhythmias when flecainide given with l SAQUINAVIR—avoid concomitant use; caution with flecainide advised by manufacturer of

l TELAPREVIR (risk of ventricular arrhythmias)

l Beta-blockers: increased risk of myocardial depression and bradycardia when flecainide given with l BETA-BLOCKERS; increased myocardial depression when anti-arrhythmics given with l BETA-BLOCKERS

l Calcium-channel Blockers: increased risk of myocardial depression and asystole when flecainide given with l VERAPAMIL

l Diuretics: increased cardiac toxicity with flecainide if

hypokalaemia occurs with l ACETAZOLAMIDE, l LOOP DIURETICS

or l THIAZIDES AND RELATED DIURETICS

▶ Ulcer-healing Drugs: metabolism of flecainide inhibited by

CIMETIDINE (increased plasma concentration)

Flucloxacillin *see* Penicillins Fluconazole *see* Antifungals, Triazole Flucytosine

▶ Antifungals: renal excretion of flucytosine decreased and

cellular uptake increased by AMPHOTERICIN (toxicity possibly increased)

▶ Cytotoxics: plasma concentration of flucytosine possibly reduced by CYTARABINE

Fludarabine

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Cytotoxics: fludarabine increases intracellular concentration of CYTARABINE; increased pulmonary toxicity when

Fludarabine

l Cytotoxics (continued)

fludarabine given with l PENTOSTATIN (unacceptably high incidence of fatalities)

▶ Dipyridamole: effects of fludarabine possibly reduced by

DIPYRIDAMOLE

Fludrocortisone *see* Corticosteroids

Fluorides

▶ Calcium Salts: absorption of fluorides reduced by CALCIUM SALTS

Fluorouracil

▶ Antibacterials: metabolism of fluorouracil inhibited by

METRONIDAZOLE (increased toxicity)

l Anticoagulants: fluorouracil enhances anticoagulant effect of

l COUMARINS

▶ Antiepileptics: fluorouracil possibly inhibits metabolism of

FOSPHENYTOIN and PHENYTOIN (increased risk of toxicity)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Filgrastim: neutropenia possibly exacerbated when fluorouracil given with FILGRASTIM

l Folates: toxicity of fluorouracil increased by l FOLIC ACID—

avoid concomitant use

▶ Lipegfilgrastim: neutropenia possibly exacerbated when fluorouracil given with LIPEGFILGRASTIM

▶ Pegfilgrastim: neutropenia possibly exacerbated when fluorouracil given with PEGFILGRASTIM

l Temoporfin: increased skin photosensitivity when *topical*

fluorouracil used with l TEMOPORFIN

▶ Ulcer-healing Drugs: metabolism of fluorouracil inhibited by

CIMETIDINE (increased plasma concentration) Fluoxetine *see* Antidepressants, SSRI Flupentixol *see* Antipsychotics

Fluphenazine *see* Antipsychotics Flurazepam *see* Anxiolytics and Hypnotics Flurbiprofen *see* NSAIDs

Flutamide

l Anticoagulants: flutamide enhances anticoagulant effect of

l COUMARINS

Fluticasone *see* Corticosteroids

Fluvastatin *see* Statins

Fluvoxamine *see* Antidepressants, SSRI

Folates

▶ Aminosalicylates: absorption of folic acid possibly reduced by

SULFASALAZINE

▶ Antacids: absorption of folic acid possibly reduced by ANTACIDS

(manufacturer of folic acid advises give at least 2 hours apart)

▶ Antiepileptics: folates possibly reduce plasma concentration of

FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Cytotoxics: folic acid increases toxicity of l CAPECITABINE, l FLUOROURACIL and l TEGAFUR—avoid concomitant use; avoidance of folates advised by manufacturer of

l RALTITREXED

Folic Acid *see* Folates Folinic Acid *see* Folates Fondaparinux

l Analgesics: increased risk of haemorrhage when

anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins)

l Anticoagulants: increased risk of haemorrhage when other anticoagulants given with l APIXABAN, l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

Formoterol *see* Sympathomimetics, Beta2

Fosamprenavir

NOTE Fosamprenavir is a prodrug of amprenavir

▶ Analgesics: fosamprenavir reduces plasma concentration of

METHADONE

l Anti-arrhythmics: fosamprenavir possibly increases plasma concentration of l AMIODARONE, l FLECAINIDE and

l PROPAFENONE (increased risk of ventricular arrhythmias—

Fosamprenavir

l Anti-arrhythmics (continued)

avoid concomitant use); fosamprenavir possibly increases plasma concentration of l LIDOCAINE—avoid concomitant use

l Antibacterials: fosamprenavir increases plasma concentration of l RIFABUTIN (reduce dose of rifabutin); plasma concentration of fosamprenavir significantly reduced by

l RIFAMPICIN—avoid concomitant use; avoidance of concomitant fosamprenavir in severe renal and hepatic impairment advised by manufacturer of l TELITHROMYCIN

▶ Anticoagulants: avoidance of fosamprenavir advised by manufacturer of APIXABAN and RIVAROXABAN; fosamprenavir may enhance or reduce anticoagulant effect of COUMARINS

l Antidepressants: plasma concentration of fosamprenavir reduced by l ST JOHN’S WORT—avoid concomitant use

▶ Antiepileptics: plasma concentration of fosamprenavir possibly reduced by CARBAMAZEPINE, PHENOBARBITAL and PRIMIDONE

▶ Antifungals: fosamprenavir increases plasma concentration of KETOCONAZOLE (also plasma concentration of fosamprenavir possibly increased); plasma concentration of both drugs may increase when fosamprenavir given with ITRACONAZOLE; fosamprenavir possibly reduces plasma concentration of POSACONAZOLE

l Antimalarials: caution with fosamprenavir advised by manufacturer of ARTEMETHER WITH LUMEFANTRINE; fosamprenavir possibly increases plasma concentration of l QUININE (increased risk of toxicity)

▶ Antimuscarinics: avoidance of fosamprenavir advised by manufacturer of DARIFENACIN and TOLTERODINE

l Antipsychotics: fosamprenavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); fosamprenavir increases plasma concentration of l PIMOZIDE (increased risk of ventricular arrhythmias—avoid concomitant use); fosamprenavir possibly increases plasma concentration of l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: manufacturer of fosamprenavir advises avoid

concomitant use with l BOCEPREVIR and l RALTEGRAVIR; fosamprenavir reduces plasma concentration of

l DOLUTEGRAVIR; plasma concentration of fosamprenavir increased by l ETRAVIRINE (consider reducing dose of fosamprenavir); plasma concentration of fosamprenavir reduced by LOPINAVIR, effect on lopinavir plasma concentration not predictable—avoid concomitant use; plasma concentration of fosamprenavir reduced by

l MARAVIROC—avoid concomitant use; plasma concentration of fosamprenavir possibly reduced by NEVIRAPINE—avoid unboosted fosamprenavir; manufacturers advise avoid concomitant use of fosamprenavir with l TELAPREVIR; plasma concentration of fosamprenavir reduced by l TIPRANAVIR

l Anxiolytics and Hypnotics: fosamprenavir possibly increases plasma concentration of l MIDAZOLAM (risk of prolonged sedation—avoid concomitant use of *oral* midazolam)

l Avanafil: fosamprenavir possibly increases plasma

concentration of l AVANAFIL—see under Avanafil, p. 698

l Ciclosporin: fosamprenavir increases plasma concentration of

l CICLOSPORIN

l Cytotoxics: fosamprenavir possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; fosamprenavir possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

▶ Dapoxetine: manufacturer of dapoxetine advises dose reduction when fosamprenavir given with DAPOXETINE (see under Dapoxetine, p. 703)

l Ergot Alkaloids: increased risk of ergotism when fosamprenavir given with l ERGOTAMINE—avoid concomitant use

l Lipid-regulating Drugs: possible increased risk of myopathy when fosamprenavir given with ATORVASTATIN; possible increased risk of myopathy when fosamprenavir given with l ROSUVASTATIN—manufacturer of rosuvastatin advises avoid concomitant use; possible increased risk of myopathy when fosamprenavir given with l SIMVASTATIN—avoid concomitant

Fosamprenavir

l Lipid-regulating Drugs (continued)

Interactions | Appendix 1

use; avoidance of fosamprenavir advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

l Orlistat: absorption of fosamprenavir possibly reduced by

l ORLISTAT

l Ranolazine: fosamprenavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

▶ Sildenafil: fosamprenavir possibly increases plasma concentration of SILDENAFIL

l Tacrolimus: fosamprenavir increases plasma concentration of

l TACROLIMUS

▶ Tadalafil: fosamprenavir possibly increases plasma concentration of TADALAFIL

▶ Vardenafil: fosamprenavir possibly increases plasma concentration of VARDENAFIL

Fosaprepitant

▶ Antibacterials: plasma concentration of fosaprepitant possibly increased by CLARITHROMYCIN and TELITHROMYCIN; plasma concentration of fosaprepitant reduced by RIFAMPICIN

▶ Anticoagulants: fosaprepitant possibly reduces anticoagulant effect of WARFARIN

l Antidepressants: manufacturer of fosaprepitant advises avoid concomitant use with l ST JOHN’S WORT

▶ Antidiabetics: fosaprepitant reduces plasma concentration of

TOLBUTAMIDE

▶ Antiepileptics: plasma concentration of fosaprepitant possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

▶ Antifungals: plasma concentration of fosaprepitant increased by KETOCONAZOLE

l Antipsychotics: manufacturer of fosaprepitant advises avoid concomitant use with l PIMOZIDE

▶ Antivirals: plasma concentration of fosaprepitant possibly increased by RITONAVIR

▶ Anxiolytics and Hypnotics: fosaprepitant increases plasma concentration of MIDAZOLAM (risk of prolonged sedation)

▶ Avanafil: fosaprepitant possibly increases plasma concentration of AVANAFIL

▶ Calcium-channel Blockers: plasma concentration of both drugs may increase when fosaprepitant given with DILTIAZEM

▶ Corticosteroids: fosaprepitant inhibits metabolism of DEXAMETHASONE and METHYLPREDNISOLONE (reduce dose of dexamethasone and methylprednisolone)

l Cytotoxics: fosaprepitant possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; fosaprepitant possibly increases plasma concentration of IBRUTINIB

▶ Lipid-regulating Drugs: separating administration from fosaprepitant by 12 hours advised by manufacturer of LOMITAPIDE

l Oestrogens: fosaprepitant possibly causes contraceptive

failure of hormonal contraceptives containing l OESTROGENS

(alternative contraception recommended)

l Progestogens: fosaprepitant possibly causes contraceptive failure of hormonal contraceptives containing

l PROGESTOGENS (alternative contraception recommended)

Foscarnet

l Pentamidine Isetionate: increased risk of hypocalcaemia when foscarnet given with *parenteral* l PENTAMIDINE ISETIONATE

Fosfomycin

▶ Metoclopramide: plasma concentration of fosfomycin reduced by METOCLOPRAMIDE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Fosinopril *see* ACE Inhibitors

Fosphenytoin

▶ Alcohol: plasma concentration of fosphenytoin possibly reduced by chronic heavy consumption of ALCOHOL

l Aminophylline: plasma concentration of both drugs reduced when fosphenytoin given with l AMINOPHYLLINE

l Analgesics: excretion of fosphenytoin possibly reduced by

ACEMETACIN (increased risk of toxicity); fosphenytoin possibly

Interactions | Appendix 1

Fosphenytoin

l Analgesics (continued)

accelerates metabolism of FENTANYL (reduced effect); fosphenytoin accelerates metabolism of METHADONE (reduced effect and risk of withdrawal effects); fosphenytoin possibly increases risk of l PETHIDINE toxicity; effects of fosphenytoin enhanced by ASPIRIN; fosphenytoin possibly accelerates metabolism of PARACETAMOL (also isolated reports of hepatotoxicity)

▶ Antacids: absorption of fosphenytoin reduced by ANTACIDS

l Anthelmintics: fosphenytoin reduces plasma concentration of l ALBENDAZOLE and l PRAZIQUANTEL—consider increasing albendazole and praziquantel dose when given for systemic infections; plasma concentration of fosphenytoin possibly increased by LEVAMISOLE

l Anti-arrhythmics: metabolism of fosphenytoin inhibited by

l AMIODARONE (increased plasma concentration); fosphenytoin reduces plasma concentration of DISOPYRAMIDE; fosphenytoin possibly reduces plasma concentration of

l DRONEDARONE—avoid concomitant use

l Antibacterials: metabolism of fosphenytoin inhibited by CLARITHROMYCIN (increased plasma concentration); metabolism of fosphenytoin possibly inhibited by METRONIDAZOLE (increased plasma concentration); plasma concentration of fosphenytoin increased or decreased by CIPROFLOXACIN; fosphenytoin accelerates metabolism of DOXYCYCLINE (reduced plasma concentration); fosphenytoin possibly reduces plasma concentration of l BEDAQUILINE— manufacturer of bedaquiline advises avoid concomitant use; plasma concentration of fosphenytoin increased by

l CHLORAMPHENICOL (increased risk of toxicity); metabolism of fosphenytoin possibly inhibited by ISONIAZID (increased risk of toxicity); metabolism of fosphenytoin accelerated by

l RIFAMYCINS (reduced plasma concentration); plasma concentration of fosphenytoin possibly increased by SULFONAMIDES; fosphenytoin reduces plasma concentration of l TELITHROMYCIN (avoid during and for 2 weeks after fosphenytoin); plasma concentration of fosphenytoin increased by l TRIMETHOPRIM (also increased antifolate effect)

l Anticoagulants: fosphenytoin possibly reduces plasma concentration of l APIXABAN; fosphenytoin accelerates metabolism of l COUMARINS (possibility of reduced anticoagulant effect, but enhancement also reported); fosphenytoin possibly reduces plasma concentration of DABIGATRAN—manufacturer of dabigatran advises avoid concomitant use; fosphenytoin possibly reduces plasma concentration of l RIVAROXABAN—manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antidepressants: plasma concentration of fosphenytoin

increased by l FLUOXETINE and l FLUVOXAMINE; fosphenytoin reduces plasma concentration of l MIANSERIN, MIRTAZAPINE and PAROXETINE; plasma concentration of fosphenytoin possibly increased by SERTRALINE, also plasma concentration of sertraline possibly reduced; anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC- RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered); plasma concentration of fosphenytoin possibly reduced by l ST JOHN’S WORT—avoid concomitant use; fosphenytoin possibly reduces plasma concentration of l TRICYCLICS

▶ Antidiabetics: plasma concentration of fosphenytoin transiently increased by TOLBUTAMIDE (possibility of toxicity)

l Antiepileptics: plasma concentration of both drugs often reduced when fosphenytoin given with CARBAMAZEPINE, also plasma concentration of fosphenytoin may be increased; fosphenytoin reduces plasma concentration of ESLICARBAZEPINE, also plasma concentration of fosphenytoin increased; plasma concentration of fosphenytoin possibly increased by l ETHOSUXIMIDE, also plasma concentration of ethosuximide possibly reduced; fosphenytoin reduces plasma concentration of LAMOTRIGINE, TIAGABINE and ZONISAMIDE; plasma concentration of fosphenytoin increased by OXCARBAZEPINE, also plasma concentration of an active metabolite of oxcarbazepine reduced; fosphenytoin reduces

Fosphenytoin

l Antiepileptics (continued)

plasma concentration of l PERAMPANEL (see under Perampanel, p. 398); fosphenytoin often increases plasma concentration of PHENOBARBITAL and PRIMIDONE, plasma concentration of fosphenytoin often reduced but may be increased; fosphenytoin possibly reduces plasma concentration of RETIGABINE; fosphenytoin possibly reduces plasma concentration of RUFINAMIDE, also plasma concentration of fosphenytoin possibly increased; plasma concentration of fosphenytoin increased or possibly reduced when given with SODIUM VALPROATE and VALPROIC ACID, also plasma concentration of sodium valproate and valproic acid reduced; plasma concentration of fosphenytoin increased by l STIRIPENTOL; plasma concentration of fosphenytoin increased by l TOPIRAMATE (also plasma concentration of topiramate reduced); plasma concentration of fosphenytoin reduced by VIGABATRIN

l Antifungals: fosphenytoin reduces plasma concentration of l KETOCONAZOLE and l POSACONAZOLE; anticonvulsant effect of fosphenytoin enhanced by l MICONAZOLE (plasma concentration of fosphenytoin increased); plasma concentration of fosphenytoin increased by l FLUCONAZOLE (consider reducing dose of fosphenytoin); fosphenytoin reduces plasma concentration of l ITRACONAZOLE—avoid concomitant use; plasma concentration of fosphenytoin increased by l VORICONAZOLE, also fosphenytoin reduces plasma concentration of voriconazole (increase dose of voriconazole and also monitor for fosphenytoin toxicity); fosphenytoin possibly reduces plasma concentration of CASPOFUNGIN—consider increasing dose of caspofungin

l Antimalarials: avoidance of fosphenytoin advised by

manufacturer of ARTENIMOL WITH PIPERAQUINE; anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE; anticonvulsant effect of fosphenytoin antagonised by

l PYRIMETHAMINE, also increased antifolate effect

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered); fosphenytoin reduces plasma concentration of HALOPERIDOL; plasma concentration of fosphenytoin possibly increased or decreased by CHLORPROMAZINE; fosphenytoin possibly reduces plasma concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); fosphenytoin accelerates metabolism of CLOZAPINE and QUETIAPINE (reduced plasma concentration); fosphenytoin possibly reduces plasma concentration of l LURASIDONE— avoid concomitant use

l Antivirals: fosphenytoin possibly reduces plasma

concentration of ABACAVIR, DARUNAVIR, LOPINAVIR and SAQUINAVIR; avoidance of fosphenytoin advised by manufacturer of l BOCEPREVIR and l RILPIVIRINE (plasma concentration of boceprevir and rilpivirine possibly reduced); fosphenytoin possibly reduces plasma concentration of

l DACLATASVIR and l SIMEPREVIR—manufacturer of daclatasvir and simeprevir advises avoid concomitant use; avoidance of fosphenytoin advised by manufacturer of DOLUTEGRAVIR,

l ELVITEGRAVIR, ETRAVIRINE, SOFOSBUVIR and l TELAPREVIR;

fosphenytoin possibly reduces plasma concentration of

l INDINAVIR, also plasma concentration of fosphenytoin possibly increased; fosphenytoin possibly reduces plasma concentration of RITONAVIR, also plasma concentration of fosphenytoin possibly affected; plasma concentration of fosphenytoin increased or decreased by ZIDOVUDINE

▶ Anxiolytics and Hypnotics: fosphenytoin often reduces plasma concentration of CLONAZEPAM; plasma concentration of fosphenytoin increased or decreased by DIAZEPAM; plasma concentration of fosphenytoin possibly increased or decreased by BENZODIAZEPINES

▶ Aprepitant: fosphenytoin possibly reduces plasma concentration of APREPITANT

▶ Bupropion: fosphenytoin reduces plasma concentration of

BUPROPION

▶ Caffeine citrate: fosphenytoin reduces plasma concentration of

CAFFEINE CITRATE

Fosphenytoin (continued)

l Calcium-channel Blockers: fosphenytoin reduces effects of FELODIPINE and VERAPAMIL; avoidance of fosphenytoin advised by manufacturer of ISRADIPINE; avoidance of fosphenytoin advised by manufacturer of NIMODIPINE (plasma concentration of nimodipine possibly reduced); plasma concentration of fosphenytoin increased by l DILTIAZEM but also effect of diltiazem reduced

l Cannabis Extract: fosphenytoin possibly reduces plasma concentration of l CANNABIS EXTRACT—manufacturer of cannabis extract advises avoid concomitant use

▶ Cardiac Glycosides: fosphenytoin possibly reduces plasma concentration of DIGOXIN

l Ciclosporin: fosphenytoin accelerates metabolism of

l CICLOSPORIN (reduced plasma concentration)

l Cobicistat: fosphenytoin possibly reduces plasma concentration of l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Corticosteroids: fosphenytoin accelerates metabolism of

l CORTICOSTEROIDS (reduced effect)

l Cytotoxics: fosphenytoin possibly reduces plasma concentration of BUSULFAN, ERIBULIN and ETOPOSIDE; metabolism of fosphenytoin possibly inhibited by CAPECITABINE, FLUOROURACIL and TEGAFUR (increased risk of toxicity); fosphenytoin increases antifolate effect of METHOTREXATE; plasma concentration of fosphenytoin possibly reduced by CISPLATIN; fosphenytoin possibly decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); fosphenytoin possibly reduces plasma concentration of BORTEZOMIB,

l BOSUTINIB, CRIZOTINIB, l IBRUTINIB, l IDELALISIB and

PONATINIB—manufacturer of bortezomib, bosutinib, crizotinib, ibrutinib, idelalisib and ponatinib advises avoid concomitant use; fosphenytoin possibly reduces plasma concentration of l CABOZANTINIB—avoid concomitant use; avoidance of fosphenytoin advised by manufacturer of

l CABAZITAXEL, DABRAFENIB, GEFITINIB, l LAPATINIB and

VEMURAFENIB; avoidance of fosphenytoin advised by manufacturer of DASATINIB and l VISMODEGIB (plasma concentration of dasatinib and vismodegib possibly reduced); fosphenytoin reduces plasma concentration of l IMATINIB— avoid concomitant use; fosphenytoin reduces plasma concentration of IRINOTECAN and its active metabolite; manufacturer of procarbazine advises possible increased risk of hypersensitivity reactions when fosphenytoin given with PROCARBAZINE

l Dexrazoxane: absorption of fosphenytoin possibly reduced by

l DEXRAZOXANE

▶ Diazoxide: plasma concentration of fosphenytoin reduced by

DIAZOXIDE, also effect of diazoxide may be reduced

l Disulfiram: metabolism of fosphenytoin inhibited by

l DISULFIRAM (increased risk of toxicity)

l Diuretics: plasma concentration of fosphenytoin possibly increased by l ACETAZOLAMIDE; fosphenytoin antagonises effects of FUROSEMIDE; fosphenytoin reduces plasma concentration of l EPLERENONE—avoid concomitant use; increased risk of osteomalacia when fosphenytoin given with CARBONIC ANHYDRASE INHIBITORS

▶ Dopaminergics: fosphenytoin possibly reduces effects of CO- BENELDOPA, CO-CARELDOPA and LEVODOPA

▶ Enteral Foods: absorption of fosphenytoin possibly reduced by

ENTERAL FEEDS

▶ Folates: plasma concentration of fosphenytoin possibly reduced by FOLATES

▶ Fosaprepitant: fosphenytoin possibly reduces plasma concentration of FOSAPREPITANT

l Hormone Antagonists: fosphenytoin possibly reduces plasma concentration of l ABIRATERONE—manufacturer of abiraterone advises avoid concomitant use; fosphenytoin possibly accelerates metabolism of TOREMIFENE

▶ 5HT3-receptor Antagonists: fosphenytoin accelerates metabolism of ONDANSETRON (reduced effect)

l Ivacaftor: fosphenytoin possibly reduces plasma concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

Fosphenytoin (continued)

▶ Leflunomide: plasma concentration of fosphenytoin possibly increased by LEFLUNOMIDE

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▶ Lipid-regulating Drugs: absorption of fosphenytoin possibly reduced by COLESEVELAM; combination of fosphenytoin with FLUVASTATIN may increase plasma concentration of either drug (or both)

▶ Lithium: neurotoxicity may occur when fosphenytoin given with LITHIUM without increased plasma concentration of lithium

▶ Macitentan: avoidance of fosphenytoin advised by manufacturer of MACITENTAN

▶ Modafinil: plasma concentration of fosphenytoin possibly increased by MODAFINIL

l Muscle Relaxants: *long-term use* of fosphenytoin reduces effects of l NON-DEPOLARISING MUSCLE RELAXANTS (but *acute use* of fosphenytoin might increase effects of non- depolarising muscle relaxants)

l Oestrogens: fosphenytoin accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: fosphenytoin accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

▶ Roflumilast: fosphenytoin possibly inhibits effects of ROFLUMILAST (manufacturer of roflumilast advises avoid concomitant use)

l Sulfinpyrazone: plasma concentration of fosphenytoin increased by l SULFINPYRAZONE

▶ Sympathomimetics: plasma concentration of fosphenytoin increased by METHYLPHENIDATE

▶ Tacrolimus: fosphenytoin reduces plasma concentration of TACROLIMUS, also plasma concentration of fosphenytoin possibly increased

l Theophylline: plasma concentration of both drugs reduced when fosphenytoin given with l THEOPHYLLINE

▶ Thyroid Hormones: fosphenytoin accelerates metabolism of THYROID HORMONES (may increase requirements in hypothyroidism), also plasma concentration of fosphenytoin possibly increased

▶ Tibolone: fosphenytoin accelerates metabolism of TIBOLONE

▶ Ticagrelor: fosphenytoin possibly reduces plasma concentration of TICAGRELOR

l Ulcer-healing Drugs: metabolism of fosphenytoin inhibited by l CIMETIDINE (increased plasma concentration); effects of fosphenytoin enhanced by l ESOMEPRAZOLE; effects of fosphenytoin possibly enhanced by OMEPRAZOLE; absorption of fosphenytoin reduced by l SUCRALFATE

l Ulipristal: avoidance of fosphenytoin advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

▶ Vaccines: effects of fosphenytoin enhanced by INFLUENZA VACCINE

▶ Vitamins: fosphenytoin possibly increases requirements for

ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL or VITAMIN D

Frovatriptan *see* 5HT1-receptor Agonists (under HT)

Furosemide *see* Diuretics

Fusidic Acid

l Antivirals: plasma concentration of both drugs increased when fusidic acid given with l RITONAVIR—avoid concomitant use; plasma concentration of both drugs may increase when fusidic acid given with SAQUINAVIR

l Lipid-regulating Drugs: risk of myopathy and rhabdomyolysis when fusidic acid given with l STATINS—avoid concomitant use and for 7 days after last fusidic acid dose

▶ Sugammadex: fusidic acid possibly reduces response to

SUGAMMADEX

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Fusidic Acid (continued)

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Gabapentin

▶ Analgesics: bioavailability of gabapentin increased by

MORPHINE

▶ Antacids: absorption of gabapentin reduced by ANTACIDS l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED

ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Galantamine *see* Parasympathomimetics

Ganciclovir

NOTE Increased risk of myelosuppression with other myelosuppressive drugs—consult product literature

l Antibacterials: increased risk of convulsions when ganciclovir given with l IMIPENEM WITH CILASTATIN

l Antivirals: ganciclovir possibly increases plasma concentration of DIDANOSINE; profound myelosuppression when ganciclovir given with l ZIDOVUDINE (if possible avoid concomitant administration, particularly during initial ganciclovir therapy)

▶ Mycophenolate: plasma concentration of ganciclovir possibly increased by MYCOPHENOLATE, also plasma concentration of inactive metabolite of mycophenolate possibly increased

▶ Tacrolimus: possible increased risk of nephrotoxicity when ganciclovir given with TACROLIMUS

Gefitinib

l Antibacterials: plasma concentration of gefitinib reduced by

l RIFAMPICIN—avoid concomitant use

l Anticoagulants: gefitinib possibly enhances anticoagulant effect of l WARFARIN

▶ Antidepressants: manufacturer of gefitinib advises avoid concomitant use with ST JOHN’S WORT

▶ Antiepileptics: manufacturer of gefitinib advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

▶ Antifungals: plasma concentration of gefitinib increased by

ITRACONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of gefitinib advised by manufacturer of

l BOCEPREVIR

l Ulcer-healing Drugs: plasma concentration of gefitinib reduced by l RANITIDINE

Gemcitabine

▶ Anticoagulants: gemcitabine possibly enhances anticoagulant effect of WARFARIN

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Gemeprost *see* Prostaglandins Gemfibrozil *see* Fibrates Gentamicin *see* Aminoglycosides Gestodene *see* Progestogens Glibenclamide *see* Antidiabetics Gliclazide *see* Antidiabetics Glimepiride *see* Antidiabetics Glipizide *see* Antidiabetics Glucosamine

l Anticoagulants: glucosamine enhances anticoagulant effect of

l WARFARIN (avoid concomitant use) Glyceryl Trinitrate *see* Nitrates Glycopyrronium *see* Antimuscarinics Golimumab

l Abatacept: avoid concomitant use of golimumab with

l ABATACEPT

Golimumab (continued)

l Anakinra: avoid concomitant use of golimumab with

l ANAKINRA

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Granisetron *see* 5HT3-receptor Antagonists (under HT)

Grapefruit Juice

l Aliskiren: grapefruit juice reduces plasma concentration of

l ALISKIREN—avoid concomitant use

▶ Anthelmintics: grapefruit juice increases plasma concentration of active metabolite of ALBENDAZOLE; grapefruit juice increases plasma concentration of PRAZIQUANTEL

l Anti-arrhythmics: grapefruit juice increases plasma concentration of AMIODARONE; grapefruit juice increases plasma concentration of l DRONEDARONE—avoid concomitant use

▶ Antidepressants: grapefruit juice possibly increases plasma concentration of SERTRALINE

▶ Antihistamines: grapefruit juice reduces plasma concentration of BILASTINE

▶ Antimalarials: grapefruit juice possibly increases plasma concentration of ARTEMETHER WITH LUMEFANTRINE; avoidance of grapefruit juice advised by manufacturer of ARTENIMOL WITH PIPERAQUINE

l Antipsychotics: avoidance of grapefruit juice advised by manufacturer of LURASIDONE and PIMOZIDE; grapefruit juice possibly increases plasma concentration of l QUETIAPINE— manufacturer of quetiapine advises avoid concomitant use

▶ Antivirals: grapefruit juice possibly increases plasma concentration of EFAVIRENZ

▶ Anxiolytics and Hypnotics: grapefruit juice possibly increases plasma concentration of *oral* MIDAZOLAM; grapefruit juice increases plasma concentration of BUSPIRONE

▶ Avanafil: grapefruit juice possibly increases plasma concentration of AVANAFIL— manufacturer of avanafil advises avoid grapefruit juice for 24 hours before avanafil

▶ Calcium-channel Blockers: grapefruit juice possibly increases plasma concentration of AMLODIPINE; grapefruit juice increases plasma concentration of FELODIPINE, ISRADIPINE, LACIDIPINE, LERCANIDIPINE, NICARDIPINE, NIFEDIPINE, NIMODIPINE and VERAPAMIL

l Ciclosporin: grapefruit juice increases plasma concentration of

l CICLOSPORIN (increased risk of toxicity)

l Colchicine: grapefruit juice possibly increases risk of

l COLCHICINE toxicity

l Corticosteroids: grapefruit juice increases plasma concentration of *oral* l BUDESONIDE—avoid concurrent use or separate administration by as much as possible and consider reducing *oral* budesonide dose

l Cytotoxics: grapefruit juice possibly increases plasma concentration of AXITINIB, CABOZANTINIB and PONATINIB; grapefruit juice possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; grapefruit juice possibly increases plasma concentration of l CRIZOTINIB and VINFLUNINE—manufacturer of crizotinib and vinflunine advises avoid concomitant use; avoidance of grapefruit juice advised by manufacturer of DASATINIB (plasma concentration of dasatinib possibly increased); avoidance of grapefruit juice advised by manufacturer of EVEROLIMUS, IBRUTINIB,

l LAPATINIB, l NILOTINIB and l PAZOPANIB

▶ Ivabradine: grapefruit juice increases plasma concentration of

IVABRADINE

▶ Ivacaftor: grapefruit juice possibly increases plasma concentration of IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

l Lipid-regulating Drugs: grapefruit juice possibly increases plasma concentration of ATORVASTATIN; grapefruit juice increases plasma concentration of l SIMVASTATIN—avoid concomitant use; avoidance of grapefruit juice advised by manufacturer of LOMITAPIDE

▶ Pirfenidone: avoidance of grapefruit juice advised by manufacturer of PIRFENIDONE

Grapefruit Juice (continued)

l Ranolazine: grapefruit juice possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

▶ Sildenafil: grapefruit juice possibly increases plasma concentration of SILDENAFIL

l Sirolimus: grapefruit juice increases plasma concentration of

l SIROLIMUS—avoid concomitant use

l Tacrolimus: grapefruit juice increases plasma concentration of

l TACROLIMUS

▶ Tadalafil: grapefruit juice possibly increases plasma concentration of TADALAFIL

l Tolvaptan: grapefruit juice increases plasma concentration of

l TOLVAPTAN—avoid concomitant use

▶ Ulipristal: avoidance of grapefruit juice advised by manufacturer of *low-dose* ULIPRISTAL

l Vardenafil: grapefruit juice possibly increases plasma concentration of l VARDENAFIL—avoid concomitant use

Griseofulvin

▶ Alcohol: griseofulvin possibly enhances effects of ALCOHOL

l Anticoagulants: griseofulvin reduces anticoagulant effect of

l COUMARINS

▶ Antiepileptics: absorption of griseofulvin reduced by

PHENOBARBITAL and PRIMIDONE (reduced effect)

▶ Ciclosporin: griseofulvin possibly reduces plasma concentration of CICLOSPORIN

▶ Oestrogens: anecdotal reports of contraceptive failure and menstrual irregularities when griseofulvin given with OESTROGENS

▶ Progestogens: anecdotal reports of contraceptive failure and menstrual irregularities when griseofulvin given with PROGESTOGENS

Guanethidine *see* Adrenergic Neurone Blockers

Haemophilus Vaccine *see* Vaccines Haloperidol *see* Antipsychotics Heparin *see* Heparins

Heparins

▶ ACE Inhibitors: increased risk of hyperkalaemia when heparins given with ACE INHIBITORS

▶ Aliskiren: increased risk of hyperkalaemia when heparins given with ALISKIREN

l Analgesics: possible increased risk of bleeding when heparins given with NSAIDS; increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins); anticoagulant effect of heparins enhanced by l ASPIRIN

▶ Angiotensin-II Receptor Antagonists: increased risk of hyperkalaemia when heparins given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Anticoagulants: increased risk of haemorrhage when other

anticoagulants given with l APIXABAN, l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

▶ Clopidogrel: increased risk of bleeding when heparins given with CLOPIDOGREL

▶ Dipyridamole: anticoagulant effect of heparins enhanced by

DIPYRIDAMOLE

▶ Iloprost: anticoagulant effect of heparins possibly enhanced by ILOPROST

l Nitrates: anticoagulant effect of heparins reduced by *infusion*

of l GLYCERYL TRINITRATE

Hepatitis Vaccines *see* Vaccines

Histamine

▶ Antidepressants: manufacturer of histamine advises avoid concomitant use with MAOIS; effects of histamine theoretically antagonised by TRICYCLICS—manufacturer of histamine advises avoid concomitant use

▶ Antihistamines: effects of histamine theoretically antagonised by ANTIHISTAMINES—manufacturer of histamine advises avoid concomitant use

Histamine (continued)

▶ Antimalarials: manufacturer of histamine advises avoid concomitant use with ANTIMALARIALS

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▶ Antipsychotics: effects of histamine theoretically antagonised by ANTIPSYCHOTICS—manufacturer of histamine advises avoid concomitant use

▶ Atovaquone: manufacturer of histamine advises avoid concomitant use with ATOVAQUONE

▶ Clonidine: manufacturer of histamine advises avoid concomitant use with CLONIDINE

▶ Corticosteroids: manufacturer of histamine advises avoid concomitant use with CORTICOSTEROIDS

▶ Ulcer-healing Drugs: effects of histamine theoretically antagonised by HISTAMINE H2-ANTAGONISTS—manufacturer of histamine advises avoid concomitant use

Histamine H2-antagonists

l Alpha-blockers: cimetidine and ranitidine antagonise effects of

l TOLAZOLINE

l Aminophylline: cimetidine inhibits metabolism of

l AMINOPHYLLINE (increased plasma concentration)

▶ Analgesics: cimetidine inhibits metabolism of OPIOID ANALGESICS (increased plasma concentration)

▶ Anthelmintics: cimetidine possibly enhances effects of ALBENDAZOLE; cimetidine possibly inhibits metabolism of MEBENDAZOLE (increased plasma concentration); cimetidine increases plasma concentration of PRAZIQUANTEL

l Anti-arrhythmics: cimetidine increases plasma concentration of AMIODARONE and l PROPAFENONE; cimetidine inhibits metabolism of FLECAINIDE (increased plasma concentration); cimetidine increases plasma concentration of l LIDOCAINE (increased risk of toxicity)

▶ Antibacterials: cimetidine increases plasma concentration of ERYTHROMYCIN (increased risk of toxicity, including deafness); cimetidine inhibits metabolism of METRONIDAZOLE (increased plasma concentration); metabolism of cimetidine accelerated by RIFAMPICIN (reduced plasma concentration)

l Anticoagulants: cimetidine inhibits metabolism of l COUMARINS

(enhanced anticoagulant effect)

▶ Antidepressants: cimetidine increases plasma concentration of

CITALOPRAM, ESCITALOPRAM, MIRTAZAPINE and SERTRALINE;

cimetidine inhibits metabolism of AMITRIPTYLINE, DOXEPIN, IMIPRAMINE and NORTRIPTYLINE (increased plasma concentration); cimetidine increases plasma concentration of MOCLOBEMIDE (halve dose of moclobemide); cimetidine possibly increases plasma concentration of TRICYCLICS

▶ Antidiabetics: cimetidine reduces excretion of METFORMIN (increased plasma concentration); cimetidine enhances hypoglycaemic effect of SULFONYLUREAS

l Antiepileptics: cimetidine inhibits metabolism of

l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENYTOIN, l SODIUM

VALPROATE and l VALPROIC ACID (increased plasma concentration)

l Antifungals: histamine H2-antagonists reduce absorption of ITRACONAZOLE and KETOCONAZOLE; cimetidine reduces plasma concentration of l POSACONAZOLE—manufacturer of posaconazole *suspension* advises avoid concomitant use; famotidine, nizatidine and ranitidine possibly reduce plasma concentration of l POSACONAZOLE—manufacturer of posaconazole *suspension* advises avoid concomitant use; cimetidine increases plasma concentration of TERBINAFINE

▶ Antihistamines: manufacturer of loratadine advises cimetidine possibly increases plasma concentration of LORATADINE; cimetidine increases plasma concentration of HYDROXYZINE

l Antimalarials: avoidance of cimetidine advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; cimetidine inhibits metabolism of CHLOROQUINE, HYDROXYCHLOROQUINE and QUININE (increased plasma concentration)

▶ Antipsychotics: cimetidine possibly enhances effects of

ANTIPSYCHOTICS, CHLORPROMAZINE and CLOZAPINE

l Antivirals: manufacturer of atazanavir advises adjust doses of both drugs when cimetidine and nizatidine given with ATAZANAVIR—consult atazanavir product literature; famotidine and ranitidine reduce the plasma concentration of l ATAZANAVIR (adjust doses of both drugs—consult atazanavir product literature); famotidine increases plasma

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Histamine H2-antagonists

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l Antivirals (continued)

concentration of RALTEGRAVIR; avoidance of histamine H2- antagonists for 12 hours before or 4 hours after RILPIVIRINE advised by manufacturer of rilpivirine—consult product literature; cimetidine possibly increases plasma concentration of SAQUINAVIR

▶ Anxiolytics and Hypnotics: cimetidine inhibits metabolism of

BENZODIAZEPINES, CLOMETHIAZOLE and ZALEPLON (increased

plasma concentration); cimetidine increases plasma concentration of MELATONIN

▶ Beta-blockers: cimetidine increases plasma concentration of

LABETALOL, METOPROLOL and PROPRANOLOL; cimetidine

possibly increases plasma concentration of *oral* TIMOLOL

▶ Caffeine citrate: cimetidine increases plasma concentration of

CAFFEINE CITRATE

▶ Calcium-channel Blockers: cimetidine possibly inhibits metabolism of CALCIUM-CHANNEL BLOCKERS (increased plasma concentration); cimetidine increases plasma concentration of ISRADIPINE (halve dose of isradipine)

l Ciclosporin: cimetidine possibly increases plasma concentration of l CICLOSPORIN

l Clopidogrel: cimetidine possibly reduces antiplatelet effect of

l CLOPIDOGREL

l Cytotoxics: cimetidine possibly enhances myelosuppressive effects of CARMUSTINE and LOMUSTINE; cimetidine reduces plasma concentration of DOXORUBICIN; cimetidine increases plasma concentration of l EPIRUBICIN; cimetidine inhibits metabolism of CAPECITABINE, FLUOROURACIL and TEGAFUR (increased plasma concentration); famotidine possibly reduces plasma concentration of DASATINIB; avoidance of cimetidine, famotidine and nizatidine advised by manufacturer of l ERLOTINIB; ranitidine reduces plasma concentration of l ERLOTINIB—manufacturer of erlotinib advises give at least 2 hours before or 10 hours after ranitidine; ranitidine reduces plasma concentration of

l GEFITINIB; histamine H2-antagonists possibly reduce absorption of LAPATINIB; histamine H2-antagonists possibly reduce absorption of PAZOPANIB—manufacturer of pazopanib advises give at least 2 hours before or 10 hours after histamine H2-antagonists

▶ Dopaminergics: cimetidine reduces excretion of PRAMIPEXOLE

(increased plasma concentration)

l Ergot Alkaloids: increased risk of ergotism when cimetidine given with l ERGOTAMINE—avoid concomitant use

l Fampridine: avoidance of cimetidine advised by manufacturer of l FAMPRIDINE

▶ Histamine: histamine H2-antagonists theoretically antagonise effects of HISTAMINE—manufacturer of histamine advises avoid concomitant use

▶ Hormone Antagonists: absorption of cimetidine possibly delayed by OCTREOTIDE

▶ 5HT1-receptor Agonists: cimetidine inhibits metabolism of

ZOLMITRIPTAN (reduce dose of zolmitriptan)

▶ Lipid-regulating Drugs: separating administration from cimetidine and ranitidine by 12 hours advised by manufacturer of LOMITAPIDE

▶ Roflumilast: cimetidine inhibits the metabolism of

ROFLUMILAST

▶ Sildenafil: cimetidine increases plasma concentration of SILDENAFIL—consider reducing dose of sildenafil for erectile dysfunction

▶ Sympathomimetics: cimetidine possibly inhibits metabolism of

DOBUTAMINE

l Theophylline: cimetidine inhibits metabolism of

l THEOPHYLLINE (increased plasma concentration)

▶ Thyroid Hormones: cimetidine reduces absorption of

LEVOTHYROXINE

Homatropine *see* Antimuscarinics

Hormone Antagonists *see* Abiraterone, Bicalutamide, Danazol, Dutasteride, Enzalutamide, Exemestane, Flutamide, Lanreotide, Octreotide, Pasireotide, Tamoxifen, and Toremifene

5HT1-receptor Agonists

l Antibacterials: plasma concentration of eletriptan increased by

l CLARITHROMYCIN and l ERYTHROMYCIN (risk of toxicity)—

5HT1-receptor Agonists

l Antibacterials (continued)

avoid concomitant use; metabolism of zolmitriptan possibly inhibited by QUINOLONES (reduce dose of zolmitriptan)

l Antidepressants: increased risk of CNS toxicity when 5HT1 agonists given with l CITALOPRAM (manufacturer of citalopram advises avoid concomitant use); increased risk of CNS toxicity when sumatriptan given with l CITALOPRAM,

l ESCITALOPRAM, l FLUOXETINE, l FLUVOXAMINE or

l PAROXETINE; metabolism of frovatriptan inhibited by FLUVOXAMINE; metabolism of zolmitriptan possibly inhibited by FLUVOXAMINE (reduce dose of zolmitriptan); CNS toxicity reported when sumatriptan given with SERTRALINE; possible increased serotonergic effects when 5HT1 agonists given with DULOXETINE or VENLAFAXINE; risk of CNS toxicity when rizatriptan or sumatriptan given with l MAOIS (avoid rizatriptan or sumatriptan for 2 weeks after MAOIs); risk of CNS toxicity when zolmitriptan given with l MAOIS or

l MOCLOBEMIDE (reduce dose of zolmitriptan); risk of CNS toxicity when rizatriptan or sumatriptan given with

l MOCLOBEMIDE (avoid rizatriptan or sumatriptan for 2 weeks after moclobemide); possible increased serotonergic effects when naratriptan given with SSRIS; increased serotonergic effects when 5HT1 agonists given with l ST JOHN’S WORT— avoid concomitant use

l Antifungals: plasma concentration of eletriptan increased by l ITRACONAZOLE and l KETOCONAZOLE (risk of toxicity)—avoid concomitant use; plasma concentration of almotriptan increased by KETOCONAZOLE (increased risk of toxicity)

l Antivirals: plasma concentration of eletriptan increased by l INDINAVIR and l RITONAVIR (risk of toxicity)—avoid concomitant use

▶ Beta-blockers: plasma concentration of rizatriptan increased by PROPRANOLOL (manufacturer of rizatriptan advises halve dose and avoid within 2 hours of propranolol)

l Dapoxetine: possible increased risk of serotonergic effects when 5HT1 agonists given with l DAPOXETINE (manufacturer of dapoxetine advises 5HT1 agonists should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping 5HT1agonists)

▶ Dopaminergics: avoidance of 5HT1agonists advised by manufacturer of SELEGILINE

l Ergot Alkaloids: increased risk of vasospasm when eletriptan, frovatriptan or naratriptan given with l ERGOTAMINE (avoid ergotamine for 24 hours after eletriptan, frovatriptan or naratriptan, avoid eletriptan, frovatriptan or naratriptan for 24 hours after ergotamine); increased risk of vasospasm when almotriptan, rizatriptan, sumatriptan or zolmitriptan given with l ERGOTAMINE (avoid ergotamine for 6 hours after almotriptan, rizatriptan, sumatriptan or zolmitriptan, avoid almotriptan, rizatriptan, sumatriptan or zolmitriptan for 24 hours after ergotamine)

▶ Lithium: possible risk of toxicity when sumatriptan given with

LITHIUM

▶ Ulcer-healing Drugs: metabolism of zolmitriptan inhibited by

CIMETIDINE (reduce dose of zolmitriptan)

5HT3-receptor Antagonists

▶ Analgesics: ondansetron possibly antagonises effects of

TRAMADOL

▶ Antibacterials: metabolism of ondansetron accelerated by

RIFAMPICIN (reduced effect)

▶ Antidepressants: possible increased serotonergic effects when 5HT3 antagonists given with SSRI-RELATED ANTIDEPRESSANTS or SSRIS

▶ Antiepileptics: metabolism of ondansetron accelerated by

CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN (reduced

effect)

l Cytotoxics: increased risk of ventricular arrhythmias when ondansetron given with l VANDETANIB—avoid concomitant use

l Dopaminergics: possible increased hypotensive effect when ondansetron given with l APOMORPHINE—avoid concomitant use

Human papillomavirus Vaccine *see* Vaccines

Hydralazine *see* Vasodilator Antihypertensives

Hydrochlorothiazide *see* Diuretics Hydrocortisone *see* Corticosteroids Hydroflumethiazide *see* Diuretics Hydromorphone *see* Opioid Analgesics Hydrotalcite *see* Antacids Hydroxocobalamin

▶ Antibacterials: response to hydroxocobalamin reduced by

CHLORAMPHENICOL

Hydroxycarbamide

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: increased risk of toxicity when hydroxycarbamide given with l DIDANOSINE and l STAVUDINE—avoid concomitant use

Hydroxychloroquine

▶ Adsorbents: absorption of hydroxychloroquine reduced by

KAOLIN

▶ Agalsidase Alfa and Beta: hydroxychloroquine possibly inhibits effects of AGALSIDASE ALFA AND BETA (manufacturers of agalsidase alfa and beta advise avoid concomitant use)

▶ Antacids: absorption of hydroxychloroquine reduced by

ANTACIDS

l Anti-arrhythmics: increased risk of ventricular arrhythmias when hydroxychloroquine given with l AMIODARONE—avoid concomitant use

l Antibacterials: increased risk of ventricular arrhythmias when hydroxychloroquine given with l MOXIFLOXACIN—avoid concomitant use

l Antimalarials: avoidance of antimalarials advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; increased risk of convulsions when hydroxychloroquine given with

l MEFLOQUINE

l Antipsychotics: increased risk of ventricular arrhythmias when hydroxychloroquine given with l DROPERIDOL—avoid concomitant use

l Cardiac Glycosides: hydroxychloroquine possibly increases plasma concentration of l DIGOXIN

l Ciclosporin: hydroxychloroquine increases plasma concentration of l CICLOSPORIN (increased risk of toxicity)

l Cytotoxics: possible increased risk of ventricular arrhythmias when hydroxychloroquine given with l BOSUTINIB

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

▶ Lanthanum: absorption of hydroxychloroquine possibly reduced by LANTHANUM (give at least 2 hours apart)

▶ Laronidase: hydroxychloroquine possibly inhibits effects of LARONIDASE (manufacturer of laronidase advises avoid concomitant use)

▶ Parasympathomimetics: hydroxychloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of NEOSTIGMINE and PYRIDOSTIGMINE

▶ Ulcer-healing Drugs: metabolism of hydroxychloroquine inhibited by CIMETIDINE (increased plasma concentration)

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Hydroxyzine *see* Antihistamines Hyoscine *see* Antimuscarinics Ibandronic Acid *see* Bisphosphonates Ibrutinib

l Anti-arrhythmics: plasma concentration of ibrutinib possibly

increased by l AMIODARONE and l DRONEDARONE—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Antibacterials: plasma concentration of ibrutinib possibly increased by l CIPROFLOXACIN, l CLARITHROMYCIN,

l ERYTHROMYCIN and l TELITHROMYCIN—reduce dose of ibrutinib (see under Ibrutinib, p. 809); plasma concentration of ibrutinib reduced by l RIFAMPICIN—avoid concomitant use

▶ Anticoagulants: manufacturer of ibrutinib advises avoid concomitant use with COUMARINS and PHENINDIONE

l Antidepressants: plasma concentration of ibrutinib possibly reduced by l ST JOHN’S WORT—manufacturer of ibrutinib advises avoid concomitant use

l Antiepileptics: plasma concentration of ibrutinib possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN and

Ibrutinib

l Antiepileptics (continued)

Interactions | Appendix 1

l PHENYTOIN—manufacturer of ibrutinib advises avoid concomitant use

l Antifungals: plasma concentration of ibrutinib increased by

l KETOCONAZOLE—reduce dose of ibrutinib (see under Ibrutinib, p. 809); plasma concentration of ibrutinib possibly increased by l FLUCONAZOLE, l ITRACONAZOLE and

l VORICONAZOLE—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: plasma concentration of ibrutinib possibly increased by l ATAZANAVIR, l DARUNAVIR, l FOSAMPRENAVIR,

l INDINAVIR, l RITONAVIR and l SAQUINAVIR—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Aprepitant: plasma concentration of ibrutinib possibly increased by l APREPITANT—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Calcium-channel Blockers: plasma concentration of ibrutinib possibly increased by l DILTIAZEM and l VERAPAMIL—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

▶ Cardiac Glycosides: manufacturer of ibrutinib advises give

DIGOXIN at least 6 hours before or after ibrutinib

l Cobicistat: plasma concentration of ibrutinib possibly increased by l COBICISTAT—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

l Cytotoxics: plasma concentration of ibrutinib possibly

increased by l CRIZOTINIB and l IMATINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

▶ Fosaprepitant: plasma concentration of ibrutinib possibly increased by FOSAPREPITANT

▶ Grapefruit Juice: manufacturer of ibrutinib advises avoid concomitant use with GRAPEFRUIT JUICE

▶ Vitamins: manufacturer of ibrutinib advises avoid concomitant use with VITAMIN E

Ibuprofen *see* NSAIDs

Idarubicin

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Ciclosporin: plasma concentration of idarubicin increased by

l CICLOSPORIN

Idelalisib

▶ Alpha-blockers: manufacturer of idelalisib advises avoid concomitant use with ALFUZOSIN

▶ Anti-arrhythmics: manufacturer of idelalisib advises avoid concomitant use with AMIODARONE

l Antibacterials: plasma concentration of idelalisib reduced by

l RIFAMPICIN—avoid concomitant use

l Antidepressants: plasma concentration of idelalisib possibly reduced by l ST JOHN’S WORT—manufacturer of idelalisib advises avoid concomitant use

l Antiepileptics: plasma concentration of idelalisib possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN and

l PHENYTOIN—manufacturer of idelalisib advises avoid concomitant use

▶ Antifungals: plasma concentration of idelalisib increased by

KETOCONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis); manufacturer of idelalisib advises avoid concomitant use with PIMOZIDE and QUETIAPINE

▶ Anxiolytics and Hypnotics: manufacturer of idelalisib advises avoid concomitant use of *oral* MIDAZOLAM

▶ Ergot Alkaloids: manufacturer of idelalisib advises avoid concomitant use with ERGOTAMINE

▶ Lipid-regulating Drugs: manufacturer of idelalisib advises avoid concomitant use with SIMVASTATIN

▶ Sildenafil: manufacturer of idelalisib advises avoid concomitant use of SILDENAFIL for pulmonary arterial hypertension

▶ Sympathomimetics, Beta2: manufacturer of idelalisib advises avoid concomitant use with SALMETEROL

Ifosfamide

l Anticoagulants: ifosfamide possibly enhances anticoagulant effect of l COUMARINS

Interactions | Appendix 1

Ifosfamide (continued)

▶ Antifungals: metabolism of ifosfamide inhibited by

KETOCONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cytotoxics: increased risk of otoxicity when ifosfamide given with CISPLATIN

Iloprost

▶ Analgesics: increased risk of bleeding when iloprost given with

NSAIDS or ASPIRIN

▶ Anticoagulants: iloprost possibly enhances anticoagulant effect of COUMARINS and HEPARINS; increased risk of bleeding when iloprost given with PHENINDIONE

▶ Clopidogrel: increased risk of bleeding when iloprost given with CLOPIDOGREL

▶ Eptifibatide: increased risk of bleeding when iloprost given with EPTIFIBATIDE

▶ Tirofiban: increased risk of bleeding when iloprost given with

TIROFIBAN

Imatinib

▶ Analgesics: manufacturer of imatinib advises caution with

PARACETAMOL

l Antibacterials: plasma concentration of imatinib reduced by

l RIFAMPICIN—avoid concomitant use

▶ Anticoagulants: manufacturer of imatinib advises replacement of WARFARIN with a heparin (possibility of enhanced warfarin effect)

l Antidepressants: plasma concentration of imatinib reduced by

l ST JOHN’S WORT—avoid concomitant use

l Antiepileptics: plasma concentration of imatinib reduced by

l CARBAMAZEPINE, l FOSPHENYTOIN, l OXCARBAZEPINE and

l PHENYTOIN—avoid concomitant use

▶ Antifungals: plasma concentration of imatinib increased by

KETOCONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of imatinib advised by manufacturer of

l BOCEPREVIR

▶ Ciclosporin: imatinib possibly increases plasma concentration of CICLOSPORIN

l Cytotoxics: imatinib possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; imatinib increases plasma concentration of l EVEROLIMUS (consider reducing the dose of everolimus —consult everolimus product literature); imatinib possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib, p. 809)

▶ Lipid-regulating Drugs: imatinib increases plasma concentration of SIMVASTATIN

▶ Tacrolimus: imatinib increases plasma concentration of

TACROLIMUS

▶ Thyroid Hormones: imatinib possibly reduces plasma concentration of LEVOTHYROXINE

Imidapril *see* ACE Inhibitors

Imipenem with Cilastatin

l Antiepileptics: carbapenems reduce plasma concentration of

l SODIUM VALPROATE and l VALPROIC ACID—avoid concomitant use

l Antivirals: increased risk of convulsions when imipenem with cilastatin given with l GANCICLOVIR or l VALGANCICLOVIR

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Imipramine *see* Antidepressants, Tricyclic

Immunoglobulins

l Vaccines: anti-d immunoglobulins and normal immunoglobulin might impair immune response to l BCG VACCINE—give BCG vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to

l MMR VACCINE—give MMR vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to live

Immunoglobulins

l Vaccines (continued)

l INFLUENZA VACCINE—give live influenza vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to l ORAL TYPHOID VACCINE—give oral typhoid vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to *oral* l POLIOMYELITIS VACCINE—give *oral* poliomyelitis vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to l ROTAVIRUS VACCINE—give rotavirus vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to l SMALLPOX VACCINE—give smallpox vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to l VARICELLA-ZOSTER VACCINE—give varicella-zoster vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; anti-d immunoglobulins and normal immunoglobulin might impair immune response to l YELLOW FEVER VACCINE—give

yellow fever vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin

Indacaterol *see* Sympathomimetics, Beta2

Indapamide *see* Diuretics

Indinavir

▶ Aldesleukin: plasma concentration of indinavir possibly increased by ALDESLEUKIN

l Anti-arrhythmics: indinavir possibly increases plasma concentration of l AMIODARONE—avoid concomitant use; indinavir possibly increases plasma concentration of

l FLECAINIDE (increased risk of ventricular arrhythmias—avoid concomitant use)

l Antibacterials: indinavir increases plasma concentration of

l RIFABUTIN, also plasma concentration of indinavir decreased (reduce dose of rifabutin and increase dose of indinavir); metabolism of indinavir accelerated by l RIFAMPICIN (reduced plasma concentration—avoid concomitant use); avoidance of concomitant indinavir in severe renal and hepatic impairment advised by manufacturer of l TELITHROMYCIN

▶ Anticoagulants: avoidance of indinavir advised by manufacturer of APIXABAN and RIVAROXABAN

l Antidepressants: plasma concentration of indinavir reduced by

l ST JOHN’S WORT—avoid concomitant use

l Antiepileptics: plasma concentration of indinavir possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN and

l PHENYTOIN, also plasma concentration of carbamazepine, fosphenytoin and phenytoin possibly increased; plasma concentration of indinavir possibly reduced by

l PHENOBARBITAL and l PRIMIDONE

l Antifungals: plasma concentration of indinavir increased by

l ITRACONAZOLE and l KETOCONAZOLE (consider reducing dose of indinavir)

l Antimalarials: caution with indinavir advised by manufacturer of ARTEMETHER WITH LUMEFANTRINE; indinavir possibly increases plasma concentration of l QUININE (increased risk of toxicity)

▶ Antimuscarinics: avoidance of indinavir advised by manufacturer of DARIFENACIN and TOLTERODINE; manufacturer of fesoterodine advises dose reduction when indinavir given with FESOTERODINE—consult fesoterodine product literature

l Antipsychotics: indinavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); indinavir possibly increases plasma concentration of

l LURASIDONE—avoid concomitant use; indinavir possibly increases plasma concentration of l PIMOZIDE (increased risk of ventricular arrhythmias—avoid concomitant use); indinavir possibly increases plasma concentration of

Indinavir

l Antipsychotics (continued)

l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: avoid concomitant use of indinavir with

l ATAZANAVIR; plasma concentration of both drugs increased when indinavir given with DARUNAVIR; absorption of indinavir reduced by DIDANOSINE *tablets* (give at least 1 hour apart); plasma concentration of indinavir reduced by EFAVIRENZ and NEVIRAPINE; plasma concentration of indinavir possibly reduced by l ETRAVIRINE—avoid concomitant use; indinavir increases plasma concentration of l MARAVIROC (consider reducing dose of maraviroc); plasma concentration of indinavir increased by RITONAVIR; indinavir increases plasma concentration of SAQUINAVIR

l Anxiolytics and Hypnotics: increased risk of prolonged sedation when indinavir given with l ALPRAZOLAM—avoid concomitant use; indinavir possibly increases plasma concentration of

l MIDAZOLAM (risk of prolonged sedation—avoid concomitant use of *oral* midazolam)

▶ Atovaquone: plasma concentration of indinavir possibly reduced by ATOVAQUONE

l Avanafil: indinavir possibly increases plasma concentration of l AVANAFIL—manufacturer of avanafil advises avoid concomitant use

▶ Bosentan: plasma concentration of indinavir possibly reduced by BOSENTAN

l Ciclosporin: indinavir increases plasma concentration of

l CICLOSPORIN

l Colchicine: indinavir possibly increases risk of l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

▶ Corticosteroids: plasma concentration of indinavir possibly reduced by DEXAMETHASONE

l Cytotoxics: indinavir possibly increases plasma concentration of AXITINIB (reduce dose of axitinib—consult axitinib product literature); indinavir possibly increases the plasma concentration of l BOSUTINIB and l CABAZITAXEL— manufacturer of bosutinib and cabazitaxel advises avoid or consider reducing dose of bosutinib and cabazitaxel; indinavir possibly increases plasma concentration of

l CRIZOTINIB and l EVEROLIMUS—manufacturer of crizotinib and everolimus advises avoid concomitant use; indinavir possibly increases the plasma concentration of l IBRUTINIB— reduce dose of ibrutinib (see under Ibrutinib, p. 809); indinavir possibly increases plasma concentration of

l PAZOPANIB (reduce dose of pazopanib); indinavir possibly increases plasma concentration of PONATINIB—consider reducing initial dose of ponatinib (see under Ponatinib,

p. 814); manufacturer of ruxolitinib advises dose reduction when indinavir given with l RUXOLITINIB—consult ruxolitinib product literature; indinavir possibly increases plasma concentration of l DOCETAXEL—manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose

l Ergot Alkaloids: increased risk of ergotism when indinavir given with l ERGOMETRINE or l ERGOTAMINE—avoid concomitant use

l 5HT1-receptor Agonists: indinavir increases plasma

concentration of l ELETRIPTAN (risk of toxicity)—avoid concomitant use

l Lipid-regulating Drugs: possible increased risk of myopathy when indinavir given with ATORVASTATIN; possible increased risk of myopathy when indinavir given with l ROSUVASTATIN— manufacturer of rosuvastatin advises avoid concomitant use; increased risk of myopathy when indinavir given with

l SIMVASTATIN (avoid concomitant use); avoidance of indinavir advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

l Orlistat: absorption of indinavir possibly reduced by

l ORLISTAT

l Ranolazine: indinavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

l Sildenafil: indinavir increases plasma concentration of

l SILDENAFIL—reduce initial dose of sildenafil

Indinavir (continued)

▶ Tadalafil: indinavir possibly increases plasma concentration of

Interactions | Appendix 1

TADALAFIL

l Vardenafil: indinavir increases plasma concentration of

l VARDENAFIL—avoid concomitant use

Indometacin *see* NSAIDs Indoramin *see* Alpha-blockers Infliximab

l Abatacept: avoid concomitant use of infliximab with

l ABATACEPT

l Anakinra: avoid concomitant use of infliximab with

l ANAKINRA

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Influenza Vaccine *see* Vaccines Insulin *see* Antidiabetics Interferon Alfa *see* Interferons Interferon Gamma *see* Interferons Interferons

l Aminophylline: interferon alfa and peginterferon alfa inhibit

metabolism of l AMINOPHYLLINE (consider reducing dose of aminophylline)

l Antivirals: caution with peginterferon alfa advised by manufacturer of ADEFOVIR; increased risk of peripheral neuropathy when interferon alfa and peginterferon alfa given with l TELBIVUDINE

l Theophylline: interferon alfa and peginterferon alfa inhibit metabolism of l THEOPHYLLINE (consider reducing dose of theophylline)

▶ Vaccines: manufacturer of interferon gamma advises avoid concomitant use with VACCINES

Ipilimumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cytotoxics: manufacturer of ipilimumab advises avoid concomitant use with VEMURAFENIB

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Ipratropium *see* Antimuscarinics

Irbesartan *see* Angiotensin-II Receptor Antagonists

Irinotecan

l Antidepressants: metabolism of irinotecan accelerated by l ST JOHN’S WORT (reduced plasma concentration—avoid concomitant use)

▶ Antiepileptics: plasma concentration of irinotecan and its active metabolite reduced by CARBAMAZEPINE, FOSPHENYTOIN,

PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Antifungals: plasma concentration of irinotecan reduced by

l KETOCONAZOLE (but concentration of active metabolite of irinotecan increased)—avoid concomitant use; increased risk of toxicity when irinotecan given with l ITRACONAZOLE—avoid concomitant use

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: metabolism of irinotecan possibly inhibited by

l ATAZANAVIR (increased risk of toxicity)

l Cytotoxics: plasma concentration of active metabolite of irinotecan increased by l LAPATINIB—consider reducing dose of irinotecan; plasma concentration of irinotecan increased by REGORAFENIB; plasma concentration of irinotecan possibly increased by SORAFENIB

Iron Salts

▶ Antacids: absorption of *oral* iron salts reduced by ORAL MAGNESIUM SALTS (as magnesium trisilicate)

▶ Antibacterials: *oral* iron salts reduce absorption of

CIPROFLOXACIN, LEVOFLOXACIN, MOXIFLOXACIN and OFLOXACIN;

*oral* iron salts reduce absorption of NORFLOXACIN (give at least 2 hours apart); *oral* iron salts reduce absorption of TETRACYCLINES, also absorption of *oral* iron salts reduced by tetracyclines

▶ Antivirals: *oral* iron salts reduce absoption of DOLUTEGRAVIR— manufacturer of dolutegravir advises give at least 2 hours before or 6 hours after *oral* iron salts

Interactions | Appendix 1

Iron Salts (continued)

▶ Bisphosphonates: *oral* iron salts reduce absorption of

BISPHOSPHONATES

▶ Calcium Salts: absorption of *oral* iron salts reduced by CALCIUM SALTS

▶ Dopaminergics: *oral* iron salts possibly reduce absorption of

CO-BENELDOPA, CO-CARELDOPA and LEVODOPA; *oral* iron salts reduce absorption of ENTACAPONE

▶ Eltrombopag: *oral* iron salts possibly reduce absorption of

ELTROMBOPAG (give at least 4 hours apart)

▶ Methyldopa: *oral* iron salts antagonise hypotensive effect of

METHYLDOPA

▶ Mycophenolate: *oral* iron salts reduce absorption of

MYCOPHENOLATE

▶ Penicillamine: *oral* iron salts reduce absorption of

PENICILLAMINE

▶ Thyroid Hormones: *oral* iron salts reduce absorption of

LEVOTHYROXINE (give at least 2 hours apart)

▶ Trientine: absorption of *oral* iron salts reduced by TRIENTINE

▶ Zinc: *oral* iron salts reduce absorption of ZINC, also absorption of *oral* iron salts reduced by zinc

Isocarboxazid *see* MAOIs

Isoflurane *see* Anaesthetics, General Isometheptene *see* Sympathomimetics Isoniazid

▶ Aminophylline: isoniazid possibly increases plasma

concentration of AMINOPHYLLINE

▶ Anaesthetics, General: increased risk of hepatotoxicity when isoniazid given with ISOFLURANE

▶ Analgesics: avoidance of isoniazid advised by manufacturer of

PETHIDINE

▶ Antacids: absorption of isoniazid reduced by ANTACIDS

l Antibacterials: increased risk of hepatotoxicity when isoniazid given with l RIFAMPICIN; increased risk of CNS toxicity when isoniazid given with CYCLOSERINE

l Antiepileptics: isoniazid increases plasma concentration of l CARBAMAZEPINE (also possibly increased isoniazid hepatotoxicity); isoniazid inhibits metabolism of

l ETHOSUXIMIDE (increased plasma concentration and risk of toxicity); isoniazid possibly inhibits metabolism of FOSPHENYTOIN and PHENYTOIN (increased risk of toxicity)

▶ Antifungals: isoniazid possibly reduces plasma concentration of KETOCONAZOLE

▶ Anxiolytics and Hypnotics: isoniazid inhibits the metabolism of

DIAZEPAM

▶ Corticosteroids: plasma concentration of isoniazid possibly reduced by CORTICOSTEROIDS

▶ Disulfiram: isoniazid possibly increases CNS effects of

DISULFIRAM

▶ Dopaminergics: isoniazid possibly reduces effects of CO- BENELDOPA, CO-CARELDOPA and LEVODOPA

▶ Lipid-regulating Drugs: separating administration from isoniazid by 12 hours advised by manufacturer of LOMITAPIDE

▶ Theophylline: isoniazid possibly increases plasma concentration of THEOPHYLLINE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Isosorbide Dinitrate *see* Nitrates Isosorbide Mononitrate *see* Nitrates Isotretinoin *see* Retinoids

Isradipine *see* Calcium-channel Blockers Itraconazole *see* Antifungals, Triazole Ivabradine

l Anti-arrhythmics: increased risk of ventricular arrhythmias

when ivabradine given with l AMIODARONE or l DISOPYRAMIDE

l Antibacterials: plasma concentration of ivabradine possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN—avoid concomitant use; increased risk of ventricular arrhythmias when ivabradine given with l ERYTHROMYCIN—avoid concomitant use

▶ Antidepressants: plasma concentration of ivabradine reduced by ST JOHN’S WORT—avoid concomitant use

l Antifungals: plasma concentration of ivabradine increased by l KETOCONAZOLE—avoid concomitant use; plasma concentration of ivabradine increased by FLUCONAZOLE—

Ivabradine

l Antifungals (continued)

reduce initial dose of ivabradine; plasma concentration of ivabradine possibly increased by l ITRACONAZOLE—avoid concomitant use

l Antimalarials: increased risk of ventricular arrhythmias when ivabradine given with l MEFLOQUINE

l Antipsychotics: increased risk of ventricular arrhythmias when ivabradine given with l PIMOZIDE

l Antivirals: plasma concentration of ivabradine possibly increased by l RITONAVIR—avoid concomitant use

l Beta-blockers: increased risk of ventricular arrhythmias when ivabradine given with l SOTALOL

l Calcium-channel Blockers: plasma concentration of ivabradine increased by l DILTIAZEM and l VERAPAMIL—avoid concomitant use

▶ Grapefruit Juice: plasma concentration of ivabradine increased by GRAPEFRUIT JUICE

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when ivabradine given with l PENTAMIDINE ISETIONATE

Ivacaftor

l Antibacterials: plasma concentration of ivacaftor possibly increased by l CLARITHROMYCIN, l ERYTHROMYCIN and

l TELITHROMYCIN (see under Ivacaftor, p. 257); plasma concentration of ivacaftor possibly reduced by l RIFABUTIN— manufacturer of ivacaftor advises avoid concomitant use; plasma concentration of ivacaftor reduced by l RIFAMPICIN— manufacturer of ivacaftor advises avoid concomitant use

l Antidepressants: plasma concentration of ivacaftor possibly reduced by l ST JOHN’S WORT—manufacturer of ivacaftor advises avoid concomitant use

l Antiepileptics: plasma concentration of ivacaftor possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—

manufacturer of ivacaftor advises avoid concomitant use

l Antifungals: plasma concentration of ivacaftor increased by

l FLUCONAZOLE and l KETOCONAZOLE (see under Ivacaftor,

p. 257); plasma concentration of ivacaftor possibly increased by l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE (see under Ivacaftor, p. 257)

▶ Anxiolytics and Hypnotics: ivacaftor increases plasma concentration of MIDAZOLAM

▶ Cardiac Glycosides: ivacaftor increases plasma concentration of

DIGOXIN

▶ Grapefruit Juice: plasma concentration of ivacaftor possibly increased by GRAPEFRUIT JUICE—manufacturer of ivacaftor advises avoid concomitant use

▶ Lipid-regulating Drugs: separating administration from ivacaftor by 12 hours advised by manufacturer of LOMITAPIDE

Ivermectin

▶ Anthelmintics: plasma concentration of ivermectin possibly increased by LEVAMISOLE

▶ Anticoagulants: ivermectin possibly enhances anticoagulant effect of COUMARINS

Japanese Encephalitis Vaccine *see* Vaccines

Kaolin

▶ Analgesics: kaolin possibly reduces absorption of ASPIRIN

▶ Antibacterials: kaolin possibly reduces absorption of

TETRACYCLINES

▶ Antimalarials: kaolin reduces absorption of CHLOROQUINE and

HYDROXYCHLOROQUINE

▶ Antipsychotics: kaolin possibly reduces absorption of

PHENOTHIAZINES

Ketamine *see* Anaesthetics, General Ketoconazole *see* Antifungals, Imidazole Ketoprofen *see* NSAIDs

Ketorolac *see* NSAIDs Ketotifen *see* Antihistamines Labetalol *see* Beta-blockers

Lacidipine *see* Calcium-channel Blockers

Lacosamide

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered);

Lacosamide

l Antidepressants (continued)

anticonvulsant effect of antiepileptics antagonised by l SSRIS

and l TRICYCLICS (convulsive threshold lowered)

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Lactulose

▶ Anticoagulants: lactulose possibly enhances anticoagulant effect of COUMARINS

Lamivudine

▶ Antibacterials: plasma concentration of lamivudine increased by TRIMETHOPRIM (as co-trimoxazole)—avoid concomitant use of high-dose co-trimoxazole

▶ Antivirals: avoidance of lamivudine advised by manufacturer of EMTRICITABINE

l Cytotoxics: manufacturer of lamivudine advises avoid concomitant use with l CLADRIBINE

l Orlistat: absorption of lamivudine possibly reduced by

l ORLISTAT

Lamotrigine

l Antibacterials: plasma concentration of lamotrigine reduced by l RIFAMPICIN

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antiepileptics: plasma concentration of lamotrigine often reduced by CARBAMAZEPINE, also plasma concentration of an active metabolite of carbamazepine sometimes raised (but evidence is conflicting); plasma concentration of lamotrigine reduced by FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and

PRIMIDONE; plasma concentration of lamotrigine increased by l SODIUM VALPROATE and l VALPROIC ACID (increased risk of toxicity—reduce lamotrigine dose)

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

▶ Antivirals: plasma concentration of lamotrigine possibly reduced by RITONAVIR

l Oestrogens: plasma concentration of lamotrigine reduced by

l OESTROGENS—consider increasing dose of lamotrigine

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

▶ Progestogens: plasma concentration of lamotrigine possibly increased by DESOGESTREL

Lanreotide

▶ Antidiabetics: lanreotide possibly reduces requirements for

ANTIDIABETICS

▶ Ciclosporin: lanreotide reduces plasma concentration of

CICLOSPORIN

Lansoprazole *see* Proton Pump Inhibitors

Lanthanum

▶ Antibacterials: lanthanum possibly reduces absorption of QUINOLONES (give at least 2 hours before or 4 hours after lanthanum)

▶ Antifungals: lanthanum possibly reduces absorption of

KETOCONAZOLE (give at least 2 hours apart)

▶ Antimalarials: lanthanum possibly reduces absorption of CHLOROQUINE and HYDROXYCHLOROQUINE (give at least 2 hours apart)

▶ Thyroid Hormones: lanthanum reduces absorption of

LEVOTHYROXINE (give at least 2 hours apart)

Lapatinib

l Antibacterials: manufacturer of lapatinib advises avoid concomitant use with l RIFABUTIN, l RIFAMPICIN and

l TELITHROMYCIN

Lapatinib (continued)

l Antidepressants: manufacturer of lapatinib advises avoid concomitant use with l ST JOHN’S WORT

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l Antidiabetics: manufacturer of lapatinib advises avoid concomitant use with l REPAGLINIDE

l Antiepileptics: plasma concentration of lapatinib reduced by

l CARBAMAZEPINE—avoid concomitant use; manufacturer of lapatinib advises avoid concomitant use with l FOSPHENYTOIN and l PHENYTOIN

l Antifungals: plasma concentration of lapatinib increased by

l KETOCONAZOLE—avoid concomitant use; manufacturer of lapatinib advises avoid concomitant use with l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis); manufacturer of lapatinib advises avoid concomitant use with l PIMOZIDE

l Antivirals: avoidance of lapatinib advised by manufacturer of l BOCEPREVIR; manufacturer of lapatinib advises avoid concomitant use with l RITONAVIR and l SAQUINAVIR

l Cytotoxics: lapatinib increases plasma concentration of PAZOPANIB; possible increased risk of neutropenia when lapatinib given with DOCETAXEL; increased risk of neutropenia when lapatinib given with l PACLITAXEL; lapatinib increases plasma concentration of active metabolite of l IRINOTECAN— consider reducing dose of irinotecan

l Grapefruit Juice: manufacturer of lapatinib advises avoid concomitant use with l GRAPEFRUIT JUICE

▶ Lipid-regulating Drugs: separating administration from lapatinib by 12 hours advised by manufacturer of LOMITAPIDE

▶ Ulcer-healing Drugs: absorption of lapatinib possibly reduced by HISTAMINE H2-ANTAGONISTS and PROTON PUMP INHIBITORS

Laronidase

▶ Antimalarials: effects of laronidase possibly inhibited by CHLOROQUINE and HYDROXYCHLOROQUINE (manufacturer of laronidase advises avoid concomitant use)

Leflunomide

NOTE Increased risk of toxicity with other haematotoxic and hepatotoxic drugs

▶ Antibacterials: plasma concentration of active metabolite of leflunomide possibly increased by RIFAMPICIN

▶ Anticoagulants: leflunomide possibly enhances anticoagulant effect of WARFARIN

▶ Antidiabetics: leflunomide possibly enhances hypoglycaemic effect of TOLBUTAMIDE

▶ Antiepileptics: leflunomide possibly increases plasma concentration of FOSPHENYTOIN and PHENYTOIN

l Cytotoxics: risk of toxicity when leflunomide given with

l METHOTREXATE

▶ Lipid-regulating Drugs: the effect of leflunomide is significantly decreased by COLESTYRAMINE (enhanced elimination)—avoid unless drug elimination desired

l Vaccines: risk of generalised infections when leflunomide given with live l VACCINES—avoid concomitant use

Lenalidomide

l Antibacterials: plasma concentration of lenalidomide possibly increased by l CLARITHROMYCIN (increased risk of toxicity)

l Antifungals: plasma concentration of lenalidomide possibly increased by l ITRACONAZOLE and l KETOCONAZOLE (increased risk of toxicity)

l Calcium-channel Blockers: plasma concentration of lenalidomide possibly increased by l VERAPAMIL (increased risk of toxicity)

▶ Cardiac Glycosides: lenalidomide possibly increases plasma concentration of DIGOXIN

l Ciclosporin: plasma concentration of lenalidomide possibly increased by l CICLOSPORIN (increased risk of toxicity)

Lercanidipine *see* Calcium-channel Blockers

Leukotriene Receptor Antagonists

▶ Aminophylline: zafirlukast possibly increases plasma concentration of AMINOPHYLLINE, also plasma concentration of zafirlukast reduced

▶ Analgesics: plasma concentration of zafirlukast increased by

ASPIRIN

▶ Antibacterials: plasma concentration of zafirlukast reduced by

ERYTHROMYCIN

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Leukotriene Receptor Antagonists (continued)

▶ Anticoagulants: zafirlukast enhances anticoagulant effect of

WARFARIN

▶ Antiepileptics: plasma concentration of montelukast reduced by PHENOBARBITAL and PRIMIDONE

▶ Antifungals: plasma concentration of zafirlukast increased by

FLUCONAZOLE

▶ Lipid-regulating Drugs: plasma concentration of montelukast increased by GEMFIBROZIL

▶ Theophylline: zafirlukast possibly increases plasma concentration of THEOPHYLLINE, also plasma concentration of zafirlukast reduced

Levamisole

▶ Alcohol: possibility of disulfiram-like reaction when levamisole given with ALCOHOL

▶ Anthelmintics: plasma concentration of both drugs possibly reduced when levamisole given with ALBENDAZOLE; levamisole possibly increases plasma concentration of IVERMECTIN

l Anticoagulants: levamisole possibly enhances anticoagulant effect of l WARFARIN

▶ Antiepileptics: levamisole possibly increases plasma concentration of FOSPHENYTOIN and PHENYTOIN

Levetiracetam

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antiepileptics: levetiracetam possibly increases risk of

CARBAMAZEPINE toxicity

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Levobunolol *see* Beta-blockers

Levobupivacaine

▶ Anti-arrhythmics: increased myocardial depression when levobupivacaine given with ANTI-ARRHYTHMICS

Levocarnitine

▶ Anticoagulants: levocarnitine possibly enhances anticoagulant effect of COUMARINS

Levocetirizine *see* Antihistamines

Levodopa

▶ ACE Inhibitors: enhanced hypotensive effect when levodopa given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when levodopa given with ADRENERGIC NEURONE BLOCKERS

▶ Alpha-blockers: enhanced hypotensive effect when levodopa given with ALPHA-BLOCKERS

l Anaesthetics, General: increased risk of arrhythmias when levodopa given with l VOLATILE LIQUID GENERAL ANAESTHETICS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when levodopa given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antibacterials: effects of levodopa possibly reduced by

ISONIAZID

l Antidepressants: risk of hypertensive crisis when levodopa given with l MAOIS, avoid levodopa for at least 2 weeks after stopping MAOIs; increased risk of side-effects when levodopa given with MOCLOBEMIDE

▶ Antiepileptics: effects of levodopa possibly reduced by

FOSPHENYTOIN and PHENYTOIN

▶ Antimuscarinics: absorption of levodopa possibly reduced by

ANTIMUSCARINICS

▶ Antipsychotics: effects of levodopa antagonised by ANTIPSYCHOTICS; avoidance of levodopa advised by manufacturer of AMISULPRIDE (antagonism of effect)

▶ Anxiolytics and Hypnotics: effects of levodopa possibly antagonised by BENZODIAZEPINES

▶ Beta-blockers: enhanced hypotensive effect when levodopa given with BETA-BLOCKERS

Levodopa (continued)

▶ Bupropion: increased risk of side-effects when levodopa given with BUPROPION

▶ Calcium-channel Blockers: enhanced hypotensive effect when levodopa given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when levodopa given with CLONIDINE

▶ Diazoxide: enhanced hypotensive effect when levodopa given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when levodopa given with DIURETICS

▶ Dopaminergics: enhanced effects and increased toxicity of levodopa when given with SELEGILINE (reduce dose of levodopa)

▶ Iron Salts: absorption of levodopa possibly reduced by *oral*

IRON SALTS

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: enhanced hypotensive effect when levodopa given with METHYLDOPA; antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Moxonidine: enhanced hypotensive effect when levodopa given with MOXONIDINE

▶ Muscle Relaxants: possible agitation, confusion and hallucinations when levodopa given with BACLOFEN

▶ Nitrates: enhanced hypotensive effect when levodopa given with NITRATES

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when levodopa given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

▶ Vitamins: effects of levodopa reduced by PYRIDOXINE when given without dopa-decarboxylase inhibitor

Levofloxacin *see* Quinolones Levofolinic Acid *see* Folates Levomepromazine *see* Antipsychotics Levonorgestrel *see* Progestogens Levothyroxine *see* Thyroid Hormones Lidocaine

NOTE Interactions less likely when lidocaine used topically

▶ Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with BUPIVACAINE, LEVOBUPIVACAINE,

PRILOCAINE or ROPIVACAINE

l Anti-arrhythmics: increased myocardial depression when anti- arrhythmics given with other l ANTI-ARRHYTHMICS

l Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with

l ANTIPSYCHOTICS that prolong the QT interval

l Antivirals: plasma concentration of lidocaine possibly increased by l ATAZANAVIR and LOPINAVIR; plasma concentration of lidocaine possibly increased by DARUNAVIR and l FOSAMPRENAVIR—avoid concomitant use; increased risk of ventricular arrhythmias when lidocaine given with

l SAQUINAVIR—avoid concomitant use; caution with

*intravenous* lidocaine advised by manufacturer of TELAPREVIR

l Beta-blockers: increased myocardial depression when anti- arrhythmics given with l BETA-BLOCKERS; possible increased risk of lidocaine toxicity when given with NADOLOL; increased risk of lidocaine toxicity when given with l PROPRANOLOL

l Diuretics: action of lidocaine antagonised by hypokalaemia caused by l ACETAZOLAMIDE, l LOOP DIURETICS or l THIAZIDES AND RELATED DIURETICS

▶ Muscle Relaxants: neuromuscular blockade enhanced and prolonged when lidocaine given with SUXAMETHONIUM

l Ulcer-healing Drugs: plasma concentration of lidocaine increased by l CIMETIDINE (increased risk of toxicity)

Linagliptin *see* Antidiabetics

Linezolid

NOTE Linezolid is a reversible, non-selective MAO inhibitor— see interactions of MAOIs

▶ Antibacterials: plasma concentration of linezolid reduced by

RIFAMPICIN (possible therapeutic failure of linezolid)

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Liothyronine *see* Thyroid Hormones

Lipegfilgrastim

▶ Cytotoxics: neutropenia possibly exacerbated when lipegfilgrastim given with CAPECITABINE, FLUOROURACIL or TEGAFUR

Lipid-regulating Drugs *see* Colesevelam, Colestipol, Colestyramine, Ezetimibe, Fibrates, Lomitapide, Nicotinic Acid, and Statins

Liraglutide *see* Antidiabetics Lisdexamfetamine *see* Sympathomimetics Lisinopril *see* ACE Inhibitors

Lithium

l ACE Inhibitors: excretion of lithium reduced by l ACE INHIBITORS (increased plasma concentration)

▶ Aminophylline: excretion of lithium increased by

AMINOPHYLLINE (reduced plasma concentration)

l Analgesics: excretion of lithium reduced by l NSAIDS (increased risk of toxicity); excretion of lithium reduced by l KETOROLAC (increased risk of toxicity)—avoid concomitant use

l Angiotensin-II Receptor Antagonists: excretion of lithium reduced by l ANGIOTENSIN-II RECEPTOR ANTAGONISTS (increased plasma concentration)

▶ Antacids: excretion of lithium increased by SODIUM BICARBONATE (reduced plasma concentration)

l Anti-arrhythmics: avoidance of lithium advised by manufacturer of l AMIODARONE (risk of ventricular arrhythmias)

▶ Antibacterials: increased risk of lithium toxicity when given with METRONIDAZOLE

l Antidepressants: possible increased serotonergic effects when lithium given with VENLAFAXINE; increased risk of CNS effects when lithium given with l SSRIS (lithium toxicity reported); risk of toxicity when lithium given with TRICYCLICS

▶ Antiepileptics: neurotoxicity may occur when lithium given with CARBAMAZEPINE, FOSPHENYTOIN or PHENYTOIN without

increased plasma concentration of lithium; plasma concentration of lithium possibly affected by TOPIRAMATE

l Antipsychotics: increased risk of extrapyramidal side-effects and possibly neurotoxicity when lithium given with CLOZAPINE, FLUPENTIXOL, HALOPERIDOL, PHENOTHIAZINES,

l RISPERIDONE or ZUCLOPENTHIXOL; possible risk of toxicity when lithium given with OLANZAPINE; lithium possibly increases extrapyramidal side-effects of QUETIAPINE; increased risk of extrapyramidal side-effects when lithium given with SULPIRIDE

▶ Anxiolytics and Hypnotics: increased risk of neurotoxicity when lithium given with CLONAZEPAM

▶ Calcium-channel Blockers: neurotoxicity may occur when lithium given with DILTIAZEM or VERAPAMIL without increased plasma concentration of lithium

l Cytotoxics: increased risk of ventricular arrhythmias when lithium given with l ARSENIC TRIOXIDE

l Dapoxetine: possible increased risk of serotonergic effects when lithium given with l DAPOXETINE (manufacturer of dapoxetine advises lithium should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping lithium)

l Diuretics: excretion of lithium increased by l ACETAZOLAMIDE; excretion of lithium reduced by l LOOP DIURETICS and

l THIAZIDES AND RELATED DIURETICS (increased plasma concentration and risk of toxicity)—loop diuretics safer than thiazides; excretion of lithium reduced by l POTASSIUM- SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS (increased

plasma concentration and risk of toxicity)

▶ 5HT1-receptor Agonists: possible risk of toxicity when lithium given with SUMATRIPTAN

l Methyldopa: neurotoxicity may occur when lithium given with l METHYLDOPA without increased plasma concentration of lithium

▶ Muscle Relaxants: lithium enhances effects of MUSCLE RELAXANTS; hyperkinesis caused by lithium possibly aggravated by BACLOFEN

▶ Parasympathomimetics: lithium antagonises effects of

NEOSTIGMINE

Lithium (continued)

▶ Theophylline: excretion of lithium increased by THEOPHYLLINE

Interactions | Appendix 1

(reduced plasma concentration)

Lixisenatide *see* Antidiabetics

Lofepramine *see* Antidepressants, Tricyclic

Lofexidine

▶ Alcohol: increased sedative effect when lofexidine given with

ALCOHOL

▶ Anxiolytics and Hypnotics: increased sedative effect when lofexidine given with ANXIOLYTICS AND HYPNOTICS

Lomitapide

▶ Alcohol: manufacturer of lomitapide advises avoid concomitant use with ALCOHOL

l Anti-arrhythmics: manufacturer of lomitapide advises separating administration from AMIODARONE by 12 hours; manufacturer of lomitapide advises avoid concomitant use with l DRONEDARONE (plasma concentration of lomitapide possibly increased)

l Antibacterials: manufacturer of lomitapide advises separating administration from AZITHROMYCIN and ISONIAZID by 12 hours; manufacturer of lomitapide advises avoid concomitant use with l CLARITHROMYCIN, l ERYTHROMYCIN and l TELITHROMYCIN

(plasma concentration of lomitapide possibly increased)

▶ Anticoagulants: lomitapide possibly enhances anticoagulant effect of WARFARIN

▶ Antidepressants: manufacturer of lomitapide advises separating administration from FLUOXETINE and FLUVOXAMINE by 12 hours

▶ Antidiabetics: manufacturer of lomitapide advises separating administration from LINAGLIPTIN by 12 hours

l Antifungals: plasma concentration of lomitapide increased by l KETOCONAZOLE—avoid concomitant use; manufacturer of lomitapide advises avoid concomitant use with l TRIAZOLES (plasma concentration of lomitapide possibly increased)

l Antivirals: manufacturer of lomitapide advises avoid concomitant use with l DARUNAVIR, l FOSAMPRENAVIR, l INDINAVIR, l LOPINAVIR, l RITONAVIR, l SAQUINAVIR,

l TELAPREVIR and l TIPRANAVIR (plasma concentration of lomitapide possibly increased)

▶ Anxiolytics and Hypnotics: manufacturer of lomitapide advises separating administration from ALPRAZOLAM by 12 hours

l Calcium-channel Blockers: manufacturer of lomitapide advises separating administration from AMLODIPINE and LACIDIPINE by 12 hours; manufacturer of lomitapide advises avoid concomitant use with l DILTIAZEM and l VERAPAMIL (plasma concentration of lomitapide possibly increased)

▶ Ciclosporin: manufacturer of lomitapide advises separating administration from CICLOSPORIN by 12 hours

▶ Cilostazol: manufacturer of lomitapide advises separating administration from CILOSTAZOL by 12 hours

▶ Cytotoxics: manufacturer of lomitapide advises separating administration from LAPATINIB, NILOTINIB and PAZOPANIB by 12 hours

▶ Fosaprepitant: manufacturer of lomitapide advises separating administration from FOSAPREPITANT by 12 hours

▶ Grapefruit Juice: manufacturer of lomitapide advises avoid concomitant use with GRAPEFRUIT JUICE

▶ Hormone Antagonists: manufacturer of lomitapide advises separating administration from BICALUTAMIDE by 12 hours

▶ Ivacaftor: manufacturer of lomitapide advises separating administration from IVACAFTOR by 12 hours

l Lipid-regulating Drugs: lomitapide increases plasma concentration of ATORVASTATIN—manufacturer of lomitapide advises reduce dose of atorvastatin by half or separate administration by 12 hours; lomitapide increases plasma concentration of l SIMVASTATIN (see under Simvastatin,

p. 181); absorption of lomitapide possibly reduced by BILE ACID SEQUESTRANTS (give at least 4 hours apart)

▶ Oestrogens: manufacturer of lomitapide advises separating administration from OESTROGENS by 12 hours

▶ Ranolazine: manufacturer of lomitapide advises separating administration from RANOLAZINE by 12 hours

▶ Tacrolimus: manufacturer of lomitapide advises separating administration from TACROLIMUS by 12 hours

▶ Ticagrelor: manufacturer of lomitapide advises separating administration from TICAGRELOR by 12 hours

Interactions | Appendix 1

Lomitapide (continued)

▶ Tolvaptan: manufacturer of lomitapide advises separating administration from TOLVAPTAN by 12 hours

▶ Ulcer-healing Drugs: manufacturer of lomitapide advises separating administration from CIMETIDINE and RANITIDINE by 12 hours

Lomustine

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Ulcer-healing Drugs: myelosuppressive effects of lomustine possibly enhanced by CIMETIDINE

Loperamide

▶ Desmopressin: loperamide increases plasma concentration of

*oral* DESMOPRESSIN

Lopinavir

NOTE In combination with ritonavir as *Kaletra* ® (ritonavir is present to inhibit lopinavir metabolism and increase plasma- lopinavir concentration)—see also Ritonavir

l Anti-arrhythmics: lopinavir possibly increases plasma concentration of l FLECAINIDE (increased risk of ventricular arrhythmias—avoid concomitant use); lopinavir possibly increases plasma concentration of LIDOCAINE

l Antibacterials: plasma concentration of lopinavir reduced by l RIFAMPICIN—avoid concomitant use; lopinavir increases plasma concentration of DELAMANID; avoidance of concomitant lopinavir in severe renal and hepatic impairment advised by manufacturer of l TELITHROMYCIN

▶ Anticoagulants: avoidance of lopinavir advised by manufacturer of APIXABAN; manufacturers advise avoid concomitant use of lopinavir with RIVAROXABAN

l Antidepressants: plasma concentration of lopinavir reduced by

l ST JOHN’S WORT—avoid concomitant use

l Antiepileptics: plasma concentration of lopinavir possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, l PHENOBARBITAL, PHENYTOIN and l PRIMIDONE

▶ Antihistamines: lopinavir possibly increases plasma concentration of CHLORPHENAMINE

▶ Antimalarials: caution with lopinavir advised by manufacturer of ARTEMETHER WITH LUMEFANTRINE

▶ Antimuscarinics: avoidance of lopinavir advised by manufacturer of DARIFENACIN and TOLTERODINE

l Antipsychotics: lopinavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); lopinavir possibly increases plasma concentration of

l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: manufacturers advise avoid concomitant use of lopinavir with l BOCEPREVIR and l TELAPREVIR; avoidance of lopinavir advised by manufacturer of DACLATASVIR (plasma concentration of daclatasvir possibly increased); lopinavir reduces plasma concentration of l DARUNAVIR, also plasma concentration of lopinavir increased (avoid concomitant use); plasma concentration of lopinavir reduced by

l EFAVIRENZ—consider increasing dose of lopinavir; lopinavir boosted with ritonavir increases plasma concentration of

l ELVITEGRAVIR (reduce dose of elvitegravir); lopinavir reduces plasma concentration of FOSAMPRENAVIR, effect on lopinavir plasma concentration not predictable—avoid concomitant use; lopinavir increases plasma concentration of l MARAVIROC (consider reducing dose of maraviroc); plasma concentration of lopinavir possibly reduced by l NEVIRAPINE—consider increasing dose of lopinavir; increased risk of ventricular arrhythmias when lopinavir given with l SAQUINAVIR—avoid concomitant use; lopinavir increases plasma concentration of TENOFOVIR; plasma concentration of lopinavir reduced by

l TIPRANAVIR

l Bosentan: lopinavir increases plasma concentration of

l BOSENTAN (consider reducing dose of bosentan)

▶ Corticosteroids: plasma concentration of lopinavir possibly reduced by DEXAMETHASONE

l Cytotoxics: manufacturer of ruxolitinib advises dose reduction when lopinavir given with l RUXOLITINIB—consult ruxolitinib product literature

▶ Eltrombopag: lopinavir possibly reduces plasma concentration of ELTROMBOPAG

Lopinavir (continued)

l Lipid-regulating Drugs: possible increased risk of myopathy when lopinavir given with ATORVASTATIN; lopinavir increases plasma concentration of l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature); possible increased risk of myopathy when lopinavir given with l SIMVASTATIN— avoid concomitant use; avoidance of lopinavir advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

l Orlistat: absorption of lopinavir possibly reduced by

l ORLISTAT

l Ranolazine: lopinavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

▶ Sirolimus: lopinavir possibly increases plasma concentration of SIROLIMUS

▶ Sympathomimetics, Beta2: manufacturer of lopinavir advises avoid concomitant use with SALMETEROL

Loprazolam *see* Anxiolytics and Hypnotics

Loratadine *see* Antihistamines

Lorazepam *see* Anxiolytics and Hypnotics Lormetazepam *see* Anxiolytics and Hypnotics Losartan *see* Angiotensin-II Receptor Antagonists Lurasidone *see* Antipsychotics

Lymecycline *see* Tetracyclines

Macitentan

l Antibacterials: plasma concentration of macitentan reduced by

l RIFAMPICIN—avoid concomitant use

▶ Antidepressants: manufacturer of macitentan advises avoid concomitant use with ST JOHN’S WORT

▶ Antiepileptics: manufacturer of macitentan advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN

▶ Antifungals: plasma concentration of macitentan increased by

KETOCONAZOLE

Macrogols

NOTE Some manufacturers suggest taking other oral medication 1 hour before or 1 hour after macrogols to reduce possible interference with absorption

Macrolides

NOTE *See also* Telithromycin

NOTE Interactions do not apply to small amounts of erythromycin used topically

l Aminophylline: clarithromycin possibly increases plasma concentration of AMINOPHYLLINE; erythromycin increases plasma concentration of l AMINOPHYLLINE (also aminophylline may reduce absorption of *oral* erythromycin)

▶ Analgesics: erythromycin increases plasma concentration of ALFENTANIL; clarithromycin possibly increases plasma concentration of FENTANYL

▶ Antacids: absorption of azithromycin reduced by ANTACIDS l Anti-arrhythmics: increased risk of ventricular arrhythmias when *parenteral* erythromycin given with l AMIODARONE—

avoid concomitant use; azithromycin possibly increases plasma concentration of l DISOPYRAMIDE (increased risk of toxicity); erythromycin increases plasma concentration of l DISOPYRAMIDE (increased risk of toxicity); clarithromycin possibly increases plasma concentration of l DISOPYRAMIDE (increased risk of ventricular arrhythmias); avoidance of clarithromycin advised by manufacturer of l DRONEDARONE (risk of ventricular arrhythmias); erythromycin increases plasma concentration of l DRONEDARONE (increased risk of ventricular arrhythmias—avoid concomitant use)

l Antibacterials: increased risk of ventricular arrhythmias when *parenteral* erythromycin given with l MOXIFLOXACIN—avoid concomitant use; increased risk of side-effects including neutropenia when azithromycin given with l RIFABUTIN; clarithromycin increases plasma concentration of l RIFABUTIN (increased risk of toxicity—reduce rifabutin dose); erythromycin possibly increases plasma concentration of

l RIFABUTIN (increased risk of toxicity—reduce rifabutin dose); clarithromycin and erythromycin possibly increase plasma concentration of BEDAQUILINE—avoid concomitant use if clarithromycin and erythromycin given for more than 14 days; possible increased risk of ventricular arrhythmias

Macrolides

l Antibacterials (continued)

when clarithromycin and erythromycin given with

l DELAMANID; avoidance of clarithromycin and erythromycin advised by manufacturer of FIDAXOMICIN; plasma concentration of clarithromycin reduced by RIFAMYCINS

l Anticoagulants: avoidance of clarithromycin advised by manufacturer of APIXABAN; clarithromycin and erythromycin enhance anticoagulant effect of l COUMARINS; azithromycin possibly enhances anticoagulant effect of l COUMARINS; possible increased risk of bleeding when clarithromycin given with DABIGATRAN

l Antidepressants: avoidance of macrolides advised by manufacturer of l REBOXETINE; avoidance of *intravenous* erythromycin advised by manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); clarithromycin possibly increases plasma concentration of TRAZODONE

▶ Antidiabetics: clarithromycin enhances effects of REPAGLINIDE

l Antiepileptics: clarithromycin increases plasma concentration of l CARBAMAZEPINE (consider reducing dose of carbamazepine); erythromycin increases plasma concentration of l CARBAMAZEPINE; clarithromycin inhibits metabolism of FOSPHENYTOIN and PHENYTOIN (increased plasma concentration); erythromycin possibly inhibits metabolism of SODIUM VALPROATE and VALPROIC ACID (increased plasma concentration)

l Antifungals: avoidance of concomitant clarithromycin in severe renal imapirment advised by manufacturer of

l KETOCONAZOLE; avoidance of erythromycin advised by manufacturer of FLUCONAZOLE; clarithromycin increases plasma concentration of ITRACONAZOLE

l Antihistamines: manufacturer of loratadine advises erythromycin possibly increases plasma concentration of LORATADINE; macrolides possibly inhibit metabolism of

l MIZOLASTINE (avoid concomitant use); erythromycin inhibits metabolism of l MIZOLASTINE—avoid concomitant use

l Antimalarials: avoidance of macrolides advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; avoidance of macrolides advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

▶ Antimuscarinics: erythromycin possibly increases plasma concentration of DARIFENACIN; manufacturer of fesoterodine advises dose reduction when clarithromycin given with FESOTERODINE—consult fesoterodine product literature; avoidance of clarithromycin and erythromycin advised by manufacturer of TOLTERODINE

l Antipsychotics: avoidance of macrolides advised by manufacturer of l DROPERIDOL (risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when *parenteral* erythromycin given with l ZUCLOPENTHIXOL—avoid concomitant use; increased risk of ventricular arrhythmias when erythromycin given with l AMISULPRIDE—avoid concomitant use; erythromycin possibly increases plasma concentration of l CLOZAPINE (possible increased risk of convulsions); clarithromycin possibly increases plasma concentration of l LURASIDONE—avoid concomitant use; erythromycin possibly increases the plasma concentration of l LURASIDONE (see under Lurasidone, p. 315); increased risk of ventricular arrhythmias when clarithromycin given with

l PIMOZIDE—avoid concomitant use; possible increased risk of ventricular arrhythmias when erythromycin given with

l PIMOZIDE—avoid concomitant use; clarithromycin possibly increases plasma concentration of l QUETIAPINE— manufacturer of quetiapine advises avoid concomitant use; erythromycin increases plasma concentration of

l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use; increased risk of ventricular arrhythmias when *parenteral* erythromycin given with l SULPIRIDE

l Antivirals: plasma concentration of both drugs increased when clarithromycin given with ATAZANAVIR; clarithromycin possibly increases the plasma concentration of

l DACLATASVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); plasma concentration of clarithromycin reduced by EFAVIRENZ, also plasma concentration of active

Macrolides

l Antivirals (continued)

Interactions | Appendix 1

metabolite of clarithromycin increased; plasma concentration of clarithromycin reduced by l ETRAVIRINE and NEVIRAPINE (but concentration of an active metabolite increased), also plasma concentration of etravirine and nevirapine increased; clarithromycin possibly increases plasma concentration of l MARAVIROC (consider reducing dose of maraviroc); avoidance of clarithromycin and erythromycin advised by manufacturer of l RILPIVIRINE (plasma concentration of rilpivirine possibly increased); plasma concentration of azithromycin and erythromycin possibly increased by RITONAVIR; plasma concentration of clarithromycin increased by l RITONAVIR (reduce dose of clarithromycin in renal impairment); increased risk of ventricular arrhythmias when erythromycin given with

l SAQUINAVIR—avoid concomitant use; plasma concentration of both drugs possibly increased when clarithromycin given with l SAQUINAVIR and l TELAPREVIR (increased risk of ventricular arrhythmias); plasma concentration of both drugs increased when erythromycin given with l SIMEPREVIR— manufacturer of simeprevir advises avoid concomitant use; clarithromycin possibly increases plasma concentration of

l SIMEPREVIR—manufacturer of simeprevir advises avoid concomitant use; plasma concentration of both drugs possibly increased when erythromycin given with

l TELAPREVIR (increased risk of ventricular arrhythmias); plasma concentration of clarithromycin increased by

l TIPRANAVIR (reduce dose of clarithromycin in renal impairment), also clarithromycin increases plasma concentration of tipranavir; clarithromycin tablets reduce absorption of ZIDOVUDINE (give at least 2 hours apart)

l Anxiolytics and Hypnotics: clarithromycin and erythromycin inhibit metabolism of l MIDAZOLAM (increased plasma concentration with increased sedation); erythromycin increases plasma concentration of BUSPIRONE (reduce dose of buspirone); erythromycin inhibits the metabolism of ZOPICLONE

▶ Aprepitant: clarithromycin possibly increases plasma concentration of APREPITANT

l Atomoxetine: increased risk of ventricular arrhythmias when

*parenteral* erythromycin given with l ATOMOXETINE

l Avanafil: clarithromycin possibly increases plasma concentration of l AVANAFIL—manufacturer of avanafil advises avoid concomitant use; erythromycin increases plasma concentration of l AVANAFIL—see under Avanafil, p. 698

l Calcium-channel Blockers: clarithromycin and erythromycin possibly inhibit metabolism of l CALCIUM-CHANNEL BLOCKERS (increased risk of side-effects); avoidance of erythromycin advised by manufacturer of LERCANIDIPINE

▶ Cardiac Glycosides: macrolides increase plasma concentration of DIGOXIN (increased risk of toxicity)

l Ciclosporin: macrolides possibly inhibit metabolism of

l CICLOSPORIN (increased plasma concentration); clarithromycin and erythromycin inhibit metabolism of l CICLOSPORIN (increased plasma concentration)

l Cilostazol: clarithromycin possibly increases plasma concentration of l CILOSTAZOL (see under Cilostazol, p. 206); erythromycin increases plasma concentration of l CILOSTAZOL (see under Cilostazol, p. 206)

l Clopidogrel: erythromycin possibly reduces antiplatelet effect of l CLOPIDOGREL

l Colchicine: azithromycin, clarithromycin and erythromycin possibly increase risk of l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

▶ Corticosteroids: erythromycin possibly inhibits metabolism of CORTICOSTEROIDS; erythromycin inhibits the metabolism of METHYLPREDNISOLONE; clarithromycin possibly increases plasma concentration of METHYLPREDNISOLONE

l Cytotoxics: erythromycin possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of erythromycin by 6 to 12 hours; clarithromycin and erythromycin possibly increase plasma concentration of AXITINIB (reduce dose of axitinib—consult

Interactions | Appendix 1

Macrolides

l Cytotoxics (continued)

axitinib product literature); clarithromycin and erythromycin possibly increase the plasma concentration of l BOSUTINIB— manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; clarithromycin and erythromycin possibly increase plasma concentration of CABOZANTINIB; clarithromycin possibly increases plasma concentration of

l CRIZOTINIB and l EVEROLIMUS—manufacturer of crizotinib and everolimus advises avoid concomitant use; avoidance of clarithromycin and erythromycin advised by manufacturer of DASATINIB (plasma concentration of dasatinib possibly increased); erythromycin increases plasma concentration of l EVEROLIMUS (consider reducing the dose of everolimus — consult everolimus product literature); clarithromycin and erythromycin possibly increase the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib,

p. 809); avoidance of clarithromycin advised by manufacturer of l NILOTINIB; clarithromycin possibly increases plasma concentration of l PAZOPANIB (reduce dose of pazopanib); clarithromycin possibly increases plasma concentration of PONATINIB—consider reducing initial dose of ponatinib (see under Ponatinib, p. 814); manufacturer of ruxolitinib advises dose reduction when clarithromycin given with

l RUXOLITINIB—consult ruxolitinib product literature; possible increased risk of ventricular arrhythmias when *parenteral* erythromycin given with l VANDETANIB—avoid concomitant use; clarithromycin possibly increases the plasma concentration of l CABAZITAXEL—manufacturer of cabazitaxel advises avoid or consider reducing dose of cabazitaxel; clarithromycin possibly increases plasma concentration of

l DOCETAXEL—manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose; increased risk of ventricular arrhythmias when erythromycin given with l ARSENIC TRIOXIDE; erythromycin increases toxicity of l VINBLASTINE—avoid concomitant use; possible increased risk of neutropenia when clarithromycin given with l VINORELBINE

▶ Dapoxetine: manufacturer of dapoxetine advises dose reduction when clarithromycin and erythromycin given with DAPOXETINE (see under Dapoxetine, p. 703)

l Diuretics: clarithromycin increases plasma concentration of l EPLERENONE—avoid concomitant use; erythromycin increases plasma concentration of EPLERENONE (reduce dose of eplerenone)

l Domperidone: possible increased risk of ventricular arrhythmias when clarithromycin given with

l DOMPERIDONE—avoid concomitant use; erythromycin increases plasma concentration of l DOMPERIDONE (increased risk of ventricular arrhythmias—avoid concomitant use)

▶ Dopaminergics: erythromycin increases plasma concentration of BROMOCRIPTINE and CABERGOLINE (increased risk of toxicity); macrolides possibly increase plasma concentration of BROMOCRIPTINE and CABERGOLINE (increased risk of toxicity)

l Ergot Alkaloids: increased risk of ergotism when clarithromycin or erythromycin given with l ERGOMETRINE— avoid concomitant use; increased risk of ergotism when macrolides given with l ERGOTAMINE—avoid concomitant use

▶ Fosaprepitant: clarithromycin possibly increases plasma concentration of FOSAPREPITANT

l 5HT1-receptor Agonists: clarithromycin and erythromycin increase plasma concentration of l ELETRIPTAN (risk of toxicity)—avoid concomitant use

l Ivabradine: clarithromycin possibly increases plasma

concentration of l IVABRADINE—avoid concomitant use; increased risk of ventricular arrhythmias when erythromycin given with l IVABRADINE—avoid concomitant use

l Ivacaftor: clarithromycin and erythromycin possibly increase plasma concentration of l IVACAFTOR (see under Ivacaftor, p. 257)

l Lenalidomide: clarithromycin possibly increases plasma concentration of l LENALIDOMIDE (increased risk of toxicity)

▶ Leukotriene Receptor Antagonists: erythromycin reduces plasma concentration of ZAFIRLUKAST

l Lipid-regulating Drugs: clarithromycin increases plasma concentration of l ATORVASTATIN and PRAVASTATIN; possible

Macrolides

l Lipid-regulating Drugs (continued)

increased risk of myopathy when erythromycin given with ATORVASTATIN; erythromycin increases plasma concentration of PRAVASTATIN; erythromycin reduces plasma concentration of ROSUVASTATIN; increased risk of myopathy when clarithromycin or erythromycin given with l SIMVASTATIN (avoid concomitant use); separating administration from azithromycin by 12 hours advised by manufacturer of LOMITAPIDE; avoidance of clarithromycin and erythromycin advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

▶ Mirabegron: when given with clarithromycin avoid or reduce dose of MIRABEGRON in hepatic or renal impairment—see Mirabegron, p. 671

▶ Oestrogens: erythromycin increases plasma concentration of

ESTRADIOL

▶ Parasympathomimetics: erythromycin increases plasma concentration of GALANTAMINE

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when *parenteral* erythromycin given with l PENTAMIDINE ISETIONATE

▶ Progestogens: erythromycin increases plasma concentration of DIENOGEST

l Ranolazine: clarithromycin possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

l Sildenafil: clarithromycin increases the plasma concentration of l SILDENAFIL—consider reducing initial dose of sildenafil for erectile dysfunction or reduce sildenafil dose frequency to once daily for pulmonary hypertension; erythromycin increases plasma concentration of SILDENAFIL—reduce initial dose of sildenafil for erectile dysfunction or reduce sildenafil dose frequency to twice daily for pulmonary hypertension

l Sirolimus: clarithromycin increases plasma concentration of l SIROLIMUS—avoid concomitant use; plasma concentration of both drugs increased when erythromycin given with

l SIROLIMUS

l Tacrolimus: clarithromycin and erythromycin increase plasma concentration of l TACROLIMUS

▶ Tadalafil: clarithromycin and erythromycin possibly increase plasma concentration of TADALAFIL

l Theophylline: clarithromycin possibly increases plasma concentration of THEOPHYLLINE; erythromycin increases plasma concentration of l THEOPHYLLINE (also theophylline may reduce absorption of *oral* erythromycin)

l Ticagrelor: clarithromycin possibly increases plasma concentration of l TICAGRELOR—manufacturer of ticagrelor advises avoid concomitant use; erythromycin possibly increases plasma concentration of TICAGRELOR

▶ Ulcer-healing Drugs: plasma concentration of erythromycin increased by CIMETIDINE (increased risk of toxicity, including deafness); plasma concentration of both drugs increased when clarithromycin given with OMEPRAZOLE

▶ Ulipristal: avoidance of clarithromycin advised by manufacturer of *low-dose* ULIPRISTAL; erythromycin increases plasma concentration of *low-dose* ULIPRISTAL—manufacturer of *low-dose* ulipristal advises avoid concomitant use

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

▶ Vardenafil: clarithromycin possibly increases plasma concentration of VARDENAFIL (consider reducing initial dose of vardenafil); erythromycin increases plasma concentration of VARDENAFIL (reduce dose of vardenafil)

Magnesium (parenteral)

l Calcium-channel Blockers: profound hypotension reported with concomitant use of parenteral magnesium and l NIFEDIPINE in pre-eclampsia

▶ Muscle Relaxants: parenteral magnesium enhances effects of

NON-DEPOLARISING MUSCLE RELAXANTS and SUXAMETHONIUM

Magnesium Salts (oral) *see* Antacids

Mannitol

▶ Antibacterials: avoidance of mannitol advised by manufacturer of TOBRAMYCIN

Mannitol (continued)

▶ Ciclosporin: possible increased risk of nephrotoxicity when mannitol given with CICLOSPORIN

MAOIs

NOTE For interactions of reversible MAO-A inhibitors (RIMAs) see Moclobemide, and for interactions of MAO-B inhibitors see Rasagiline and Selegiline; the antibacterial Linezolid is a reversible, non-selective MAO inhibitor

▶ ACE Inhibitors: MAOIs possibly enhance hypotensive effect of

ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when MAOIs given with ADRENERGIC NEURONE BLOCKERS

l Alcohol: MAOIs interact with tyramine found in some beverages containing l ALCOHOL and some dealcoholised beverages (hypertensive crisis)—if no tyramine, enhanced hypotensive effect

▶ Alpha2-adrenoceptor Stimulants: avoidance of MAOIs advised by manufacturer of APRACLONIDINE and BRIMONIDINE

l Alpha-blockers: avoidance of MAOIs advised by manufacturer of l INDORAMIN; enhanced hypotensive effect when MAOIs given with ALPHA-BLOCKERS

l Analgesics: possible increased serotonergic effects when MAOIs given with FENTANYL; CNS excitation or depression (hypertension or hypotension) when MAOIs given with

l PETHIDINE—avoid concomitant use and for 2 weeks after stopping MAOIs; possible increased serotonergic effects and increased risk of convulsions when MAOIs given with

l TRAMADOL—some manufacturers advise avoid concomitant use and for 2 weeks after stopping MAOIs; avoidance of MAOIs advised by manufacturer of l NEFOPAM; possible CNS excitation or depression (hypertension or hypotension) when MAOIs given with l OPIOID ANALGESICS—some manufacturers advise avoid concomitant use and for 2 weeks after stopping MAOIs

▶ Angiotensin-II Receptor Antagonists: MAOIs possibly enhance hypotensive effect of ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Antidepressants: increased risk of hypertension and CNS excitation when MAOIs given with l REBOXETINE (MAOIs should not be started until 1 week after stopping reboxetine, avoid reboxetine for 2 weeks after stopping MAOIs); after stopping MAOIs do not start l CITALOPRAM, l ESCITALOPRAM, l FLUVOXAMINE, l PAROXETINE or l SERTRALINE for 2 weeks,

also MAOIs should not be started until at least 1 week after stopping citalopram, escitalopram, fluvoxamine, paroxetine or sertraline; after stopping MAOIs do not start l FLUOXETINE for 2 weeks, also MAOIs should not be started until at least 5 weeks after stopping fluoxetine; after stopping MAOIs do not start l DULOXETINE for 2 weeks, also MAOIs should not be started until at least 5 days after stopping duloxetine; enhanced CNS effects and toxicity when MAOIs given with

l VENLAFAXINE (venlafaxine should not be started until 2 weeks after stopping MAOIs, avoid MAOIs for 1 week after stopping venlafaxine); increased risk of hypertension and CNS excitation when MAOIs given with other l MAOIS (avoid for at least 2 weeks after stopping previous MAOIs and then start at a reduced dose); after stopping MAOIs do not start

l MOCLOBEMIDE for at least 1 week; MAOIs increase CNS effects of l SSRIS (risk of serious toxicity); after stopping MAOIs do not start l MIRTAZAPINE for 2 weeks, also MAOIs should not be started until at least 2 weeks after stopping mirtazapine; after stopping MAOIs do not start l TRICYCLIC- RELATED ANTIDEPRESSANTS for 2 weeks, also MAOIs should not be started until at least 1–2 weeks after stopping tricyclic- related antidepressants; increased risk of hypertension and CNS excitation when MAOIs given with l TRICYCLICS, tricyclics should not be started until 2 weeks after stopping MAOIs (3 weeks if starting clomipramine or imipramine), also MAOIs should not be started for at least 1–2 weeks after stopping tricyclics (3 weeks in the case of clomipramine or imipramine)

▶ Antidiabetics: MAOIs possibly enhance hypoglycaemic effect of ANTIDIABETICS; MAOIs enhance hypoglycaemic effect of INSULIN, METFORMIN and SULFONYLUREAS

l Antiepileptics: MAOIs possibly antagonise anticonvulsant effect of ANTIEPILEPTICS (convulsive threshold lowered);

MAOIs

l Antiepileptics (continued)

Interactions | Appendix 1

avoidance for 2 weeks after stopping MAOIs advised by manufacturer of l CARBAMAZEPINE, also antagonism of anticonvulsant effect

▶ Antihistamines: avoidance of MAOIs advised by manufacturer of HYDROXYZINE; avoidance of promethazine for 2 weeks after stopping MAOIs advised by manufacturer of PROMETHAZINE; increased antimuscarinic and sedative effects when MAOIs given with ANTIHISTAMINES

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

▶ Antimuscarinics: increased risk of antimuscarinic side-effects when MAOIs given with ANTIMUSCARINICS

l Antipsychotics: CNS effects of MAOIs possibly increased by

l CLOZAPINE

l Anxiolytics and Hypnotics: avoidance of MAOIs advised by manufacturer of BUSPIRONE; manufacturer of tranylcypromine advises avoid l BUSPIRONE for 14 days after stopping tranylcypromine

l Atomoxetine: after stopping MAOIs do not start l ATOMOXETINE for 2 weeks, also MAOIs should not be started until at least 2 weeks after stopping atomoxetine; possible increased risk of convulsions when antidepressants given with ATOMOXETINE

▶ Beta-blockers: enhanced hypotensive effect when MAOIs given with BETA-BLOCKERS

l Bupropion: avoidance of bupropion for 2 weeks after stopping MAOIs advised by manufacturer of l BUPROPION

▶ Calcium-channel Blockers: enhanced hypotensive effect when MAOIs given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when MAOIs given with CLONIDINE

l Dapoxetine: increased risk of serotonergic effects when MAOIs given with l DAPOXETINE (MAOIs should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping MAOIs)

▶ Diazoxide: enhanced hypotensive effect when MAOIs given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when MAOIs given with DIURETICS

l Dopaminergics: risk of hypertensive crisis when MAOIs given with l CO-BENELDOPA, l CO-CARELDOPA or l LEVODOPA, avoid

co-beneldopa, co-careldopa or levodopa for at least 2 weeks after stopping MAOIs; avoid concomitant use of non- selective MAOIs with l ENTACAPONE; risk of hypertensive crisis when MAOIs given with l RASAGILINE, avoid MAOIs for at least 2 weeks after stopping rasagiline; enhanced hypotensive effect when MAOIs given with l SELEGILINE— manufacturer of selegiline advises avoid concomitant use; avoid concomitant use of MAOIs with TOLCAPONE

▶ Doxapram: MAOIs enhance effects of DOXAPRAM

▶ Histamine: avoidance of MAOIs advised by manufacturer of

HISTAMINE

l 5HT1-receptor Agonists: risk of CNS toxicity when MAOIs given with l RIZATRIPTAN or l SUMATRIPTAN (avoid rizatriptan or sumatriptan for 2 weeks after MAOIs); risk of CNS toxicity when MAOIs given with l ZOLMITRIPTAN (reduce dose of zolmitriptan)

l Methyldopa: avoidance of MAOIs advised by manufacturer of

l METHYLDOPA

▶ Moxonidine: enhanced hypotensive effect when MAOIs given with MOXONIDINE

▶ Muscle Relaxants: phenelzine enhances effects of

SUXAMETHONIUM

▶ Nicorandil: enhanced hypotensive effect when MAOIs given with NICORANDIL

▶ Nitrates: enhanced hypotensive effect when MAOIs given with

NITRATES

▶ Pholcodine: avoidance of pholcodine for 2 weeks after stopping MAOIs advised by manufacturer of PHOLCODINE

l Sympathomimetics: risk of hypertensive crisis when MAOIs given with l ADRENALINE (EPINEPHRINE), l DOBUTAMINE,

l DOPAMINE, l NORADRENALINE (NOREPINEPHRINE) or

l XYLOMETAZOLINE; risk of hypertensive crisis when MAOIs given with l DEXAMFETAMINE, l EPHEDRINE, l ISOMETHEPTENE,

Interactions | Appendix 1

MAOIs

l Sympathomimetics (continued)

l LISDEXAMFETAMINE, l METARAMINOL, l METHYLPHENIDATE,

l PHENYLEPHRINE or l PSEUDOEPHEDRINE, avoid

dexamfetamine, ephedrine, isometheptene, lisdexamfetamine, metaraminol, methylphenidate, phenylephrine or pseudoephedrine for at least 2 weeks after stopping MAOIs; risk of hypertensive crisis when MAOIs given with l OXYMETAZOLINE, some manufacturers advise avoid oxymetazoline for at least 2 weeks after stopping MAOIs

l Tetrabenazine: risk of CNS toxicity when MAOIs given with l TETRABENAZINE (avoid tetrabenazine for 2 weeks after MAOIs)

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when MAOIs given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

MAOIs, reversible *see* Moclobemide

Maraviroc

l Antibacterials: plasma concentration of maraviroc possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN (consider reducing dose of maraviroc); plasma concentration of maraviroc reduced by l RIFAMPICIN—consider increasing dose of maraviroc

l Antidepressants: plasma concentration of maraviroc possibly

reduced by l ST JOHN’S WORT—avoid concomitant use

l Antifungals: plasma concentration of maraviroc increased by

l KETOCONAZOLE (consider reducing dose of maraviroc)

l Antivirals: plasma concentration of maraviroc increased by

l ATAZANAVIR, BOCEPREVIR, l DARUNAVIR, l INDINAVIR,

l LOPINAVIR, l SAQUINAVIR and TELAPREVIR (consider reducing dose of maraviroc); plasma concentration of maraviroc possibly reduced by l EFAVIRENZ—consider increasing dose of maraviroc; plasma concentration of maraviroc possibly reduced by ETRAVIRINE; maraviroc reduces plasma concentration of l FOSAMPRENAVIR—avoid concomitant use; plasma concentration of maraviroc increased by RITONAVIR

l Cobicistat: plasma concentration of maraviroc possibly increased by l COBICISTAT (reduce dose of maraviroc)

l Orlistat: absorption of maraviroc possibly reduced by

l ORLISTAT

Mebendazole

▶ Ulcer-healing Drugs: metabolism of mebendazole possibly inhibited by CIMETIDINE (increased plasma concentration)

Medroxyprogesterone *see* Progestogens

Mefenamic Acid *see* NSAIDs

Mefloquine

l Anti-arrhythmics: increased risk of ventricular arrhythmias when mefloquine given with l AMIODARONE—avoid concomitant use

l Antibacterials: increased risk of ventricular arrhythmias when mefloquine given with l MOXIFLOXACIN—avoid concomitant use; plasma concentration of mefloquine reduced by

l RIFAMPICIN—avoid concomitant use

l Antiepileptics: mefloquine antagonises anticonvulsant effect of l ANTIEPILEPTICS

▶ Antifungals: plasma concentration of mefloquine increased by

KETOCONAZOLE

l Antimalarials: avoidance of antimalarials advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; increased risk of convulsions when mefloquine given with

l CHLOROQUINE or l HYDROXYCHLOROQUINE; increased risk of convulsions when mefloquine given with l QUININE (but should not prevent the use of *intravenous* quinine in severe cases)

l Antipsychotics: possible increased risk of ventricular arrhythmias when mefloquine given with l HALOPERIDOL— avoid concomitant use; avoidance of mefloquine advised by manufacturer of AMISULPRIDE; increased risk of ventricular arrhythmias when mefloquine given with l PIMOZIDE—avoid concomitant use; manufacturer of risperidone advises possible risk of ventricular arrhythmias when mefloquine given with l RISPERIDONE

▶ Antivirals: mefloquine possibly reduces plasma concentration of RITONAVIR

Mefloquine (continued)

l Atomoxetine: increased risk of ventricular arrhythmias when mefloquine given with l ATOMOXETINE

▶ Beta-blockers: increased risk of bradycardia when mefloquine given with BETA-BLOCKERS

▶ Calcium-channel Blockers: possible increased risk of bradycardia when mefloquine given with CALCIUM-CHANNEL BLOCKERS

▶ Cardiac Glycosides: possible increased risk of bradycardia when mefloquine given with DIGOXIN

▶ Cytotoxics: possible increased risk of bradycardia when mefloquine given with CRIZOTINIB

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

l Ivabradine: increased risk of ventricular arrhythmias when mefloquine given with l IVABRADINE

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Megestrol *see* Progestogens

Melatonin *see* Anxiolytics and Hypnotics

Meloxicam *see* NSAIDs

Melphalan

▶ Antibacterials: increased risk of melphalan toxicity when given with NALIDIXIC ACID

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: melphalan possibly reduces absorption of

DIGOXIN *tablets*

l Ciclosporin: increased risk of nephrotoxicity when melphalan given with l CICLOSPORIN

Memantine

l Anaesthetics, General: increased risk of CNS toxicity when memantine given with l KETAMINE (manufacturer of memantine advises avoid concomitant use)

l Analgesics: increased risk of CNS toxicity when memantine given with l DEXTROMETHORPHAN (manufacturer of memantine advises avoid concomitant use)

▶ Anticoagulants: memantine possibly enhances anticoagulant effect of WARFARIN

▶ Antimuscarinics: memantine possibly enhances effects of

ANTIMUSCARINICS

▶ Antipsychotics: memantine possibly reduces effects of

ANTIPSYCHOTICS

l Dopaminergics: memantine possibly enhances effects of DOPAMINERGICS and SELEGILINE; increased risk of CNS toxicity when memantine given with l AMANTADINE (manufacturer of memantine advises avoid concomitant use)

▶ Muscle Relaxants: memantine possibly modifies effects of

BACLOFEN and DANTROLENE

Meningococcal Vaccines *see* Vaccines

Mepacrine

▶ Antimalarials: mepacrine increases plasma concentration of

PRIMAQUINE (increased risk of toxicity) Meprobamate *see* Anxiolytics and Hypnotics Meptazinol *see* Opioid Analgesics Mercaptopurine

l Allopurinol: enhanced effects and increased toxicity of

mercaptopurine when given with l ALLOPURINOL (reduce dose of mercaptopurine to one quarter of usual dose)

l Antibacterials: increased risk of haematological toxicity when mercaptopurine given with l SULFAMETHOXAZOLE (as co- trimoxazole); increased risk of haematological toxicity when mercaptopurine given with l TRIMETHOPRIM (also with co- trimoxazole)

l Anticoagulants: mercaptopurine possibly reduces anticoagulant effect of l COUMARINS

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Dairy Products: plasma concentration of mercaptopurine possibly reduced by DAIRY PRODUCTS—manufacturer of mercaptopurine advises give at least 1 hour before or 2 hours after dairy products

l Febuxostat: avoidance of mercaptopurine advised by manufacturer of l FEBUXOSTAT

Meropenem

l Antiepileptics: carbapenems reduce plasma concentration of

l SODIUM VALPROATE and l VALPROIC ACID—avoid concomitant use

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Mestranol *see* Oestrogens Metaraminol *see* Sympathomimetics Metformin *see* Antidiabetics Methadone *see* Opioid Analgesics Methenamine

▶ Antacids: avoid concomitant use of methenamine with

ANTACIDS

l Antibacterials: increased risk of crystalluria when methenamine given with l SULFONAMIDES

l Diuretics: effects of methenamine antagonised by

l ACETAZOLAMIDE

▶ Potassium Salts: avoid concomitant use of methenamine with

POTASSIUM CITRATE

▶ Sodium Citrate: avoid concomitant use of methenamine with

SODIUM CITRATE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Methocarbamol *see* Muscle Relaxants

Methotrexate

▶ Aminophylline: methotrexate possibly increases plasma concentration of AMINOPHYLLINE

l Anaesthetics, General: antifolate effect of methotrexate increased by l NITROUS OXIDE—avoid concomitant use

l Analgesics: excretion of methotrexate probably reduced by l NSAIDS (increased risk of toxicity); excretion of methotrexate reduced by l ASPIRIN, l DICLOFENAC,

l IBUPROFEN, l INDOMETACIN, l KETOPROFEN, l MELOXICAM and

l NAPROXEN (increased risk of toxicity)

l Antibacterials: absorption of methotrexate possibly reduced by NEOMYCIN; excretion of methotrexate possibly reduced by CIPROFLOXACIN (increased risk of toxicity); increased risk of haematological toxicity when methotrexate given with

l SULFAMETHOXAZOLE (as co-trimoxazole); increased risk of methotrexate toxicity when given with DOXYCYCLINE, SULFONAMIDES or TETRACYCLINE; excretion of methotrexate reduced by PENICILLINS (increased risk of toxicity); increased risk of haematological toxicity when methotrexate given with l TRIMETHOPRIM (also with co-trimoxazole)

▶ Antiepileptics: antifolate effect of methotrexate increased by

FOSPHENYTOIN and PHENYTOIN

l Antimalarials: antifolate effect of methotrexate increased by

l PYRIMETHAMINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: methotrexate possibly reduces absorption of DIGOXIN *tablets*

l Ciclosporin: risk of toxicity when methotrexate given with

l CICLOSPORIN

▶ Corticosteroids: possible increased risk of hepatoxicity when

*high-dose* methotrexate given with DEXAMETHASONE

l Cytotoxics: increased pulmonary toxicity when methotrexate given with l CISPLATIN

▶ Diuretics: excretion of methotrexate increased by alkaline urine due to ACETAZOLAMIDE

l Leflunomide: risk of toxicity when methotrexate given with

l LEFLUNOMIDE

l Retinoids: plasma concentration of methotrexate increased by l ACITRETIN (also increased risk of hepatotoxicity)—avoid concomitant use

▶ Theophylline: methotrexate possibly increases plasma concentration of THEOPHYLLINE

▶ Ulcer-healing Drugs: excretion of methotrexate possibly reduced by PROTON PUMP INHIBITORS (increased risk of toxicity)

Methyldopa

▶ ACE Inhibitors: enhanced hypotensive effect when methyldopa given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when methyldopa given with ADRENERGIC NEURONE BLOCKERS

Methyldopa (continued)

▶ Alcohol: enhanced hypotensive effect when methyldopa given with ALCOHOL

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▶ Aldesleukin: enhanced hypotensive effect when methyldopa given with ALDESLEUKIN

▶ Alpha-blockers: enhanced hypotensive effect when methyldopa given with ALPHA-BLOCKERS

▶ Anaesthetics, General: enhanced hypotensive effect when methyldopa given with GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of methyldopa antagonised by

NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when methyldopa given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Antidepressants: manufacturer of methyldopa advises avoid

concomitant use with l MAOIS

▶ Antipsychotics: enhanced hypotensive effect when methyldopa given with ANTIPSYCHOTICS (also increased risk of extrapyramidal effects)

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when methyldopa given with ANXIOLYTICS AND HYPNOTICS

▶ Beta-blockers: enhanced hypotensive effect when methyldopa given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when methyldopa given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when methyldopa given with CLONIDINE

▶ Corticosteroids: hypotensive effect of methyldopa antagonised by CORTICOSTEROIDS

▶ Diazoxide: enhanced hypotensive effect when methyldopa given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when methyldopa given with DIURETICS

▶ Dopaminergics: methyldopa antagonises antiparkinsonian effect of DOPAMINERGICS; increased risk of extrapyramidal side-effects when methyldopa given with AMANTADINE; enhanced hypotensive effect when methyldopa given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA; effects of

methyldopa possibly enhanced by ENTACAPONE

▶ Iron Salts: hypotensive effect of methyldopa antagonised by

*oral* IRON SALTS

l Lithium: neurotoxicity may occur when methyldopa given with l LITHIUM without increased plasma concentration of lithium

▶ Moxisylyte: enhanced hypotensive effect when methyldopa given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when methyldopa given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when methyldopa given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when methyldopa given with NITRATES

▶ Oestrogens: hypotensive effect of methyldopa antagonised by

OESTROGENS

▶ Prostaglandins: enhanced hypotensive effect when methyldopa given with ALPROSTADIL

l Sympathomimetics, Beta2: acute hypotension reported when methyldopa given with *infusion* of l SALBUTAMOL

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when methyldopa given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Methylphenidate *see* Sympathomimetics Methylprednisolone *see* Corticosteroids Methylthioninium

l Antidepressants: risk of CNS toxicity when methylthioninium

given with l SSRI-RELATED ANTIDEPRESSANTS, l SSRIS and

l CLOMIPRAMINE—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration); possible risk of CNS toxicity when methylthioninium given with l MIRTAZAPINE—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

l Anxiolytics and Hypnotics: possible risk of CNS toxicity when methylthioninium given with l BUSPIRONE—avoid concomitant use (if avoidance not possible, use lowest

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Methylthioninium

l Anxiolytics and Hypnotics (continued)

possible dose of methylthioninium and observe patient for up to 4 hours after administration)

l Bupropion: possible risk of CNS toxicity when methylthioninium given with l BUPROPION—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

Metoclopramide

▶ Alcohol: metoclopramide possibly increases absorption of

ALCOHOL

▶ Anaesthetics, General: metoclopramide enhances effects of

THIOPENTAL

▶ Analgesics: metoclopramide increases rate of absorption of ASPIRIN (enhanced effect); effects of metoclopramide on gastro-intestinal activity antagonised by OPIOID ANALGESICS; metoclopramide increases rate of absorption of PARACETAMOL

▶ Antibacterials: metoclopramide reduces plasma concentration of FOSFOMYCIN

▶ Antidepressants: CNS toxicity reported when metoclopramide given with SSRIS

▶ Antimuscarinics: effects of metoclopramide on gastro- intestinal activity antagonised by ANTIMUSCARINICS

▶ Antipsychotics: increased risk of extrapyramidal side-effects when metoclopramide given with ANTIPSYCHOTICS

▶ Atovaquone: metoclopramide reduces plasma concentration of

ATOVAQUONE—avoid concomitant use

l Ciclosporin: metoclopramide increases plasma concentration of l CICLOSPORIN

▶ Dopaminergics: metoclopramide antagonises hypoprolactinaemic effects of BROMOCRIPTINE and CABERGOLINE; metoclopramide antagonises antiparkinsonian effect of PERGOLIDE; avoidance of metoclopramide advised by manufacturer of ROPINIROLE and ROTIGOTINE (antagonism of effect)

▶ Muscle Relaxants: metoclopramide enhances effects of

SUXAMETHONIUM

▶ Tetrabenazine: increased risk of extrapyramidal side-effects when metoclopramide given with TETRABENAZINE

Metolazone *see* Diuretics Metoprolol *see* Beta-blockers Metronidazole

NOTE Interactions do not apply to topical metronidazole preparations

▶ Alcohol: disulfiram-like reaction when metronidazole given with ALCOHOL

l Anticoagulants: metronidazole enhances anticoagulant effect of l COUMARINS

▶ Antiepileptics: metronidazole possibly inhibits metabolism of FOSPHENYTOIN and PHENYTOIN (increased plasma concentration); metabolism of metronidazole accelerated by PHENOBARBITAL and PRIMIDONE (reduced effect)

l Cytotoxics: metronidazole increases plasma concentration of l BUSULFAN (increased risk of toxicity); metronidazole inhibits metabolism of CAPECITABINE, FLUOROURACIL and TEGAFUR (increased toxicity)

▶ Disulfiram: psychotic reaction reported when metronidazole given with DISULFIRAM

▶ Lithium: metronidazole increases risk of LITHIUM toxicity

▶ Mycophenolate: metronidazole possibly reduces bioavailability of MYCOPHENOLATE

▶ Ulcer-healing Drugs: metabolism of metronidazole inhibited by

CIMETIDINE (increased plasma concentration)

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Mianserin *see* Antidepressants, Tricyclic (related)

Micafungin

▶ Antifungals: micafungin possibly increases plasma concentration of AMPHOTERICIN; micafungin increases plasma concentration of ITRACONAZOLE (consider reducing dose of itraconazole)

▶ Calcium-channel Blockers: micafungin increases plasma concentration of NIFEDIPINE

Micafungin (continued)

▶ Ciclosporin: micafungin possibly increases plasma concentration of CICLOSPORIN

▶ Sirolimus: micafungin increases plasma concentration of

SIROLIMUS

Miconazole *see* Antifungals, Imidazole Midazolam *see* Anxiolytics and Hypnotics Mifamurtide

▶ Analgesics: manufacturer of mifamurtide advises avoid

concomitant use with high doses of NSAIDS

▶ Ciclosporin: manufacturer of mifamurtide advises avoid concomitant use with CICLOSPORIN

▶ Corticosteroids: manufacturer of mifamurtide advises avoid concomitant use with CORTICOSTEROIDS

▶ Tacrolimus: manufacturer of mifamurtide advises avoid concomitant use with TACROLIMUS

Mifepristone

▶ Corticosteroids: mifepristone may reduce effect of CORTICOSTEROIDS (including *inhaled* corticosteroids) for 3–4 days

Milrinone *see* Phosphodiesterase Inhibitors

Minocycline *see* Tetracyclines

Minoxidil *see* Vasodilator Antihypertensives

Mirabegron

▶ Antibacterials: avoid or reduce dose of mirabegron in hepatic or renal impairment when given with CLARITHROMYCIN—see Mirabegron, p. 671

▶ Antifungals: avoid or reduce dose of mirabegron in hepatic or renal impairment when given with ITRACONAZOLE and KETOCONAZOLE—see Mirabegron, p. 671

▶ Antivirals: avoid or reduce dose of mirabegron in hepatic or renal impairment when given with RITONAVIR—see Mirabegron, p. 671

▶ Beta-blockers: mirabegron increases plasma concentration of

METOPROLOL

▶ Cardiac Glycosides: mirabegron increases plasma concentration of DIGOXIN—reduce initial dose of digoxin

Mirtazapine

l Alcohol: increased sedative effect when mirtazapine given with l ALCOHOL

▶ Analgesics: possible increased serotonergic effects when mirtazapine given with TRAMADOL

▶ Anticoagulants: mirtazapine enhances anticoagulant effect of

WARFARIN

l Antidepressants: possible increased serotonergic effects when mirtazapine given with FLUOXETINE, FLUVOXAMINE or VENLAFAXINE; mirtazapine should not be started until 2 weeks after stopping l MAOIS, also MAOIs should not be started until at least 2 weeks after stopping mirtazapine; after stopping mirtazapine do not start l MOCLOBEMIDE for at least 1 week

▶ Antiepileptics: plasma concentration of mirtazapine reduced by CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN

▶ Antifungals: plasma concentration of mirtazapine increased by

KETOCONAZOLE

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

▶ Anxiolytics and Hypnotics: increased sedative effect when mirtazapine given with ANXIOLYTICS AND HYPNOTICS

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

▶ Clonidine: mirtazapine possibly antagonises hypotensive effect of CLONIDINE

l Methylthioninium: possible risk of CNS toxicity when mirtazapine given with l METHYLTHIONINIUM—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

▶ Ulcer-healing Drugs: plasma concentration of mirtazapine increased by CIMETIDINE

Mitomycin

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Mitotane

l Anticoagulants: mitotane possibly reduces anticoagulant effect of l COUMARINS

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Diuretics: manufacturer of mitotane advises avoid concomitant use of SPIRONOLACTONE (antagonism of effect)

Mitoxantrone

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Ciclosporin: excretion of mitoxantrone reduced by CICLOSPORIN

(increased plasma concentration) Mivacurium *see* Muscle Relaxants Mizolastine *see* Antihistamines MMR Vaccine *see* Vaccines Moclobemide

l Analgesics: possible CNS excitation or depression

(hypertension or hypotension) when moclobemide given with l DEXTROMETHORPHAN or l PETHIDINE—avoid concomitant use; possible CNS excitation or depression (hypertension or hypotension) when moclobemide given with l OPIOID ANALGESICS—manufacturer of moclobemide advises consider reducing dose of opioid analgesics

l Antidepressants: moclobemide should not be started for at least 1 week after stopping l MAOIS, l SSRI-RELATED ANTIDEPRESSANTS, l CITALOPRAM, l FLUVOXAMINE,

l MIRTAZAPINE, l PAROXETINE, l SERTRALINE, l TRICYCLIC-

RELATED ANTIDEPRESSANTS or l TRICYCLICS; increased risk of CNS toxicity when moclobemide given with l ESCITALOPRAM, preferably avoid concomitant use; moclobemide should not be started until 5 weeks after stopping l FLUOXETINE; possible increased serotonergic effects when moclobemide given with l DULOXETINE

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

l Bupropion: avoidance of moclobemide advised by manufacturer of l BUPROPION

l Clopidogrel: moclobemide possibly reduces antiplatelet effect of l CLOPIDOGREL

l Dopaminergics: increased risk of side-effects when moclobemide given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA; caution with moclobemide advised by manufacturer of ENTACAPONE; avoid concomitant use of moclobemide with l SELEGILINE

l 5HT1-receptor Agonists: risk of CNS toxicity when moclobemide given with l RIZATRIPTAN or l SUMATRIPTAN (avoid rizatriptan or sumatriptan for 2 weeks after moclobemide); risk of CNS toxicity when moclobemide given with l ZOLMITRIPTAN (reduce dose of zolmitriptan)

l Sympathomimetics: risk of hypertensive crisis when moclobemide given with l SYMPATHOMIMETICS

▶ Ulcer-healing Drugs: plasma concentration of moclobemide increased by CIMETIDINE (halve dose of moclobemide)

Modafinil

▶ Antiepileptics: modafinil possibly increases plasma concentration of FOSPHENYTOIN and PHENYTOIN

l Ciclosporin: modafinil reduces plasma concentration of

l CICLOSPORIN

l Cytotoxics: modafinil possibly reduces plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid concomitant use

l Oestrogens: modafinil accelerates metabolism of l OESTROGENS

(reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

Moexipril *see* ACE Inhibitors Mometasone *see* Corticosteroids Monobactams *see* Aztreonam

Monoclonal antibodies *see* individual drugs Montelukast *see* Leukotriene Receptor Antagonists Morphine *see* Opioid Analgesics

Moxifloxacin *see* Quinolones

Moxisylyte

▶ ACE Inhibitors: enhanced hypotensive effect when moxisylyte given with ACE INHIBITORS

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▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when moxisylyte given with ADRENERGIC NEURONE BLOCKERS

l Alpha-blockers: possible severe postural hypotension when moxisylyte given with l ALPHA-BLOCKERS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when moxisylyte given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Beta-blockers: possible severe postural hypotension when

moxisylyte given with l BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when moxisylyte given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when moxisylyte given with CLONIDINE

▶ Diazoxide: enhanced hypotensive effect when moxisylyte given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when moxisylyte given with DIURETICS

▶ Methyldopa: enhanced hypotensive effect when moxisylyte given with METHYLDOPA

▶ Moxonidine: enhanced hypotensive effect when moxisylyte given with MOXONIDINE

▶ Nitrates: enhanced hypotensive effect when moxisylyte given with NITRATES

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when moxisylyte given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Moxonidine

▶ ACE Inhibitors: enhanced hypotensive effect when moxonidine given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when moxonidine given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when moxonidine given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when moxonidine given with ALDESLEUKIN

▶ Alpha-blockers: enhanced hypotensive effect when moxonidine given with ALPHA-BLOCKERS

▶ Anaesthetics, General: enhanced hypotensive effect when moxonidine given with GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of moxonidine antagonised by

NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when moxonidine given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antidepressants: enhanced hypotensive effect when moxonidine given with MAOIS; hypotensive effect of moxonidine possibly antagonised by TRICYCLICS (manufacturer of moxonidine advises avoid concomitant use)

▶ Antipsychotics: enhanced hypotensive effect when moxonidine given with PHENOTHIAZINES

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when moxonidine given with ANXIOLYTICS AND HYPNOTICS; sedative effects possibly increased when moxonidine given with BENZODIAZEPINES

▶ Beta-blockers: enhanced hypotensive effect when moxonidine given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when moxonidine given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when moxonidine given with CLONIDINE

▶ Corticosteroids: hypotensive effect of moxonidine antagonised by CORTICOSTEROIDS

▶ Diazoxide: enhanced hypotensive effect when moxonidine given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when moxonidine given with DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when moxonidine given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Methyldopa: enhanced hypotensive effect when moxonidine given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when moxonidine given with MOXISYLYTE

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Moxonidine (continued)

▶ Muscle Relaxants: enhanced hypotensive effect when moxonidine given with BACLOFEN or TIZANIDINE

▶ Nitrates: enhanced hypotensive effect when moxonidine given with NITRATES

▶ Oestrogens: hypotensive effect of moxonidine antagonised by

OESTROGENS

▶ Prostaglandins: enhanced hypotensive effect when moxonidine given with ALPROSTADIL

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when moxonidine given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Muscle Relaxants

▶ ACE Inhibitors: enhanced hypotensive effect when baclofen or tizanidine given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when baclofen or tizanidine given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: increased sedative effect when baclofen, methocarbamol or tizanidine given with ALCOHOL

▶ Alpha-blockers: enhanced hypotensive effect when baclofen or tizanidine given with ALPHA-BLOCKERS

l Anaesthetics, General: effects of atracurium enhanced by KETAMINE; increased risk of myocardial depression and bradycardia when suxamethonium given with l PROPOFOL; effects of non-depolarising muscle relaxants and suxamethonium enhanced by VOLATILE LIQUID GENERAL ANAESTHETICS

▶ Analgesics: excretion of baclofen possibly reduced by NSAIDS (increased risk of toxicity); excretion of baclofen reduced by IBUPROFEN (increased risk of toxicity); increased sedative effect when baclofen given with FENTANYL or MORPHINE

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when baclofen or tizanidine given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Anti-arrhythmics: neuromuscular blockade enhanced and prolonged when suxamethonium given with LIDOCAINE

l Antibacterials: effects of non-depolarising muscle relaxants and suxamethonium enhanced by PIPERACILLIN; plasma concentration of tizanidine increased by l CIPROFLOXACIN (increased risk of toxicity)—avoid concomitant use; plasma concentration of tizanidine possibly increased by NORFLOXACIN (increased risk of toxicity); plasma concentration of tizanidine possibly reduced by RIFAMPICIN; effects of non-depolarising muscle relaxants and suxamethonium enhanced by l AMINOGLYCOSIDES; effects of non-depolarising muscle relaxants and suxamethonium enhanced by l CLINDAMYCIN; effects of non-depolarising muscle relaxants and suxamethonium enhanced by

l POLYMYXINS; effects of suxamethonium enhanced by

l VANCOMYCIN

l Antidepressants: plasma concentration of tizanidine increased by l FLUVOXAMINE (increased risk of toxicity)—avoid concomitant use; effects of suxamethonium enhanced by PHENELZINE; muscle relaxant effect of baclofen enhanced by TRICYCLICS

l Antiepileptics: muscle relaxant effect of non-depolarising muscle relaxants antagonised by CARBAMAZEPINE (accelerated recovery from neuromuscular blockade); effects of non- depolarising muscle relaxants reduced by *long-term use* of

l FOSPHENYTOIN and l PHENYTOIN (but effects of non- depolarising muscle relaxants might be increased by *acute use* of fosphenytoin and phenytoin)

▶ Antimalarials: effects of suxamethonium possibly enhanced by

QUININE

▶ Antipsychotics: effects of suxamethonium possibly enhanced by PROMAZINE

▶ Anxiolytics and Hypnotics: increased sedative effect when baclofen or tizanidine given with ANXIOLYTICS AND HYPNOTICS

▶ Beta-blockers: enhanced hypotensive effect when baclofen given with BETA-BLOCKERS; possible enhanced hypotensive effect and bradycardia when tizanidine given with BETA- BLOCKERS; effects of muscle relaxants enhanced by PROPRANOLOL

▶ Calcium-channel Blockers: enhanced hypotensive effect when baclofen or tizanidine given with CALCIUM-CHANNEL BLOCKERS;

Muscle Relaxants

Calcium-channel Blockers (continued)

effects of non-depolarising muscle relaxants possibly enhanced by CALCIUM-CHANNEL BLOCKERS; possible increased risk of ventricular arrhythmias when *intravenous* dantrolene given with DILTIAZEM—manufacturer of diltiazem advises avoid concomitant use; effects of non-depolarising muscle relaxants and suxamethonium enhanced by VERAPAMIL; avoidance of *intravenous* dantrolene advised by manufacturer of VERAPAMIL

▶ Cardiac Glycosides: possible increased risk of bradycardia when tizanidine given with CARDIAC GLYCOSIDES; risk of ventricular arrhythmias when suxamethonium given with CARDIAC GLYCOSIDES

▶ Clonidine: enhanced hypotensive effect when baclofen or tizanidine given with CLONIDINE

▶ Corticosteroids: effects of pancuronium and vecuronium possibly antagonised by CORTICOSTEROIDS

▶ Cytotoxics: effects of suxamethonium enhanced by

CYCLOPHOSPHAMIDE and THIOTEPA

▶ Deferasirox: avoidance of tizanidine advised by manufacturer of DEFERASIROX

▶ Diazoxide: enhanced hypotensive effect when baclofen or tizanidine given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when baclofen or tizanidine given with DIURETICS

▶ Dopaminergics: possible agitation, confusion and hallucinations when baclofen given with CO-BENELDOPA, CO- CARELDOPA or LEVODOPA

▶ Lithium: effects of muscle relaxants enhanced by LITHIUM; baclofen possibly aggravates hyperkinesis caused by LITHIUM

▶ Magnesium (parenteral): effects of non-depolarising muscle relaxants and suxamethonium enhanced by PARENTERAL MAGNESIUM

▶ Memantine: effects of baclofen and dantrolene possibly modified by MEMANTINE

▶ Methyldopa: enhanced hypotensive effect when baclofen or tizanidine given with METHYLDOPA

▶ Metoclopramide: effects of suxamethonium enhanced by

METOCLOPRAMIDE

▶ Moxonidine: enhanced hypotensive effect when baclofen or tizanidine given with MOXONIDINE

▶ Nitrates: enhanced hypotensive effect when baclofen or tizanidine given with NITRATES

▶ Oestrogens: plasma concentration of tizanidine possibly increased by OESTROGENS (increased risk of toxicity)

▶ Parasympathomimetics: effects of non-depolarising muscle relaxants possibly antagonised by DONEPEZIL; effects of suxamethonium possibly enhanced by DONEPEZIL; effects of suxamethonium enhanced by GALANTAMINE, NEOSTIGMINE, PYRIDOSTIGMINE and RIVASTIGMINE; effects of non-depolarising muscle relaxants antagonised by NEOSTIGMINE, PYRIDOSTIGMINE and RIVASTIGMINE

▶ Progestogens: plasma concentration of tizanidine possibly increased by PROGESTOGENS (increased risk of toxicity)

▶ Sympathomimetics, Beta2: effects of suxamethonium enhanced by BAMBUTEROL

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when baclofen or tizanidine given with HYDRALAZINE; enhanced hypotensive effect when baclofen or tizanidine given with MINOXIDIL; enhanced hypotensive effect when baclofen or tizanidine given with SODIUM NITROPRUSSIDE

Muscle Relaxants, depolarising *see* Muscle Relaxants Muscle Relaxants, non-depolarising *see* Muscle Relaxants Mycophenolate

▶ Antacids: absorption of mycophenolate reduced by ANTACIDS

l Antibacterials: bioavailability of mycophenolate possibly reduced by METRONIDAZOLE and NORFLOXACIN; plasma concentration of mycophenolate possibly reduced by CO- AMOXICLAV; plasma concentration of active metabolite of mycophenolate reduced by l RIFAMPICIN

▶ Antivirals: mycophenolate increases plasma concentration of ACICLOVIR and VALACICLOVIR, also plasma concentration of inactive metabolite of mycophenolate increased; mycophenolate possibly increases plasma concentration of

Mycophenolate

Antivirals (continued)

GANCICLOVIR and VALGANCICLOVIR, also plasma concentration of inactive metabolite of mycophenolate possibly increased

▶ Colestilan: manufacturer of colestilan advises give mycophenolate at least 1 hour before or 3 hours after COLESTILAN

▶ Iron Salts: absorption of mycophenolate reduced by *oral* IRON SALTS

▶ Lipid-regulating Drugs: absorption of mycophenolate reduced

by COLESTYRAMINE

▶ Sevelamer: plasma concentration of mycophenolate possibly reduced by SEVELAMER

Nabumetone *see* NSAIDs Nadolol *see* Beta-blockers Nalidixic Acid *see* Quinolones Nalmefene

l Analgesics: manufacturer of nalmefene advises avoid

concomitant use with l OPIOID ANALGESICS Nandrolone *see* Anabolic Steroids Naproxen *see* NSAIDs

Naratriptan *see* 5HT1-receptor Agonists (under HT)

Natalizumub

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Nateglinide *see* Antidiabetics Nebivolol *see* Beta-blockers Nefopam

l Antidepressants: manufacturer of nefopam advises avoid

concomitant use with l MAOIS; side-effects possibly increased when nefopam given with TRICYCLICS

▶ Antimuscarinics: increased risk of antimuscarinic side-effects when nefopam given with ANTIMUSCARINICS

Neomycin *see* Aminoglycosides Neostigmine *see* Parasympathomimetics Nevirapine

▶ Analgesics: nevirapine possibly reduces plasma concentration

of METHADONE

l Antibacterials: nevirapine reduces plasma concentration of CLARITHROMYCIN (but concentration of an active metabolite increased), also plasma concentration of nevirapine increased; nevirapine possibly increases plasma concentration of RIFABUTIN; plasma concentration of nevirapine reduced by l RIFAMPICIN—avoid concomitant use

l Anticoagulants: nevirapine may enhance or reduce anticoagulant effect of l WARFARIN

l Antidepressants: plasma concentration of nevirapine reduced by l ST JOHN’S WORT—avoid concomitant use

▶ Antiepileptics: plasma concentration of nevirapine reduced by

CARBAMAZEPINE

l Antifungals: nevirapine reduces plasma concentration of l KETOCONAZOLE—avoid concomitant use; plasma concentration of nevirapine increased by l FLUCONAZOLE; nevirapine possibly reduces plasma concentration of

CASPOFUNGIN and ITRACONAZOLE—consider increasing dose of caspofungin and itraconazole

l Antipsychotics: nevirapine possibly reduces plasma concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature)

l Antivirals: nevirapine possibly reduces plasma concentration of l ATAZANAVIR and l ETRAVIRINE—avoid concomitant use; manufacturer of nevirapine advises avoid concomitant use with BOCEPREVIR and RILPIVIRINE; avoidance of nevirapine advised by manufacturer of DACLATASVIR (plasma concentration of daclatasvir possibly reduced); nevirapine possibly reduces the plasma concentration of l DOLUTEGRAVIR (see under Dolutegravir, p. 557); nevirapine reduces plasma concentration of l EFAVIRENZ—avoid concomitant use; avoidance of nevirapine advised by manufacturer of ELVITEGRAVIR; nevirapine possibly reduces plasma concentration of FOSAMPRENAVIR—avoid unboosted fosamprenavir; nevirapine reduces plasma concentration of

Nevirapine

l Antivirals (continued)

Interactions | Appendix 1

INDINAVIR; nevirapine possibly reduces plasma concentration of l LOPINAVIR and TELAPREVIR—consider increasing dose of lopinavir and telaprevir; nevirapine possibly reduces plasma concentration of l SIMEPREVIR—manufacturer of simeprevir advises avoid concomitant use; increased risk of granulocytopenia when nevirapine given with l ZIDOVUDINE

▶ Cobicistat: manufacturer of nevirapine advises avoid concomitant use with COBICISTAT

l Oestrogens: nevirapine accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: absorption of nevirapine possibly reduced by

l ORLISTAT

l Progestogens: nevirapine accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

Nicardipine *see* Calcium-channel Blockers

Nicorandil

▶ Alcohol: hypotensive effect of nicorandil possibly enhanced by

ALCOHOL

▶ Antidepressants: enhanced hypotensive effect when nicorandil given with MAOIS; hypotensive effect of nicorandil possibly enhanced by TRICYCLICS

l Avanafil: hypotensive effect of nicorandil significantly enhanced by l AVANAFIL (avoid concomitant use)

l Sildenafil: hypotensive effect of nicorandil significantly enhanced by l SILDENAFIL (avoid concomitant use)

l Tadalafil: hypotensive effect of nicorandil significantly enhanced by l TADALAFIL (avoid concomitant use)

l Vardenafil: possible increased hypotensive effect when nicorandil given with l VARDENAFIL—avoid concomitant use

▶ Vasodilator Antihypertensives: possible enhanced hypotensive effect when nicorandil given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Nicotine

▶ Anti-arrhythmics: nicotine possibly enhances effects of

ADENOSINE

Nicotinic Acid

l Lipid-regulating Drugs: increased risk of myopathy when nicotinic acid given with l STATINS (applies to lipid regulating doses of nicotinic acid)

Nifedipine *see* Calcium-channel Blockers

Nilotinib

l Antibacterials: manufacturer of nilotinib advises avoid concomitant use with l CLARITHROMYCIN and l TELITHROMYCIN; plasma concentration of nilotinib reduced by l RIFAMPICIN— avoid concomitant use

l Antifungals: plasma concentration of nilotinib increased by

l KETOCONAZOLE—avoid concomitant use; manufacturer of nilotinib advises avoid concomitant use with l ITRACONAZOLE and l VORICONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of nilotinib advised by manufacturer of l BOCEPREVIR; plasma concentration of nilotinib possibly increased by RITONAVIR—manufacturer of nilotinib advises avoid concomitant use

▶ Anxiolytics and Hypnotics: nilotinib increases plasma concentration of MIDAZOLAM

l Grapefruit Juice: manufacturer of nilotinib advises avoid concomitant use with l GRAPEFRUIT JUICE

▶ Lipid-regulating Drugs: separating administration from nilotinib by 12 hours advised by manufacturer of LOMITAPIDE

Nimodipine *see* Calcium-channel Blockers

Nintedanib

l Antibacterials: plasma concentration of nintedanib reduced by

l RIFAMPICIN—avoid concomitant use

l Antifungals: plasma concentration of nintedanib increased by

l KETOCONAZOLE

Interactions | Appendix 1

Nitrates

▶ ACE Inhibitors: enhanced hypotensive effect when nitrates given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when nitrates given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when nitrates given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when nitrates given with ALDESLEUKIN

▶ Alpha-blockers: enhanced hypotensive effect when nitrates given with ALPHA-BLOCKERS

▶ Anaesthetics, General: enhanced hypotensive effect when nitrates given with GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of nitrates antagonised by

NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when nitrates given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Anti-arrhythmics: effects of sublingual tablets of nitrates reduced by DISOPYRAMIDE (failure to dissolve under tongue owing to dry mouth)

l Anticoagulants: *infusion* of glyceryl trinitrate reduces anticoagulant effect of l HEPARINS

▶ Antidepressants: enhanced hypotensive effect when nitrates given with MAOIS; effects of sublingual tablets of nitrates possibly reduced by TRICYCLIC-RELATED ANTIDEPRESSANTS (failure to dissolve under tongue owing to dry mouth); effects of sublingual tablets of nitrates reduced by TRICYCLICS (failure to dissolve under tongue owing to dry mouth)

▶ Antimuscarinics: effects of sublingual tablets of nitrates possibly reduced by ANTIMUSCARINICS (failure to dissolve under tongue owing to dry mouth)

▶ Antipsychotics: enhanced hypotensive effect when nitrates given with PHENOTHIAZINES

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when nitrates given with ANXIOLYTICS AND HYPNOTICS

l Avanafil: hypotensive effect of nitrates significantly enhanced by l AVANAFIL (avoid concomitant use)

▶ Beta-blockers: enhanced hypotensive effect when nitrates given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when nitrates given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when nitrates given with CLONIDINE

▶ Corticosteroids: hypotensive effect of nitrates antagonised by

CORTICOSTEROIDS

▶ Diazoxide: enhanced hypotensive effect when nitrates given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when nitrates given with DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when nitrates given with CO-BENELDOPA, CO-CARELDOPA or LEVODOPA

▶ Methyldopa: enhanced hypotensive effect when nitrates given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when nitrates given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when nitrates given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when nitrates given with BACLOFEN or TIZANIDINE

▶ Oestrogens: hypotensive effect of nitrates antagonised by

OESTROGENS

▶ Prostaglandins: enhanced hypotensive effect when nitrates given with ALPROSTADIL

l Riociguat: possible enhanced hypotensive effect when nitrates given with l RIOCIGUAT—avoid concomitant use

l Sildenafil: hypotensive effect of nitrates significantly enhanced by l SILDENAFIL (avoid concomitant use)

l Tadalafil: hypotensive effect of nitrates significantly enhanced by l TADALAFIL (avoid concomitant use)

l Vardenafil: possible increased hypotensive effect when nitrates given with l VARDENAFIL—avoid concomitant use

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when nitrates given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Nitrazepam *see* Anxiolytics and Hypnotics

Nitrofurantoin

▶ Antacids: absorption of nitrofurantoin reduced by ORAL MAGNESIUM SALTS (as magnesium trisilicate)

▶ Antibacterials: nitrofurantoin possibly antagonises effects of

NALIDIXIC ACID

▶ Sulfinpyrazone: excretion of nitrofurantoin reduced by

SULFINPYRAZONE (increased risk of toxicity)

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Nitroimidazoles *see* Metronidazole and Tinidazole Nitrous Oxide *see* Anaesthetics, General Nizatidine *see* Histamine H2-antagonists Nomegestrol *see* Progestogens

Noradrenaline (norepinephrine) *see* Sympathomimetics

Norelgestromin *see* Progestogens

Norepinephrine

NOTE Norepinephrine interactions as for noradrenaline, see under sympathomimetics

Norethisterone *see* Progestogens Norfloxacin *see* Quinolones Norgestimate *see* Progestogens Norgestrel *see* Progestogens

Normal Immunoglobulin *see* Immunoglobulins Nortriptyline *see* Antidepressants, Tricyclic NSAIDs

NOTE *See also* Aspirin. Interactions do not generally apply to topical NSAIDs

▶ ACE Inhibitors: increased risk of renal impairment when NSAIDs given with ACE INHIBITORS, also hypotensive effect antagonised

▶ Adrenergic Neurone Blockers: NSAIDs antagonise hypotensive effect of ADRENERGIC NEURONE BLOCKERS

▶ Aliskiren: NSAIDs possibly antagonise hypotensive effect of

ALISKIREN

▶ Alpha-blockers: NSAIDs antagonise hypotensive effect of

ALPHA-BLOCKERS

l Analgesics: avoid concomitant use of NSAIDs with l NSAIDS or l ASPIRIN (increased side-effects); avoid concomitant use of NSAIDs with l KETOROLAC (increased side-effects and haemorrhage); ibuprofen possibly reduces antiplatelet effect of ASPIRIN

▶ Angiotensin-II Receptor Antagonists: increased risk of renal impairment when NSAIDs given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS, also hypotensive effect antagonised

▶ Antacids: absorption of acemetacin possibly reduced by

ANTACIDS

l Antibacterials: indometacin possibly increases plasma concentration of AMIKACIN and GENTAMICIN in neonates; plasma concentration of celecoxib, diclofenac and etoricoxib reduced by RIFAMPICIN; possible increased risk of convulsions when NSAIDs given with l QUINOLONES

l Anticoagulants: increased risk of haemorrhage when *intravenous* diclofenac given with l ANTICOAGULANTS (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when ketorolac given with

l ANTICOAGULANTS (avoid concomitant use, including low- dose heparins); NSAIDs possibly enhance anticoagulant effect of l COUMARINS and l PHENINDIONE; possible increased risk of bleeding when NSAIDs given with l DABIGATRAN or HEPARINS

l Antidepressants: increased risk of bleeding when NSAIDs

given with l SSRIS or l VENLAFAXINE

l Antidiabetics: NSAIDs possibly enhance effects of

l SULFONYLUREAS

▶ Antiepileptics: acemetacin possibly reduces excretion of

FOSPHENYTOIN and PHENYTOIN (increased risk of toxicity)

▶ Antifungals: plasma concentration of parecoxib increased by FLUCONAZOLE (reduce dose of parecoxib); plasma concentration of celecoxib increased by FLUCONAZOLE (halve dose of celecoxib); plasma concentration of flurbiprofen and ibuprofen increased by FLUCONAZOLE; plasma concentration of diclofenac and ibuprofen increased by VORICONAZOLE

▶ Antipsychotics: possible severe drowsiness when acemetacin or indometacin given with HALOPERIDOL

NSAIDs (continued)

l Antivirals: plasma concentration of piroxicam increased by

l RITONAVIR (risk of toxicity)—avoid concomitant use; plasma concentration of NSAIDs possibly increased by RITONAVIR; increased risk of haematological toxicity when NSAIDs given with ZIDOVUDINE

▶ Beta-blockers: NSAIDs antagonise hypotensive effect of BETA- BLOCKERS

▶ Calcium-channel Blockers: NSAIDs antagonise hypotensive

effect of CALCIUM-CHANNEL BLOCKERS

▶ Cardiac Glycosides: NSAIDs possibly increase plasma concentration of CARDIAC GLYCOSIDES, also possible exacerbation of heart failure and reduction of renal function

l Ciclosporin: increased risk of nephrotoxicity when NSAIDs given with l CICLOSPORIN; plasma concentration of diclofenac increased by l CICLOSPORIN (halve dose of diclofenac)

▶ Clonidine: NSAIDs antagonise hypotensive effect of CLONIDINE

▶ Clopidogrel: increased risk of bleeding when NSAIDs given with CLOPIDOGREL

▶ Corticosteroids: increased risk of gastro-intestinal bleeding and ulceration when NSAIDs given with CORTICOSTEROIDS

l Cytotoxics: NSAIDs probably reduce excretion of

l METHOTREXATE (increased risk of toxicity); diclofenac, ibuprofen, indometacin, ketoprofen, meloxicam and naproxen reduce excretion of l METHOTREXATE (increased risk of toxicity); NSAIDs possibly reduce renal excretion of PEMETREXED—consult product literature; increased risk of bleeding when NSAIDs given with l ERLOTINIB; avoidance of mefenamic acid advised by manufacturer of REGORAFENIB

▶ Desmopressin: indometacin enhances effects of DESMOPRESSIN

▶ Diazoxide: NSAIDs antagonise hypotensive effect of DIAZOXIDE

l Dimethyl sulfoxide: avoid concomitant use of sulindac with

l DIMETHYL SULFOXIDE

l Diuretics: risk of nephrotoxicity of NSAIDs increased by DIURETICS, also antagonism of diuretic effect; indometacin and ketorolac antagonise effects of DIURETICS; excretion of acemetacin possibly increased by FUROSEMIDE; NSAIDs possibly antagonise diuretic effect of POTASSIUM CANRENOATE; occasional reports of reduced renal function when indometacin given with l TRIAMTERENE—avoid concomitant use; possible increased risk of hyperkalaemia when NSAIDs given with POTASSIUM-SPARING DIURETICS AND ALDOSTERONE

ANTAGONISTS; increased risk of hyperkalaemia when indometacin given with POTASSIUM-SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

▶ Iloprost: increased risk of bleeding when NSAIDs given with

ILOPROST

▶ Lipid-regulating Drugs: excretion of meloxicam increased by

COLESTYRAMINE

l Lithium: NSAIDs reduce excretion of l LITHIUM (increased risk of toxicity); ketorolac reduces excretion of l LITHIUM (increased risk of toxicity)—avoid concomitant use

▶ Methyldopa: NSAIDs antagonise hypotensive effect of

METHYLDOPA

▶ Mifamurtide: avoidance of high doses of NSAIDs advised by manufacturer of MIFAMURTIDE

▶ Moxonidine: NSAIDs antagonise hypotensive effect of

MOXONIDINE

▶ Muscle Relaxants: ibuprofen reduces excretion of BACLOFEN (increased risk of toxicity); NSAIDs possibly reduce excretion of BACLOFEN (increased risk of toxicity)

▶ Nitrates: NSAIDs antagonise hypotensive effect of NITRATES

▶ Oestrogens: etoricoxib increases plasma concentration of

ETHINYLESTRADIOL

▶ Penicillamine: possible increased risk of nephrotoxicity when NSAIDs given with PENICILLAMINE

l Pentoxifylline: possible increased risk of bleeding when NSAIDs given with PENTOXIFYLLINE; increased risk of bleeding when ketorolac given with l PENTOXIFYLLINE (avoid concomitant use)

▶ Prasugrel: possible increased risk of bleeding when NSAIDs given with PRASUGREL

l Tacrolimus: possible increased risk of nephrotoxicity when NSAIDs given with TACROLIMUS; increased risk of nephrotoxicity when ibuprofen given with l TACROLIMUS

NSAIDs (continued)

▶ Vasodilator Antihypertensives: NSAIDs antagonise hypotensive effect of HYDRALAZINE, MINOXIDIL and SODIUM NITROPRUSSIDE

Interactions | Appendix 1

Obinutuzumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Octreotide

▶ Antidiabetics: octreotide possibly reduces requirements for

ANTIDIABETICS

l Ciclosporin: octreotide reduces plasma concentration of

l CICLOSPORIN

▶ Dopaminergics: octreotide increases plasma concentration of

BROMOCRIPTINE

▶ Ulcer-healing Drugs: octreotide possibly delays absorption of

CIMETIDINE

Oestrogens

▶ ACE Inhibitors: oestrogens antagonise hypotensive effect of

ACE INHIBITORS

▶ Adrenergic Neurone Blockers: oestrogens antagonise hypotensive effect of ADRENERGIC NEURONE BLOCKERS

▶ Alpha-blockers: oestrogens antagonise hypotensive effect of

ALPHA-BLOCKERS

▶ Aminophylline: oestrogens increase plasma concentration of

AMINOPHYLLINE (consider reducing dose of aminophylline)

▶ Analgesics: plasma concentration of ethinylestradiol increased by ETORICOXIB

▶ Angiotensin-II Receptor Antagonists: oestrogens antagonise hypotensive effect of ANGIOTENSIN-II RECEPTOR ANTAGONISTS

l Antibacterials: plasma concentration of estradiol increased by

ERYTHROMYCIN; metabolism of oestrogens accelerated by l RIFAMYCINS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Anticoagulants: oestrogens may enhance or reduce anticoagulant effect of COUMARINS; oestrogens antagonise anticoagulant effect of l PHENINDIONE

l Antidepressants: contraceptive effect of oestrogens reduced by l ST JOHN’S WORT (avoid concomitant use); oestrogens antagonise antidepressant effect of TRICYCLICS (but side- effects of tricyclics possibly increased due to increased plasma concentration)

▶ Antidiabetics: oestrogens antagonise hypoglycaemic effect of

ANTIDIABETICS

l Antiepileptics: metabolism of oestrogens accelerated by

l CARBAMAZEPINE, l ESLICARBAZEPINE, l FOSPHENYTOIN,

l OXCARBAZEPINE, l PHENOBARBITAL, l PHENYTOIN, l PRIMIDONE,

l RUFINAMIDE and l TOPIRAMATE (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF); oestrogens reduce plasma concentration of l LAMOTRIGINE— consider increasing dose of lamotrigine; ethinylestradiol possibly reduces plasma concentration of SODIUM VALPROATE and VALPROIC ACID

▶ Antifungals: oestrogens increase plasma concentration of VORICONAZOLE; anecdotal reports of contraceptive failure and menstrual irregularities when oestrogens given with GRISEOFULVIN; anecdotal reports of contraceptive failure when oestrogens given with IMIDAZOLES; occasional reports of breakthrough bleeding when oestrogens (used for contraception) given with TERBINAFINE

l Antivirals: plasma concentration of ethinylestradiol increased by ATAZANAVIR; metabolism of oestrogens accelerated by

l NEVIRAPINE and l RITONAVIR (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF); plasma concentration of ethinylestradiol possibly reduced by l TELAPREVIR—manufacturer of telaprevir advises additional contraceptive precautions

▶ Anxiolytics and Hypnotics: oestrogens possibly increase plasma concentration of CHLORDIAZEPOXIDE, DIAZEPAM and NITRAZEPAM; oestrogens possibly reduce plasma concentration of LORAZEPAM, OXAZEPAM and TEMAZEPAM; oestrogens increase plasma concentration of MELATONIN

Interactions | Appendix 1

Oestrogens (continued)

l Aprepitant: possible contraceptive failure of hormonal contraceptives containing oestrogens when given with l APREPITANT (alternative contraception recommended)

▶ Beta-blockers: oestrogens antagonise hypotensive effect of

BETA-BLOCKERS

l Bosentan: possible contraceptive failure of hormonal contraceptives containing oestrogens when given with l BOSENTAN (alternative contraception recommended)

▶ Calcium-channel Blockers: oestrogens antagonise hypotensive effect of CALCIUM-CHANNEL BLOCKERS

▶ Ciclosporin: oestrogens possibly increase plasma concentration of CICLOSPORIN

▶ Clonidine: oestrogens antagonise hypotensive effect of

CLONIDINE

l Cobicistat: metabolism of oestrogens accelerated by

l COBICISTAT (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

▶ Corticosteroids: oral contraceptives containing oestrogens increase plasma concentration of CORTICOSTEROIDS

l Cytotoxics: possible reduction in contraceptive effect of oestrogens advised by manufacturer of l CRIZOTINIB and l VEMURAFENIB; possible reduced contraceptive effect of

hormonal contraceptives containing oestrogens advised by manufacturer of l DABRAFENIB (alternative contraception recommended)

▶ Diuretics: oestrogens antagonise diuretic effect of DIURETICS l Dopaminergics: oestrogens increase plasma concentration of ROPINIROLE; oestrogens increase plasma concentration of

l SELEGILINE—manufacturer of selegiline advises avoid concomitant use

l Fosaprepitant: possible contraceptive failure of hormonal contraceptives containing oestrogens when given with

l FOSAPREPITANT (alternative contraception recommended)

▶ Lipid-regulating Drugs: absorption of ethinylestradiol reduced by COLESEVELAM; plasma concentration of ethinylestradiol increased by ATORVASTATIN and ROSUVASTATIN; separating administration from oestrogens by 12 hours advised by manufacturer of LOMITAPIDE

▶ Methyldopa: oestrogens antagonise hypotensive effect of

METHYLDOPA

l Modafinil: metabolism of oestrogens accelerated by

l MODAFINIL (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

▶ Moxonidine: oestrogens antagonise hypotensive effect of

MOXONIDINE

▶ Muscle Relaxants: oestrogens possibly increase plasma concentration of TIZANIDINE (increased risk of toxicity)

▶ Nitrates: oestrogens antagonise hypotensive effect of NITRATES

▶ Somatropin: oestrogens (when used as oral replacement therapy) may increase dose requirements of SOMATROPIN

▶ Tacrolimus: ethinylestradiol possibly increases plasma concentration of TACROLIMUS

▶ Teriflunomide: plasma concentration of ethinylestradiol increased by TERIFLUNOMIDE

▶ Theophylline: oestrogens increase plasma concentration of

THEOPHYLLINE (consider reducing dose of theophylline)

▶ Thyroid Hormones: oestrogens may increase requirements for

THYROID HORMONES in hypothyroidism

▶ Vasodilator Antihypertensives: oestrogens antagonise hypotensive effect of HYDRALAZINE, MINOXIDIL and SODIUM NITROPRUSSIDE

Oestrogens, conjugated *see* Oestrogens

Ofatumumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Ofloxacin *see* Quinolones

Olanzapine *see* Antipsychotics

Olmesartan *see* Angiotensin-II Receptor Antagonists

Olodaterol *see* Sympathomimetics, Beta2

Omeprazole *see* Proton Pump Inhibitors

Ondansetron *see* 5HT3-receptor Antagonists (under HT)

Opioid Analgesics

▶ Alcohol: enhanced hypotensive and sedative effects when opioid analgesics given with ALCOHOL

▶ Anaesthetics, General: fentanyl inhibits metabolism of ETOMIDATE (consider reducing dose of etomidate); opioid analgesics possibly enhance effects of INTRAVENOUS GENERAL ANAESTHETICS and VOLATILE LIQUID GENERAL ANAESTHETICS

▶ Analgesics: avoidance of buprenorphine advised by manufacturer of FENTANYL; manufacturer of fentanyl advises avoid concomitant use with PENTAZOCINE

l Antibacterials: plasma concentration of fentanyl possibly increased by CLARITHROMYCIN; plasma concentration of alfentanil increased by ERYTHROMYCIN; metabolism of alfentanil, codeine, fentanyl, methadone and morphine accelerated by RIFAMPICIN (reduced effect); metabolism of oxycodone possibly accelerated by RIFAMPICIN; increased risk of ventricular arrhythmias when methadone given with

l DELAMANID; manufacturer of pethidine advises avoid concomitant use with ISONIAZID; metabolism of oxycodone inhibited by TELITHROMYCIN; possible increased risk of ventricular arrhythmias when methadone given with

l TELITHROMYCIN

l Anticoagulants: tramadol enhances anticoagulant effect of

l COUMARINS

l Antidepressants: plasma concentration of methadone possibly increased by FLUOXETINE, FLUVOXAMINE, PAROXETINE and

SERTRALINE; possible increased serotonergic effects when pethidine or tramadol given with DULOXETINE; possible increased serotonergic effects when tramadol given with MIRTAZAPINE or VENLAFAXINE; possible CNS excitation or depression (hypertension or hypotension) when opioid analgesics given with l MAOIS—some manufacturers advise avoid concomitant use and for 2 weeks after stopping MAOIs; possible increased serotonergic effects and increased risk of convulsions when tramadol given with l MAOIS—some manufacturers advise avoid concomitant use and for 2 weeks after stopping MAOIs; CNS excitation or depression (hypertension or hypotension) when pethidine given with

l MAOIS—avoid concomitant use and for 2 weeks after stopping MAOIs; possible increased serotonergic effects when fentanyl given with MAOIS, SSRI-RELATED ANTIDEPRESSANTS or SSRIS; possible CNS excitation or depression (hypertension or hypotension) when opioid analgesics given with l MOCLOBEMIDE—manufacturer of moclobemide advises consider reducing dose of opioid analgesics; possible CNS excitation or depression (hypertension or hypotension) when dextromethorphan or pethidine given with l MOCLOBEMIDE—avoid concomitant use; increased risk of CNS toxicity when tramadol given with

l SSRIS or l TRICYCLICS; plasma concentration of methadone possibly reduced by ST JOHN’S WORT; sedative effects possibly increased when opioid analgesics given with TRICYCLICS

l Antiepileptics: effects of tramadol reduced by CARBAMAZEPINE; plasma concentration of methadone reduced by CARBAMAZEPINE, PHENOBARBITAL and PRIMIDONE; metabolism

of fentanyl possibly accelerated by CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN (reduced effect); dextropropoxyphene enhances effects of l CARBAMAZEPINE; metabolism of methadone accelerated by FOSPHENYTOIN and PHENYTOIN (reduced effect and risk of withdrawal effects); possible increased risk of pethidine toxicity when given with l FOSPHENYTOIN and l PHENYTOIN; morphine increases bioavailability of GABAPENTIN

l Antifungals: metabolism of buprenorphine inhibited by

l KETOCONAZOLE (reduce dose of buprenorphine); possible increased risk of ventricular arrhythmias when methadone given with l KETOCONAZOLE—manufacturer of ketoconazole advises avoid concomitant use; plasma concentration of oxycodone increased by ITRACONAZOLE, KETOCONAZOLE and l VORICONAZOLE; metabolism of alfentanil inhibited by FLUCONAZOLE (risk of prolonged or delayed respiratory depression); plasma concentration of methadone increased

by FLUCONAZOLE; metabolism of alfentanil possibly inhibited by ITRACONAZOLE; plasma concentration of methadone

Opioid Analgesics

l Antifungals (continued)

possibly increased by l ITRACONAZOLE (increased risk of ventricular arrhythmias); plasma concentration of alfentanil and methadone increased by l VORICONAZOLE (consider reducing dose of alfentanil and methadone); plasma concentration of fentanyl possibly increased by l TRIAZOLES

l Antihistamines: sedative effects possibly increased when opioid analgesics given with l SEDATING ANTIHISTAMINES

l Antimalarials: avoidance of methadone advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

▶ Antimuscarinics: possible increased risk of antimuscarinic side-effects when codeine given with ANTIMUSCARINICS

l Antipsychotics: enhanced hypotensive and sedative effects when opioid analgesics given with ANTIPSYCHOTICS; increased risk of ventricular arrhythmias when methadone given with l ANTIPSYCHOTICS that prolong the QT interval; increased risk of convulsions when tramadol given with ANTIPSYCHOTICS; increased risk of ventricular arrhythmias when methadone given with l AMISULPRIDE—avoid concomitant use

l Antivirals: plasma concentration of methadone possibly reduced by ABACAVIR, NEVIRAPINE and RILPIVIRINE; plasma concentration of methadone possibly affected by BOCEPREVIR; possible increased risk of prolonged sedation and respiratory depression when buprenorphine given with BOCEPREVIR; methadone possibly reduces plasma concentration of DIDANOSINE; plasma concentration of methadone reduced by EFAVIRENZ, FOSAMPRENAVIR and RITONAVIR; plasma

concentration of buprenorphine possibly increased by RITONAVIR; plasma concentration of alfentanil and fentanyl increased by l RITONAVIR; plasma concentration of pethidine reduced by l RITONAVIR, but plasma concentration of toxic pethidine metabolite increased (avoid concomitant use); plasma concentration of morphine possibly reduced by RITONAVIR; plasma concentration of dextropropoxyphene increased by l RITONAVIR (risk of toxicity)—avoid concomitant use; increased risk of ventricular arrhythmias when alfentanil, fentanyl or methadone given with l SAQUINAVIR— avoid concomitant use; caution with methadone advised by manufacturer of l TELAPREVIR (risk of ventricular arrhythmias); buprenorphine possibly reduces plasma concentration of TIPRANAVIR; methadone possibly increases plasma concentration of ZIDOVUDINE

▶ Anxiolytics and Hypnotics: increased sedative effect when opioid analgesics given with ANXIOLYTICS AND HYPNOTICS; fentanyl possibly inhibits metabolism of MIDAZOLAM

l Atomoxetine: increased risk of ventricular arrhythmias when methadone given with l ATOMOXETINE; possible increased risk of convulsions when tramadol given with ATOMOXETINE

▶ Beta-blockers: morphine possibly increases plasma concentration of ESMOLOL

▶ Calcium-channel Blockers: metabolism of alfentanil inhibited by DILTIAZEM (risk of prolonged or delayed respiratory depression)

l Cytotoxics: possible increased risk of ventricular arrhythmias when methadone given with l BOSUTINIB; caution with alfentanil and fentanyl advised by manufacturer of

l CRIZOTINIB; possible increased risk of ventricular arrhythmias when methadone given with l VANDETANIB— avoid concomitant use

l Dapoxetine: possible increased risk of serotonergic effects when tramadol given with l DAPOXETINE (manufacturer of dapoxetine advises tramadol should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping tramadol)

▶ Domperidone: opioid analgesics antagonise effects of

DOMPERIDONE on gastro-intestinal activity

l Dopaminergics: avoid concomitant use of dextromethorphan with l RASAGILINE; risk of CNS toxicity when pethidine given with l RASAGILINE (avoid pethidine for 2 weeks after rasagiline); avoidance of opioid analgesics advised by manufacturer of SELEGILINE; hyperpyrexia and CNS toxicity reported when pethidine given with l SELEGILINE (avoid concomitant use)

Opioid Analgesics (continued)

▶ Hormone Antagonists: plasma concentration of dextromethorphan increased by ABIRATERONE

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▶ 5HT3-receptor Antagonists: effects of tramadol possibly antagonised by ONDANSETRON

l Memantine: increased risk of CNS toxicity when dextromethorphan given with l MEMANTINE (manufacturer of memantine advises avoid concomitant use)

▶ Metoclopramide: opioid analgesics antagonise effects of

METOCLOPRAMIDE on gastro-intestinal activity

▶ Muscle Relaxants: increased sedative effect when fentanyl or morphine given with BACLOFEN

l Nalmefene: avoidance of opioid analgesics advised by manufacturer of l NALMEFENE

l Sodium Oxybate: opioid analgesics enhance effects of l SODIUM OXYBATE (avoid concomitant use)

▶ Ulcer-healing Drugs: metabolism of opioid analgesics inhibited by CIMETIDINE (increased plasma concentration)

Oritavancin

▶ Anticoagulants: oritavancin possibly increases plasma concentration of WARFARIN

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Orlistat

▶ Anti-arrhythmics: orlistat possibly reduces plasma concentration of AMIODARONE

▶ Anticoagulants: manufacturer of orlistat recommends monitoring anticoagulant effect of COUMARINS

▶ Antidiabetics: manufacturer of orlistat advises avoid concomitant use with ACARBOSE

l Antiepileptics: possible increased risk of convulsions when orlistat given with l ANTIEPILEPTICS

l Antivirals: orlistat possibly reduces absorption of l ABACAVIR,

l ATAZANAVIR, l DARUNAVIR, l DIDANOSINE, l EFAVIRENZ,

l ELVITEGRAVIR, l EMTRICITABINE, l ENFUVIRTIDE, l ETRAVIRINE,

l FOSAMPRENAVIR, l INDINAVIR, l LAMIVUDINE, l LOPINAVIR, l MARAVIROC, l NEVIRAPINE, l RALTEGRAVIR, l RILPIVIRINE, l RITONAVIR, l SAQUINAVIR, l STAVUDINE, l TENOFOVIR,

l TIPRANAVIR and l ZIDOVUDINE

l Ciclosporin: orlistat possibly reduces absorption of

l CICLOSPORIN

▶ Thyroid Hormones: possible increased risk of hypothyroidism when orlistat given with LEVOTHYROXINE

Orphenadrine *see* Antimuscarinics Oxaliplatin *see* Platinum Compounds Oxandrolone *see* Anabolic Steroids Oxazepam *see* Anxiolytics and Hypnotics Oxcarbazepine

l Antidepressants: anticonvulsant effect of antiepileptics

possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antiepileptics: oxcarbazepine sometimes reduces plasma concentration of CARBAMAZEPINE (but concentration of an active metabolite of carbamazepine may be increased), also plasma concentration of an active metabolite of oxcarbazepine often reduced; avoidance of oxcarbazepine advised by manufacturer of ESLICARBAZEPINE; oxcarbazepine increases plasma concentration of FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE, also plasma

concentration of an active metabolite of oxcarbazepine reduced; oxcarbazepine reduces plasma concentration of l PERAMPANEL (see under Perampanel, p. 398); plasma concentration of an active metabolite of oxcarbazepine

sometimes reduced by SODIUM VALPROATE and VALPROIC ACID

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Antivirals: oxcarbazepine possibly reduces plasma concentration of l DACLATASVIR and l SIMEPREVIR— manufacturer of daclatasvir and simeprevir advises avoid concomitant use; avoidance of oxcarbazepine advised by

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Oxcarbazepine

l Antivirals (continued)

manufacturer of DOLUTEGRAVIR and SOFOSBUVIR; avoidance of oxcarbazepine advised by manufacturer of l RILPIVIRINE (plasma concentration of rilpivirine possibly reduced)

▶ Ciclosporin: oxcarbazepine possibly reduces plasma concentration of CICLOSPORIN

l Clopidogrel: oxcarbazepine possibly reduces antiplatelet effect of l CLOPIDOGREL

l Cytotoxics: oxcarbazepine reduces plasma concentration of

l IMATINIB—avoid concomitant use

l Oestrogens: oxcarbazepine accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: oxcarbazepine accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

Oxprenolol *see* Beta-blockers Oxybutynin *see* Antimuscarinics Oxycodone *see* Opioid Analgesics Oxymetazoline *see* Sympathomimetics Oxytetracycline *see* Tetracyclines Oxytocin

▶ Anaesthetics, General: oxytocic effect possibly reduced, also enhanced hypotensive effect and risk of arrhythmias when oxytocin given with VOLATILE LIQUID GENERAL ANAESTHETICS

▶ Prostaglandins: uterotonic effect of oxytocin potentiated by

PROSTAGLANDINS

▶ Sympathomimetics: risk of hypertension when oxytocin given with vasoconstrictor SYMPATHOMIMETICS (due to enhanced vasopressor effect)

Paclitaxel

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Antivirals: plasma concentration of paclitaxel increased by

RITONAVIR

l Cytotoxics: increased risk of neutropenia when paclitaxel given with l LAPATINIB

Paliperidone *see* Antipsychotics Pamidronate Disodium *see* Bisphosphonates Pancreatin

▶ Antidiabetics: pancreatin antagonises hypoglycaemic effect of

ACARBOSE

Pancuronium *see* Muscle Relaxants

Panitumumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Pantoprazole *see* Proton Pump Inhibitors Papaveretum *see* Opioid Analgesics Paracetamol

▶ Anticoagulants: prolonged regular use of paracetamol possibly enhances anticoagulant effect of COUMARINS

▶ Antidiabetics: absorption of paracetamol possibly reduced when given 1 to 4 hours after LIXISENATIDE

▶ Antiepileptics: metabolism of paracetamol possibly accelerated by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN

and PRIMIDONE (also isolated reports of hepatotoxicity)

▶ Antifungals: avoidance of paracetamol advised by manufacturer of KETOCONAZOLE

▶ Cytotoxics: paracetamol possibly inhibits metabolism of *intravenous* BUSULFAN (manufacturer of *intravenous* busulfan advises caution within 72 hours of paracetamol); caution with paracetamol advised by manufacturer of IMATINIB

▶ Lipid-regulating Drugs: absorption of paracetamol reduced by

COLESTYRAMINE

▶ Metoclopramide: rate of absorption of paracetamol increased by METOCLOPRAMIDE

Paraldehyde

l Alcohol: increased sedative effect when paraldehyde given with l ALCOHOL

l Disulfiram: risk of toxicity when paraldehyde given with

l DISULFIRAM

Parasympathomimetics

▶ Anti-arrhythmics: effects of neostigmine and pyridostigmine possibly antagonised by PROPAFENONE

l Antibacterials: plasma concentration of galantamine increased by ERYTHROMYCIN; effects of neostigmine and pyridostigmine antagonised by l AMINOGLYCOSIDES; effects of neostigmine and pyridostigmine antagonised by CLINDAMYCIN; effects of neostigmine and pyridostigmine antagonised by

l POLYMYXINS

▶ Antidepressants: plasma concentration of galantamine increased by PAROXETINE

▶ Antifungals: plasma concentration of galantamine increased by KETOCONAZOLE

▶ Antimalarials: effects of neostigmine and pyridostigmine may be diminished because of potential for CHLOROQUINE to increase symptoms of myasthenia gravis; effects of neostigmine and pyridostigmine may be diminished because of potential for HYDROXYCHLOROQUINE to increase symptoms of myasthenia gravis

▶ Antimuscarinics: effects of parasympathomimetics antagonised by ANTIMUSCARINICS

▶ Beta-blockers: increased risk of arrhythmias when pilocarpine given with BETA-BLOCKERS; effects of neostigmine and pyridostigmine antagonised by PROPRANOLOL

▶ Cytotoxics: possible increased risk of bradycardia when pilocarpine given with CRIZOTINIB

▶ Lithium: effects of neostigmine antagonised by LITHIUM

▶ Muscle Relaxants: donepezil possibly enhances effects of SUXAMETHONIUM; galantamine, neostigmine, pyridostigmine and rivastigmine enhance effects of SUXAMETHONIUM; neostigmine, pyridostigmine and rivastigmine antagonise effects of NON-DEPOLARISING MUSCLE RELAXANTS; donepezil possibly antagonises effects of NON-DEPOLARISING MUSCLE RELAXANTS

Parecoxib *see* NSAIDs

Paricalcitol *see* Vitamins

Paroxetine *see* Antidepressants, SSRI

Pasireotide

▶ Antidiabetics: pasireotide possibly reduces requirements for

ANTIDIABETICS

▶ Antifungals: avoidance of pasireotide advised by manufacturer of KETOCONAZOLE

▶ Antimuscarinics: possible increased risk of bradycardia when pasireotide given with IPRATROPIUM or OXYBUTYNIN

▶ Beta-blockers: possible increased risk of bradycardia when pasireotide given with CARTEOLOL, METOPROLOL, PROPRANOLOL or SOTALOL

▶ Calcium-channel Blockers: possible increased risk of bradycardia when pasireotide given with DILTIAZEM or VERAPAMIL

l Ciclosporin: pasireotide possibly reduces plasma concentration

of l CICLOSPORIN

Pazopanib

l Antibacterials: plasma concentration of pazopanib possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN (reduce dose of pazopanib); plasma concentration of pazopanib possibly reduced by l RIFAMPICIN

l Antifungals: plasma concentration of pazopanib increased by l KETOCONAZOLE (reduce dose of pazopanib); plasma concentration of pazopanib possibly increased by

l ITRACONAZOLE and l VORICONAZOLE (reduce dose of pazopanib)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: plasma concentration of pazopanib possibly increased by l ATAZANAVIR, l INDINAVIR and l RITONAVIR (reduce dose of pazopanib); avoidance of pazopanib advised by manufacturer of l BOCEPREVIR; increased risk of ventricular arrhythmias when pazopanib given with

l SAQUINAVIR—avoid concomitant use

Pazopanib (continued)

▶ Cytotoxics: plasma concentration of pazopanib increased by

LAPATINIB

l Grapefruit Juice: manufacturer of pazopanib advises avoid concomitant use with l GRAPEFRUIT JUICE

▶ Lipid-regulating Drugs: separating administration from pazopanib by 12 hours advised by manufacturer of LOMITAPIDE

▶ Ulcer-healing Drugs: absorption of pazopanib possibly reduced by HISTAMINE H2-ANTAGONISTS—manufacturer of pazopanib advises give at least 2 hours before or 10 hours after histamine H2-antagonists; absorption of pazopanib possibly reduced by PROTON PUMP INHIBITORS—manufacturer of pazopanib advises give at the same time as proton pump inhibitors

Pegfilgrastim

▶ Cytotoxics: neutropenia possibly exacerbated when pegfilgrastim given with CAPECITABINE, FLUOROURACIL or TEGAFUR

Peginterferon Alfa *see* Interferons

Pemetrexed

▶ Analgesics: renal excretion of pemetrexed possibly reduced by

NSAIDS and ASPIRIN—consult product literature

l Antimalarials: antifolate effect of pemetrexed increased by

l PYRIMETHAMINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Penicillamine

▶ Analgesics: possible increased risk of nephrotoxicity when penicillamine given with NSAIDS

▶ Antacids: absorption of penicillamine reduced by ANTACIDS

l Antipsychotics: avoid concomitant use of penicillamine with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: penicillamine possibly reduces plasma concentration of DIGOXIN

▶ Iron Salts: absorption of penicillamine reduced by *oral* IRON SALTS

▶ Sodium Aurothiomalate: manufacturer of penicillamine advises

avoid concomitant use with SODIUM AUROTHIOMALATE

(increased risk of toxicity)

▶ Zinc: penicillamine reduces absorption of ZINC, also absorption of penicillamine reduced by zinc

Penicillins

▶ Allopurinol: increased risk of rash when amoxicillin, ampicillin or co-amoxiclav given with ALLOPURINOL

▶ Antibacterials: absorption of phenoxymethylpenicillin reduced by NEOMYCIN; effects of penicillins possibly antagonised by TETRACYCLINES

▶ Anticoagulants: an interaction between broad-spectrum penicillins and COUMARINS and PHENINDIONE has not been demonstrated in studies, but common experience in anticoagulant clinics is that INR can be altered

l Antiepileptics: manufacturer of pivmecillinam advises avoid concomitant use with l SODIUM VALPROATE and l VALPROIC ACID

▶ Cytotoxics: penicillins reduce excretion of METHOTREXATE

(increased risk of toxicity)

▶ Muscle Relaxants: piperacillin enhances effects of NON- DEPOLARISING MUSCLE RELAXANTS and SUXAMETHONIUM

▶ Mycophenolate: co-amoxiclav possibly reduces plasma concentration of MYCOPHENOLATE

▶ Sulfinpyrazone: excretion of penicillins reduced by

SULFINPYRAZONE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Pentamidine Isetionate

l Anti-arrhythmics: increased risk of ventricular arrhythmias when pentamidine isetionate given with l AMIODARONE— avoid concomitant use; possible increased risk of ventricular arrhythmias when pentamidine isetionate given with

l DISOPYRAMIDE

l Antibacterials: increased risk of ventricular arrhythmias when pentamidine isetionate given with *parenteral*

l ERYTHROMYCIN; increased risk of ventricular arrhythmias when pentamidine isetionate given with l MOXIFLOXACIN—

Pentamidine Isetionate

l Antibacterials (continued)

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avoid concomitant use; increased risk of ventricular arrhythmias when pentamidine isetionate given with l DELAMANID; possible increased risk of ventricular

arrhythmias when *parenteral* pentamidine isetionate given with l TELITHROMYCIN

l Antidepressants: avoidance of pentamidine isetionate advised by manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when pentamidine isetionate given with

l TRICYCLICS

▶ Antifungals: possible increased risk of nephrotoxicity when pentamidine isetionate given with AMPHOTERICIN

l Antimalarials: avoidance of pentamidine isetionate advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias)

l Antipsychotics: increased risk of ventricular arrhythmias when pentamidine isetionate given with l AMISULPRIDE or

l DROPERIDOL—avoid concomitant use; increased risk of ventricular arrhythmias when pentamidine isetionate given with l PHENOTHIAZINES

l Antivirals: increased risk of hypocalcaemia when *parenteral* pentamidine isetionate given with l FOSCARNET; increased risk of ventricular arrhythmias when pentamidine isetionate given with l SAQUINAVIR—avoid concomitant use

l Cytotoxics: possible increased risk of ventricular arrhythmias when pentamidine isetionate given with l VANDETANIB—avoid concomitant use

l Ivabradine: increased risk of ventricular arrhythmias when pentamidine isetionate given with l IVABRADINE

Pentazocine *see* Opioid Analgesics

Pentostatin

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Cytotoxics: increased toxicity when pentostatin given with high-dose l CYCLOPHOSPHAMIDE—avoid concomitant use; increased pulmonary toxicity when pentostatin given with l FLUDARABINE (unacceptably high incidence of fatalities)

Pentoxifylline

▶ Aminophylline: pentoxifylline increases plasma concentration of AMINOPHYLLINE

l Analgesics: possible increased risk of bleeding when pentoxifylline given with NSAIDS; increased risk of bleeding when pentoxifylline given with l KETOROLAC (avoid concomitant use)

▶ Theophylline: pentoxifylline increases plasma concentration of

THEOPHYLLINE

Perampanel

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antiepileptics: plasma concentration of perampanel reduced by l CARBAMAZEPINE, l FOSPHENYTOIN, l OXCARBAZEPINE and

l PHENYTOIN (see under Perampanel, p. 398); plasma concentration of perampanel reduced by TOPIRAMATE

▶ Antifungals: plasma concentration of perampanel increased by

KETOCONAZOLE

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

▶ Anxiolytics and Hypnotics: perampanel reduces plasma concentration of MIDAZOLAM

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: perampanel accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

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Pergolide

▶ Antipsychotics: effects of pergolide antagonised by

ANTIPSYCHOTICS

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Metoclopramide: antiparkinsonian effect of pergolide antagonised by METOCLOPRAMIDE

Pericyazine *see* Antipsychotics Perindopril *see* ACE Inhibitors Perphenazine *see* Antipsychotics Pertuzumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Pethidine *see* Opioid Analgesics Phenelzine *see* MAOIs Phenindione

NOTE Change in patient’s clinical condition particularly associated with liver disease, intercurrent illness, or drug administration, necessitates more frequent testing. Major changes in diet (especially involving salads and vegetables) and in alcohol consumption may also affect anticoagulant control

l Alcohol: anticoagulant control with phenindione may be affected by major changes in consumption of l ALCOHOL

l Anabolic Steroids: anticoagulant effect of phenindione enhanced by l ANABOLIC STEROIDS

l Analgesics: anticoagulant effect of phenindione possibly enhanced by l NSAIDS; increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins); increased risk of bleeding when phenindione given with l ASPIRIN (due to antiplatelet effect)

l Anti-arrhythmics: metabolism of phenindione inhibited by

l AMIODARONE (enhanced anticoagulant effect); anticoagulant effect of phenindione possibly enhanced by l DRONEDARONE

l Antibacterials: experience in anticoagulant clinics suggests that INR possibly altered when phenindione is given with l NEOMYCIN (given for local action on gut); anticoagulant effect of phenindione possibly enhanced by LEVOFLOXACIN and l TETRACYCLINES; an interaction between phenindione

and broad-spectrum PENICILLINS has not been demonstrated in studies, but common experience in anticoagulant clinics is that INR can be altered; metabolism of phenindione possibly inhibited by SULFONAMIDES

l Anticoagulants: increased risk of haemorrhage when other anticoagulants given with l APIXABAN, l DABIGATRAN and l RIVAROXABAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

l Antivirals: anticoagulant effect of phenindione possibly enhanced by l RITONAVIR

l Clopidogrel: anticoagulant effect of phenindione enhanced due to antiplatelet action of l CLOPIDOGREL

▶ Corticosteroids: anticoagulant effect of phenindione may be enhanced or reduced by CORTICOSTEROIDS

▶ Cytotoxics: avoidance of phenindione advised by manufacturer of IBRUTINIB

l Dipyridamole: anticoagulant effect of phenindione enhanced due to antiplatelet action of l DIPYRIDAMOLE

l Enteral Foods: anticoagulant effect of phenindione antagonised by vitamin K (present in some l ENTERAL FEEDS )

▶ Iloprost: increased risk of bleeding when phenindione given with ILOPROST

l Lipid-regulating Drugs: anticoagulant effect of phenindione may be enhanced or reduced by l COLESTYRAMINE; anticoagulant effect of phenindione possibly enhanced by l ROSUVASTATIN; anticoagulant effect of phenindione enhanced by l FIBRATES

Phenindione (continued)

l Oestrogens: anticoagulant effect of phenindione antagonised by l OESTROGENS

▶ Prasugrel: possible increased risk of bleeding when phenindione given with PRASUGREL

l Progestogens: anticoagulant effect of phenindione antagonised by l PROGESTOGENS

l Testolactone: anticoagulant effect of phenindione enhanced by l TESTOLACTONE

l Testosterone: anticoagulant effect of phenindione enhanced by l TESTOSTERONE

l Thyroid Hormones: anticoagulant effect of phenindione enhanced by l THYROID HORMONES

l Vitamins: anticoagulant effect of phenindione antagonised by

l VITAMIN K

Phenobarbital

▶ Alcohol: increased sedative effect when phenobarbital given with ALCOHOL

l Aminophylline: phenobarbital accelerates metabolism of

l AMINOPHYLLINE (reduced effect)

▶ Analgesics: phenobarbital reduces plasma concentration of METHADONE; phenobarbital possibly accelerates metabolism of PARACETAMOL (also isolated reports of hepatotoxicity)

l Anthelmintics: phenobarbital reduces plasma concentration of l ALBENDAZOLE and l PRAZIQUANTEL—consider increasing albendazole and praziquantel dose when given for systemic infections

l Anti-arrhythmics: phenobarbital accelerates metabolism of DISOPYRAMIDE (reduced plasma concentration); phenobarbital possibly reduces plasma concentration of l DRONEDARONE— avoid concomitant use; phenobarbital possibly accelerates metabolism of PROPAFENONE

l Antibacterials: phenobarbital accelerates metabolism of METRONIDAZOLE (reduced effect); phenobarbital possibly reduces plasma concentration of RIFAMPICIN; phenobarbital accelerates metabolism of DOXYCYCLINE (reduced plasma concentration); phenobarbital possibly accelerates metabolism of l CHLORAMPHENICOL (reduced plasma concentration); phenobarbital reduces plasma concentration of l TELITHROMYCIN (avoid during and for 2 weeks after phenobarbital)

l Anticoagulants: phenobarbital possibly reduces plasma concentration of l APIXABAN; phenobarbital accelerates metabolism of l COUMARINS (reduced anticoagulant effect); phenobarbital possibly reduces plasma concentration of

l RIVAROXABAN—manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antidepressants: phenobarbital possibly reduces plasma concentration of REBOXETINE; phenobarbital reduces plasma concentration of PAROXETINE; phenobarbital accelerates metabolism of l MIANSERIN (reduced plasma concentration); anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS

(convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered); plasma concentration of phenobarbital possibly reduced by l ST JOHN’S WORT—avoid concomitant use; phenobarbital possibly accelerates metabolism of l TRICYCLICS (reduced plasma concentration)

l Antiepileptics: plasma concentration of phenobarbital possibly increased by CARBAMAZEPINE; phenobarbital possibly reduces plasma concentration of ETHOSUXIMIDE, RUFINAMIDE and TOPIRAMATE; plasma concentration of phenobarbital often increased by FOSPHENYTOIN and PHENYTOIN, plasma concentration of fosphenytoin and phenytoin often reduced but may be increased; phenobarbital reduces plasma concentration of LAMOTRIGINE, TIAGABINE and ZONISAMIDE; plasma concentration of phenobarbital increased by OXCARBAZEPINE, also plasma concentration of an active metabolite of oxcarbazepine reduced; plasma concentration of phenobarbital increased by SODIUM VALPROATE and VALPROIC ACID (also plasma concentration of sodium valproate and valproic acid reduced); plasma concentration of phenobarbital increased by l STIRIPENTOL

l Antifungals: phenobarbital possibly reduces plasma concentration of ITRACONAZOLE and l POSACONAZOLE;

Phenobarbital

l Antifungals (continued)

phenobarbital possibly reduces plasma concentration of l VORICONAZOLE—avoid concomitant use; phenobarbital reduces absorption of GRISEOFULVIN (reduced effect)

l Antimalarials: avoidance of phenobarbital advised by manufacturer of ARTENIMOL WITH PIPERAQUINE; anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered); phenobarbital accelerates metabolism of HALOPERIDOL (reduced plasma concentration); plasma concentration of both drugs reduced when phenobarbital given with CHLORPROMAZINE; phenobarbital possibly reduces plasma concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); phenobarbital possibly reduces plasma concentration of CLOZAPINE; phenobarbital possibly reduces plasma concentration of l LURASIDONE— avoid concomitant use

l Antivirals: phenobarbital possibly reduces plasma concentration of ABACAVIR, DARUNAVIR, FOSAMPRENAVIR, l INDINAVIR, l LOPINAVIR and l SAQUINAVIR; avoidance of

phenobarbital advised by manufacturer of l BOCEPREVIR and l RILPIVIRINE (plasma concentration of boceprevir and rilpivirine possibly reduced); phenobarbital possibly reduces plasma concentration of l DACLATASVIR and l SIMEPREVIR— manufacturer of daclatasvir and simeprevir advises avoid concomitant use; avoidance of phenobarbital advised by manufacturer of DOLUTEGRAVIR, l ELVITEGRAVIR, ETRAVIRINE, SOFOSBUVIR and l TELAPREVIR

▶ Anxiolytics and Hypnotics: increased sedative effect when phenobarbital given with ANXIOLYTICS AND HYPNOTICS; phenobarbital often reduces plasma concentration of CLONAZEPAM

▶ Aprepitant: phenobarbital possibly reduces plasma concentration of APREPITANT

▶ Avanafil: phenobarbital possibly reduces plasma concentration of AVANAFIL—manufacturer of avanafil advises avoid concomitant use

▶ Beta-blockers: phenobarbital possibly reduces plasma concentration of PROPRANOLOL

▶ Caffeine citrate: effects of phenobarbital possibly antagonised by CAFFEINE CITRATE

l Calcium-channel Blockers: phenobarbital probably reduces effects of l CALCIUM-CHANNEL BLOCKERS; avoidance of phenobarbital advised by manufacturer of ISRADIPINE; avoidance of phenobarbital advised by manufacturer of

l NIMODIPINE (plasma concentration of nimodipine reduced)

l Cannabis Extract: phenobarbital possibly reduces plasma concentration of l CANNABIS EXTRACT—manufacturer of cannabis extract advises avoid concomitant use

l Ciclosporin: phenobarbital accelerates metabolism of

l CICLOSPORIN (reduced plasma concentration)

l Cobicistat: phenobarbital possibly reduces plasma concentration of l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Corticosteroids: phenobarbital accelerates metabolism of

l CORTICOSTEROIDS (reduced effect)

l Cytotoxics: phenobarbital possibly decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); phenobarbital possibly reduces plasma concentration of BORTEZOMIB, l BOSUTINIB, CRIZOTINIB and PONATINIB—manufacturer of bortezomib, bosutinib, crizotinib and ponatinib advises avoid concomitant use; phenobarbital possibly reduces plasma concentration of

l CABOZANTINIB—avoid concomitant use; avoidance of phenobarbital advised by manufacturer of l CABAZITAXEL, DABRAFENIB and GEFITINIB; avoidance of phenobarbital advised by manufacturer of DASATINIB and VANDETANIB (plasma concentration of dasatinib and vandetanib possibly reduced); phenobarbital possibly reduces plasma concentration of ETOPOSIDE; phenobarbital reduces plasma concentration of IRINOTECAN and its active metabolite; manufacturer of procarbazine advises possible increased risk

Phenobarbital

l Cytotoxics (continued)

Interactions | Appendix 1

of hypersensitivity reactions when phenobarbital given with

PROCARBAZINE

l Diuretics: phenobarbital reduces plasma concentration of l EPLERENONE—avoid concomitant use; increased risk of osteomalacia when phenobarbital given with CARBONIC ANHYDRASE INHIBITORS

▶ Folates: plasma concentration of phenobarbital possibly reduced by FOLATES

▶ Fosaprepitant: phenobarbital possibly reduces plasma concentration of FOSAPREPITANT

l Hormone Antagonists: phenobarbital possibly reduces plasma concentration of l ABIRATERONE—manufacturer of abiraterone advises avoid concomitant use; phenobarbital accelerates metabolism of TOREMIFENE (reduced plasma concentration)

l Ivacaftor: phenobarbital possibly reduces plasma

concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

▶ Leukotriene Receptor Antagonists: phenobarbital reduces plasma concentration of MONTELUKAST

l Oestrogens: phenobarbital accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: phenobarbital accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

▶ Roflumilast: phenobarbital possibly inhibits effects of ROFLUMILAST (manufacturer of roflumilast advises avoid concomitant use)

▶ Sodium Oxybate: avoidance of phenobarbital advised by manufacturer of SODIUM OXYBATE

▶ Sympathomimetics: plasma concentration of phenobarbital possibly increased by METHYLPHENIDATE

l Tacrolimus: phenobarbital reduces plasma concentration of

l TACROLIMUS

l Theophylline: phenobarbital accelerates metabolism of

l THEOPHYLLINE (reduced effect)

▶ Thyroid Hormones: phenobarbital accelerates metabolism of THYROID HORMONES (may increase requirements for thyroid hormones in hypothyroidism)

▶ Ticagrelor: phenobarbital possibly reduces plasma concentration of TICAGRELOR

l Ulipristal: avoidance of phenobarbital advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

▶ Vitamins: phenobarbital possibly increases requirements for ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL or VITAMIN D

Phenothiazines *see* Antipsychotics Phenoxybenzamine *see* Alpha-blockers Phenoxymethylpenicillin *see* Penicillins Phentolamine *see* Alpha-blockers Phenylephrine *see* Sympathomimetics Phenytoin

▶ Alcohol: plasma concentration of phenytoin possibly reduced by chronic heavy consumption of ALCOHOL

l Aminophylline: plasma concentration of both drugs reduced when phenytoin given with l AMINOPHYLLINE

l Analgesics: excretion of phenytoin possibly reduced by ACEMETACIN (increased risk of toxicity); phenytoin possibly accelerates metabolism of FENTANYL (reduced effect); phenytoin accelerates metabolism of METHADONE (reduced effect and risk of withdrawal effects); phenytoin possibly increases risk of l PETHIDINE toxicity; effects of phenytoin enhanced by ASPIRIN; phenytoin possibly accelerates

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Phenytoin

l Analgesics (continued)

metabolism of PARACETAMOL (also isolated reports of hepatotoxicity)

▶ Antacids: absorption of phenytoin reduced by ANTACIDS

l Anthelmintics: phenytoin reduces plasma concentration of

l ALBENDAZOLE and l PRAZIQUANTEL—consider increasing albendazole and praziquantel dose when given for systemic infections; plasma concentration of phenytoin possibly increased by LEVAMISOLE

l Anti-arrhythmics: metabolism of phenytoin inhibited by

l AMIODARONE (increased plasma concentration); phenytoin reduces plasma concentration of DISOPYRAMIDE; phenytoin possibly reduces plasma concentration of l DRONEDARONE— avoid concomitant use

l Antibacterials: metabolism of phenytoin inhibited by CLARITHROMYCIN (increased plasma concentration); metabolism of phenytoin possibly inhibited by METRONIDAZOLE (increased plasma concentration); plasma concentration of phenytoin increased or decreased by CIPROFLOXACIN; phenytoin accelerates metabolism of DOXYCYCLINE (reduced plasma concentration); phenytoin possibly reduces plasma concentration of l BEDAQUILINE— manufacturer of bedaquiline advises avoid concomitant use; plasma concentration of phenytoin increased by

l CHLORAMPHENICOL (increased risk of toxicity); metabolism of phenytoin possibly inhibited by ISONIAZID (increased risk of toxicity); metabolism of phenytoin accelerated by

l RIFAMYCINS (reduced plasma concentration); plasma concentration of phenytoin possibly increased by SULFONAMIDES; phenytoin reduces plasma concentration of l TELITHROMYCIN (avoid during and for 2 weeks after

phenytoin); plasma concentration of phenytoin increased by

l TRIMETHOPRIM (also increased antifolate effect)

l Anticoagulants: phenytoin possibly reduces plasma concentration of l APIXABAN; phenytoin accelerates metabolism of l COUMARINS (possibility of reduced anticoagulant effect, but enhancement also reported); phenytoin possibly reduces plasma concentration of DABIGATRAN—manufacturer of dabigatran advises avoid concomitant use; phenytoin possibly reduces plasma concentration of l RIVAROXABAN—manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antidepressants: plasma concentration of phenytoin increased

by l FLUOXETINE and l FLUVOXAMINE; phenytoin reduces plasma concentration of l MIANSERIN, MIRTAZAPINE and PAROXETINE; plasma concentration of phenytoin possibly increased by SERTRALINE, also plasma concentration of sertraline possibly reduced; anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC- RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered); plasma concentration of phenytoin possibly reduced by l ST JOHN’S WORT—avoid concomitant use; phenytoin possibly reduces plasma concentration of l TRICYCLICS

▶ Antidiabetics: plasma concentration of phenytoin transiently increased by TOLBUTAMIDE (possibility of toxicity)

l Antiepileptics: plasma concentration of both drugs often reduced when phenytoin given with CARBAMAZEPINE, also plasma concentration of phenytoin may be increased; phenytoin reduces plasma concentration of ESLICARBAZEPINE, also plasma concentration of phenytoin increased; plasma concentration of phenytoin possibly increased by

l ETHOSUXIMIDE, also plasma concentration of ethosuximide possibly reduced; phenytoin reduces plasma concentration of LAMOTRIGINE, TIAGABINE and ZONISAMIDE; plasma

concentration of phenytoin increased by OXCARBAZEPINE, also plasma concentration of an active metabolite of oxcarbazepine reduced; phenytoin reduces plasma concentration of l PERAMPANEL (see under Perampanel,

p. 398); phenytoin often increases plasma concentration of PHENOBARBITAL and PRIMIDONE, plasma concentration of phenytoin often reduced but may be increased; phenytoin possibly reduces plasma concentration of RETIGABINE;

Phenytoin

l Antiepileptics (continued)

phenytoin possibly reduces plasma concentration of RUFINAMIDE, also plasma concentration of phenytoin possibly increased; plasma concentration of phenytoin increased or possibly reduced when given with SODIUM VALPROATE and VALPROIC ACID, also plasma concentration of sodium valproate and valproic acid reduced; plasma concentration of phenytoin increased by l STIRIPENTOL; plasma concentration of phenytoin increased by l TOPIRAMATE (also plasma concentration of topiramate reduced); plasma concentration of phenytoin reduced by VIGABATRIN

l Antifungals: phenytoin reduces plasma concentration of

l KETOCONAZOLE and l POSACONAZOLE; anticonvulsant effect of phenytoin enhanced by l MICONAZOLE (plasma concentration of phenytoin increased); plasma concentration of phenytoin increased by l FLUCONAZOLE (consider reducing dose of phenytoin); phenytoin reduces plasma concentration of l ITRACONAZOLE—avoid concomitant use; plasma concentration of phenytoin increased by l VORICONAZOLE, also phenytoin reduces plasma concentration of voriconazole (increase dose of voriconazole and also monitor for phenytoin toxicity); phenytoin possibly reduces plasma concentration of CASPOFUNGIN—consider increasing dose of caspofungin

l Antimalarials: avoidance of phenytoin advised by manufacturer of ARTENIMOL WITH PIPERAQUINE; anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE; anticonvulsant effect of phenytoin antagonised by

l PYRIMETHAMINE, also increased antifolate effect

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered); phenytoin reduces plasma concentration of HALOPERIDOL; plasma concentration of phenytoin possibly increased or decreased by CHLORPROMAZINE; phenytoin possibly reduces plasma concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); phenytoin accelerates metabolism of CLOZAPINE and QUETIAPINE (reduced plasma concentration); phenytoin possibly reduces plasma concentration of l LURASIDONE— avoid concomitant use

l Antivirals: phenytoin possibly reduces plasma concentration

of ABACAVIR, DARUNAVIR, LOPINAVIR and SAQUINAVIR;

avoidance of phenytoin advised by manufacturer of

l BOCEPREVIR and l RILPIVIRINE (plasma concentration of boceprevir and rilpivirine possibly reduced); phenytoin possibly reduces plasma concentration of l DACLATASVIR and l SIMEPREVIR—manufacturer of daclatasvir and simeprevir advises avoid concomitant use; avoidance of phenytoin advised by manufacturer of DOLUTEGRAVIR, l ELVITEGRAVIR, ETRAVIRINE, SOFOSBUVIR and l TELAPREVIR; phenytoin possibly reduces plasma concentration of l INDINAVIR, also plasma concentration of phenytoin possibly increased; phenytoin possibly reduces plasma concentration of RITONAVIR, also plasma concentration of phenytoin possibly affected; plasma concentration of phenytoin increased or decreased by ZIDOVUDINE

▶ Anxiolytics and Hypnotics: phenytoin often reduces plasma concentration of CLONAZEPAM; plasma concentration of phenytoin increased or decreased by DIAZEPAM; plasma concentration of phenytoin possibly increased or decreased by BENZODIAZEPINES

▶ Aprepitant: phenytoin possibly reduces plasma concentration of APREPITANT

▶ Bupropion: phenytoin reduces plasma concentration of

BUPROPION

▶ Caffeine citrate: phenytoin reduces plasma concentration of

CAFFEINE CITRATE

l Calcium-channel Blockers: phenytoin reduces effects of FELODIPINE and VERAPAMIL; avoidance of phenytoin advised by manufacturer of ISRADIPINE; avoidance of phenytoin advised by manufacturer of NIMODIPINE (plasma concentration of nimodipine possibly reduced); plasma

Phenytoin

l Calcium-channel Blockers (continued)

concentration of phenytoin increased by l DILTIAZEM but also effect of diltiazem reduced

l Cannabis Extract: phenytoin possibly reduces plasma concentration of l CANNABIS EXTRACT—manufacturer of cannabis extract advises avoid concomitant use

▶ Cardiac Glycosides: phenytoin possibly reduces plasma concentration of DIGOXIN

l Ciclosporin: phenytoin accelerates metabolism of

l CICLOSPORIN (reduced plasma concentration)

l Cobicistat: phenytoin possibly reduces plasma concentration of l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Corticosteroids: phenytoin accelerates metabolism of

l CORTICOSTEROIDS (reduced effect)

l Cytotoxics: phenytoin possibly reduces plasma concentration of BUSULFAN, ERIBULIN and ETOPOSIDE; metabolism of phenytoin possibly inhibited by CAPECITABINE, FLUOROURACIL and TEGAFUR (increased risk of toxicity); phenytoin increases antifolate effect of METHOTREXATE; plasma concentration of phenytoin possibly reduced by CISPLATIN; phenytoin possibly decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); phenytoin possibly reduces plasma concentration of BORTEZOMIB,

l BOSUTINIB, CRIZOTINIB, l IBRUTINIB, l IDELALISIB and

PONATINIB—manufacturer of bortezomib, bosutinib, crizotinib, ibrutinib, idelalisib and ponatinib advises avoid concomitant use; phenytoin possibly reduces plasma concentration of l CABOZANTINIB—avoid concomitant use; avoidance of phenytoin advised by manufacturer of

l CABAZITAXEL, DABRAFENIB, GEFITINIB, l LAPATINIB and

VEMURAFENIB; avoidance of phenytoin advised by manufacturer of DASATINIB and l VISMODEGIB (plasma concentration of dasatinib and vismodegib possibly reduced); phenytoin reduces plasma concentration of l IMATINIB—avoid concomitant use; phenytoin reduces plasma concentration of IRINOTECAN and its active metabolite; manufacturer of procarbazine advises possible increased risk of hypersensitivity reactions when phenytoin given with PROCARBAZINE

l Dexrazoxane: absorption of phenytoin possibly reduced by

l DEXRAZOXANE

▶ Diazoxide: plasma concentration of phenytoin reduced by

DIAZOXIDE, also effect of diazoxide may be reduced

l Disulfiram: metabolism of phenytoin inhibited by

l DISULFIRAM (increased risk of toxicity)

l Diuretics: plasma concentration of phenytoin possibly increased by l ACETAZOLAMIDE; phenytoin antagonises effects of FUROSEMIDE; phenytoin reduces plasma concentration of

l EPLERENONE—avoid concomitant use; increased risk of osteomalacia when phenytoin given with CARBONIC ANHYDRASE INHIBITORS

▶ Dopaminergics: phenytoin possibly reduces effects of CO- BENELDOPA, CO-CARELDOPA and LEVODOPA

▶ Enteral Foods: absorption of phenytoin possibly reduced by

ENTERAL FEEDS

▶ Folates: plasma concentration of phenytoin possibly reduced by FOLATES

▶ Fosaprepitant: phenytoin possibly reduces plasma concentration of FOSAPREPITANT

l Hormone Antagonists: phenytoin possibly reduces plasma concentration of l ABIRATERONE—manufacturer of abiraterone advises avoid concomitant use; phenytoin possibly accelerates metabolism of TOREMIFENE

▶ 5HT3-receptor Antagonists: phenytoin accelerates metabolism of ONDANSETRON (reduced effect)

l Ivacaftor: phenytoin possibly reduces plasma concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

▶ Leflunomide: plasma concentration of phenytoin possibly increased by LEFLUNOMIDE

▶ Lipid-regulating Drugs: absorption of phenytoin possibly reduced by COLESEVELAM; combination of phenytoin with FLUVASTATIN may increase plasma concentration of either drug (or both)

Phenytoin (continued)

▶ Lithium: neurotoxicity may occur when phenytoin given with

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LITHIUM without increased plasma concentration of lithium

▶ Macitentan: avoidance of phenytoin advised by manufacturer of MACITENTAN

▶ Modafinil: plasma concentration of phenytoin possibly increased by MODAFINIL

l Muscle Relaxants: *long-term use* of phenytoin reduces effects of l NON-DEPOLARISING MUSCLE RELAXANTS (but *acute use* of phenytoin might increase effects of non-depolarising muscle relaxants)

l Oestrogens: phenytoin accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: phenytoin accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

▶ Roflumilast: phenytoin possibly inhibits effects of ROFLUMILAST

(manufacturer of roflumilast advises avoid concomitant use)

l Sulfinpyrazone: plasma concentration of phenytoin increased by l SULFINPYRAZONE

▶ Sympathomimetics: plasma concentration of phenytoin increased by METHYLPHENIDATE

▶ Tacrolimus: phenytoin reduces plasma concentration of TACROLIMUS, also plasma concentration of phenytoin possibly increased

l Theophylline: plasma concentration of both drugs reduced when phenytoin given with l THEOPHYLLINE

▶ Thyroid Hormones: phenytoin accelerates metabolism of THYROID HORMONES (may increase requirements in hypothyroidism), also plasma concentration of phenytoin possibly increased

▶ Tibolone: phenytoin accelerates metabolism of TIBOLONE

▶ Ticagrelor: phenytoin possibly reduces plasma concentration of TICAGRELOR

l Ulcer-healing Drugs: metabolism of phenytoin inhibited by

l CIMETIDINE (increased plasma concentration); effects of phenytoin enhanced by l ESOMEPRAZOLE; effects of phenytoin possibly enhanced by OMEPRAZOLE; absorption of phenytoin reduced by l SUCRALFATE

l Ulipristal: avoidance of phenytoin advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

▶ Vaccines: effects of phenytoin enhanced by INFLUENZA VACCINE

▶ Vitamins: phenytoin possibly increases requirements for ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL or VITAMIN D

Pholcodine

▶ Antidepressants: manufacturer of pholcodine advises avoid for 2 weeks after stopping MAOIS

Phosphodiesterase Type-3 Inhibitors

l Anagrelide: avoidance of enoximone and milrinone advised by manufacturer of l ANAGRELIDE

Pilocarpine *see* Parasympathomimetics

Pimozide *see* Antipsychotics Pindolol *see* Beta-blockers Pioglitazone *see* Antidiabetics Piperacillin *see* Penicillins

Piperaquine *see* Artenimol with Piperaquine

Pipotiazine *see* Antipsychotics

Pirfenidone

l Antibacterials: plasma concentration of pirfenidone increased by l CIPROFLOXACIN—see under Pirfenidone, p. 260

l Antidepressants: plasma concentration of pirfenidone increased by l FLUVOXAMINE—manufacturer of pirfenidone advises avoid concomitant use

▶ Grapefruit Juice: manufacturer of pirfenidone advises avoid concomitant use with GRAPEFRUIT JUICE

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Piroxicam *see* NSAIDs Pivmecillinam *see* Penicillins Pixantrone

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when pixantrone given with live l VACCINES—avoid concomitant use

Pizotifen

▶ Adrenergic Neurone Blockers: pizotifen antagonises hypotensive effect of ADRENERGIC NEURONE BLOCKERS

Platinum Compounds

l Aldesleukin: avoidance of cisplatin advised by manufacturer of

l ALDESLEUKIN

l Antibacterials: increased risk of nephrotoxicity and possibly of ototoxicity when platinum compounds given with

l AMINOGLYCOSIDES or l POLYMYXINS; increased risk of nephrotoxicity and ototoxicity when platinum compounds given with CAPREOMYCIN; increased risk of nephrotoxicity and possibly of ototoxicity when cisplatin given with VANCOMYCIN

▶ Antiepileptics: cisplatin possibly reduces plasma concentration of FOSPHENYTOIN and PHENYTOIN

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Cytotoxics: increased risk of otoxicity when cisplatin given with IFOSFAMIDE; increased pulmonary toxicity when cisplatin given with l BLEOMYCIN and l METHOTREXATE

▶ Diuretics: increased risk of nephrotoxicity and ototoxicity when platinum compounds given with DIURETICS

Pneumococcal Vaccine *see* Vaccines Poliomyelitis Vaccine *see* Vaccines Polymyxins

▶ Antibacterials: increased risk of nephrotoxicity when

colistimethate sodium or polymyxins given with AMINOGLYCOSIDES; increased risk of nephrotoxicity when colistimethate sodium or polymyxins given with CAPREOMYCIN; increased risk of nephrotoxicity when polymyxins given with VANCOMYCIN; increased risk of nephrotoxicity and ototoxicity when colistimethate sodium given with VANCOMYCIN

▶ Antifungals: increased risk of nephrotoxicity when polymyxins given with AMPHOTERICIN

l Ciclosporin: increased risk of nephrotoxicity when polymyxins given with l CICLOSPORIN

l Cytotoxics: increased risk of nephrotoxicity and possibly of ototoxicity when polymyxins given with l PLATINUM COMPOUNDS

l Diuretics: increased risk of otoxicity when polymyxins given

with l LOOP DIURETICS

l Muscle Relaxants: polymyxins enhance effects of l NON-

DEPOLARISING MUSCLE RELAXANTS and l SUXAMETHONIUM

l Parasympathomimetics: polymyxins antagonise effects of

l NEOSTIGMINE and l PYRIDOSTIGMINE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Polysaccharide-iron Complex *see* Iron salts

Polystyrene Sulfonate Resins

▶ Antacids: risk of intestinal obstruction when polystyrene sulfonate resins given with ALUMINIUM HYDROXIDE; risk of metabolic alkalosis when polystyrene sulfonate resins given with ORAL MAGNESIUM SALTS

▶ Thyroid Hormones: polystyrene sulfonate resins reduce absorption of LEVOTHYROXINE

Pomalidomide

l Antidepressants: plasma concentration of pomalidomide increased by l FLUVOXAMINE

Ponatinib

l Antibacterials: plasma concentration of ponatinib possibly increased by CLARITHROMYCIN and TELITHROMYCIN—consider reducing initial dose of ponatinib (see under Ponatinib,

p. 814); plasma concentration of ponatinib possibly reduced by RIFABUTIN—manufacturer of ponatinib advises avoid concomitant use; plasma concentration of ponatinib reduced by l RIFAMPICIN—manufacturer of ponatinib advises avoid concomitant use

Ponatinib (continued)

▶ Antidepressants: plasma concentration of ponatinib possibly reduced by ST JOHN’S WORT—manufacturer of ponatinib advises avoid concomitant use

▶ Antiepileptics: plasma concentration of ponatinib possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL,

PHENYTOIN and PRIMIDONE—manufacturer of ponatinib advises avoid concomitant use

▶ Antifungals: plasma concentration of ponatinib increased by KETOCONAZOLE; plasma concentration of ponatinib possibly increased by ITRACONAZOLE and VORICONAZOLE—consider reducing initial dose of ponatinib (see under Ponatinib,

p. 814)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Antivirals: plasma concentration of ponatinib possibly increased by INDINAVIR, RITONAVIR and SAQUINAVIR—consider reducing initial dose of ponatinib (see under Ponatinib,

p. 814)

▶ Grapefruit Juice: plasma concentration of ponatinib possibly increased by GRAPEFRUIT JUICE

Posaconazole *see* Antifungals, Triazole Potassium Canrenoate *see* Diuretics Potassium Aminobenzoate

▶ Antibacterials: potassium aminobenzoate inhibits effects of

SULFONAMIDES

Potassium Bicarbonate *see* Potassium Salts Potassium Chloride *see* Potassium Salts Potassium Citrate *see* Potassium Salts Potassium Salts

NOTE Includes salt substitutes

l ACE Inhibitors: increased risk of severe hyperkalaemia when potassium salts given with l ACE INHIBITORS

▶ Aliskiren: increased risk of hyperkalaemia when potassium salts given with ALISKIREN

l Angiotensin-II Receptor Antagonists: increased risk of hyperkalaemia when potassium salts given with

l ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antibacterials: avoid concomitant use of potassium citrate with METHENAMINE

l Ciclosporin: increased risk of hyperkalaemia when potassium salts given with l CICLOSPORIN

l Diuretics: increased risk of hyperkalaemia when potassium salts given with l POTASSIUM-SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

l Tacrolimus: increased risk of hyperkalaemia when potassium

salts given with l TACROLIMUS

▶ Ulcer-healing Drugs: avoidance of potassium citrate advised by manufacturer of SUCRALFATE

Pramipexole

▶ Antipsychotics: manufacturer of pramipexole advises avoid concomitant use of ANTIPSYCHOTICS (antagonism of effect)

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Ulcer-healing Drugs: excretion of pramipexole reduced by

CIMETIDINE (increased plasma concentration)

Prasugrel

▶ Analgesics: possible increased risk of bleeding when prasugrel given with NSAIDS

▶ Anticoagulants: possible increased risk of bleeding when prasugrel given with COUMARINS or PHENINDIONE

▶ Clopidogrel: possible increased risk of bleeding when prasugrel given with CLOPIDOGREL

Pravastatin *see* Statins

Praziquantel

l Antibacterials: plasma concentration of praziquantel reduced by l RIFAMPICIN—avoid concomitant use

l Antiepileptics: plasma concentration of praziquantel reduced by l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE—consider increasing praziquantel dose when given for systemic infections

▶ Antifungals: plasma concentration of praziquantel increased by KETOCONAZOLE

Praziquantel (continued)

l Antimalarials: plasma concentration of praziquantel reduced by l CHLOROQUINE—consider increasing praziquantel dose when given for systemic infections

▶ Corticosteroids: plasma concentration of praziquantel possibly reduced by continuous use of DEXAMETHASONE

▶ Grapefruit Juice: plasma concentration of praziquantel increased by GRAPEFRUIT JUICE

▶ Ulcer-healing Drugs: plasma concentration of praziquantel increased by CIMETIDINE

Prazosin *see* Alpha-blockers Prednisolone *see* Corticosteroids Prednisone *see* Corticosteroids Pregabalin

l Antidepressants: anticonvulsant effect of antiepileptics

possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Prilocaine

▶ Anti-arrhythmics: increased myocardial depression when prilocaine given with ANTI-ARRHYTHMICS

▶ Antibacterials: increased risk of methaemoglobinaemia when prilocaine given with SULFONAMIDES

Primaquine

l Antimalarials: avoidance of antimalarials advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

▶ Mepacrine: plasma concentration of primaquine increased by

MEPACRINE (increased risk of toxicity)

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Primidone

▶ Alcohol: increased sedative effect when primidone given with

ALCOHOL

l Aminophylline: primidone accelerates metabolism of

l AMINOPHYLLINE (reduced effect)

▶ Analgesics: primidone reduces plasma concentration of METHADONE; primidone possibly accelerates metabolism of PARACETAMOL (also isolated reports of hepatotoxicity)

l Anthelmintics: primidone reduces plasma concentration of

l ALBENDAZOLE and l PRAZIQUANTEL—consider increasing albendazole and praziquantel dose when given for systemic infections

l Anti-arrhythmics: primidone accelerates metabolism of DISOPYRAMIDE (reduced plasma concentration); primidone possibly reduces plasma concentration of l DRONEDARONE— avoid concomitant use; primidone possibly accelerates metabolism of PROPAFENONE

l Antibacterials: primidone accelerates metabolism of METRONIDAZOLE (reduced effect); primidone possibly reduces plasma concentration of RIFAMPICIN; primidone accelerates metabolism of DOXYCYCLINE (reduced plasma concentration); primidone possibly accelerates metabolism of

l CHLORAMPHENICOL (reduced plasma concentration); primidone reduces plasma concentration of l TELITHROMYCIN (avoid during and for 2 weeks after primidone)

l Anticoagulants: primidone possibly reduces plasma concentration of l APIXABAN; primidone accelerates metabolism of l COUMARINS (reduced anticoagulant effect); primidone possibly reduces plasma concentration of

l RIVAROXABAN—manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antidepressants: primidone possibly reduces plasma concentration of REBOXETINE; primidone reduces plasma concentration of PAROXETINE; primidone accelerates metabolism of l MIANSERIN (reduced plasma concentration);

Primidone

l Antidepressants (continued)

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anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS

(convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered); plasma concentration of primidone possibly reduced by l ST JOHN’S WORT—avoid concomitant use; primidone possibly accelerates metabolism of l TRICYCLICS (reduced plasma concentration)

l Antiepileptics: plasma concentration of primidone possibly increased by CARBAMAZEPINE; primidone possibly reduces plasma concentration of ETHOSUXIMIDE, RUFINAMIDE and TOPIRAMATE; plasma concentration of primidone often increased by FOSPHENYTOIN and PHENYTOIN, plasma concentration of fosphenytoin and phenytoin often reduced but may be increased; primidone reduces plasma concentration of LAMOTRIGINE, TIAGABINE and ZONISAMIDE; plasma concentration of primidone increased by OXCARBAZEPINE, also plasma concentration of an active metabolite of oxcarbazepine reduced; plasma concentration of primidone increased by SODIUM VALPROATE and VALPROIC ACID (also plasma concentration of sodium valproate and valproic acid reduced); plasma concentration of primidone increased by l STIRIPENTOL

l Antifungals: primidone possibly reduces plasma concentration of ITRACONAZOLE and l POSACONAZOLE; primidone possibly reduces plasma concentration of l VORICONAZOLE—avoid concomitant use; primidone reduces absorption of GRISEOFULVIN (reduced effect)

l Antimalarials: avoidance of primidone advised by manufacturer of ARTENIMOL WITH PIPERAQUINE; anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered); primidone accelerates metabolism of HALOPERIDOL (reduced plasma concentration); plasma concentration of both drugs reduced when primidone given with CHLORPROMAZINE; primidone possibly reduces plasma concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); primidone possibly reduces plasma concentration of CLOZAPINE; primidone possibly reduces plasma concentration of l LURASIDONE—avoid concomitant use

l Antivirals: primidone possibly reduces plasma concentration

of ABACAVIR, DARUNAVIR, FOSAMPRENAVIR, l INDINAVIR,

l LOPINAVIR and l SAQUINAVIR; avoidance of primidone advised by manufacturer of l BOCEPREVIR and l RILPIVIRINE (plasma concentration of boceprevir and rilpivirine possibly reduced); primidone possibly reduces plasma concentration of l DACLATASVIR and l SIMEPREVIR—manufacturer of daclatasvir and simeprevir advises avoid concomitant use; avoidance of primidone advised by manufacturer of DOLUTEGRAVIR, l ELVITEGRAVIR, ETRAVIRINE, SOFOSBUVIR and l TELAPREVIR

▶ Anxiolytics and Hypnotics: increased sedative effect when primidone given with ANXIOLYTICS AND HYPNOTICS; primidone often reduces plasma concentration of CLONAZEPAM

▶ Aprepitant: primidone possibly reduces plasma concentration of APREPITANT

▶ Avanafil: primidone possibly reduces plasma concentration of AVANAFIL—manufacturer of avanafil advises avoid concomitant use

▶ Beta-blockers: primidone possibly reduces plasma concentration of PROPRANOLOL

▶ Caffeine citrate: effects of primidone possibly antagonised by

CAFFEINE CITRATE

l Calcium-channel Blockers: primidone probably reduces effects of l CALCIUM-CHANNEL BLOCKERS; avoidance of primidone advised by manufacturer of ISRADIPINE; avoidance of primidone advised by manufacturer of l NIMODIPINE (plasma concentration of nimodipine reduced)

l Cannabis Extract: primidone possibly reduces plasma concentration of l CANNABIS EXTRACT—manufacturer of cannabis extract advises avoid concomitant use

Interactions | Appendix 1

Primidone (continued)

l Ciclosporin: primidone accelerates metabolism of

l CICLOSPORIN (reduced plasma concentration)

l Cobicistat: primidone possibly reduces plasma concentration of l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Corticosteroids: primidone accelerates metabolism of

l CORTICOSTEROIDS (reduced effect)

l Cytotoxics: primidone possibly decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); primidone possibly reduces plasma concentration of BORTEZOMIB, l BOSUTINIB, CRIZOTINIB and PONATINIB—manufacturer of bortezomib, bosutinib, crizotinib and ponatinib advises avoid concomitant use; primidone possibly reduces plasma concentration of

l CABOZANTINIB—avoid concomitant use; avoidance of primidone advised by manufacturer of l CABAZITAXEL, DABRAFENIB and GEFITINIB; avoidance of primidone advised by manufacturer of DASATINIB and VANDETANIB (plasma concentration of dasatinib and vandetanib possibly reduced); primidone possibly reduces plasma concentration of ETOPOSIDE; primidone reduces plasma concentration of IRINOTECAN and its active metabolite; manufacturer of procarbazine advises possible increased risk of hypersensitivity reactions when primidone given with PROCARBAZINE

l Diuretics: primidone reduces plasma concentration of

l EPLERENONE—avoid concomitant use; increased risk of osteomalacia when primidone given with CARBONIC ANHYDRASE INHIBITORS

▶ Folates: plasma concentration of primidone possibly reduced by FOLATES

▶ Fosaprepitant: primidone possibly reduces plasma concentration of FOSAPREPITANT

l Hormone Antagonists: primidone possibly reduces plasma concentration of l ABIRATERONE—manufacturer of abiraterone advises avoid concomitant use; primidone accelerates metabolism of TOREMIFENE (reduced plasma concentration)

l Ivacaftor: primidone possibly reduces plasma concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

▶ Leukotriene Receptor Antagonists: primidone reduces plasma concentration of MONTELUKAST

l Oestrogens: primidone accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: primidone accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

▶ Roflumilast: primidone possibly inhibits effects of ROFLUMILAST (manufacturer of roflumilast advises avoid concomitant use)

▶ Sodium Oxybate: avoidance of primidone advised by manufacturer of SODIUM OXYBATE

▶ Sympathomimetics: plasma concentration of primidone possibly increased by METHYLPHENIDATE

l Tacrolimus: primidone reduces plasma concentration of

l TACROLIMUS

l Theophylline: primidone accelerates metabolism of

l THEOPHYLLINE (reduced effect)

▶ Thyroid Hormones: primidone accelerates metabolism of THYROID HORMONES (may increase requirements for thyroid hormones in hypothyroidism)

▶ Ticagrelor: primidone possibly reduces plasma concentration of TICAGRELOR

l Ulipristal: avoidance of primidone advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

Primidone (continued)

▶ Vitamins: primidone possibly increases requirements for ALFACALCIDOL, CALCITRIOL, COLECALCIFEROL, DIHYDROTACHYSTEROL, ERGOCALCIFEROL, PARICALCITOL or VITAMIN D

Procarbazine

▶ Alcohol: disulfiram-like reaction when procarbazine given with ALCOHOL

▶ Antiepileptics: manufacturer of procarbazine advises possible increased risk of hypersensitivity reactions when given with CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cardiac Glycosides: procarbazine possibly reduces absorption of DIGOXIN *tablets*

Prochlorperazine *see* Antipsychotics Procyclidine *see* Antimuscarinics Progesterone *see* Progestogens Progestogens

l Antibacterials: plasma concentration of dienogest increased by

ERYTHROMYCIN; metabolism of progestogens accelerated by l RIFAMYCINS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

l Anticoagulants: progestogens may enhance or reduce anticoagulant effect of COUMARINS; progestogens antagonise anticoagulant effect of l PHENINDIONE

l Antidepressants: contraceptive effect of progestogens reduced by l ST JOHN’S WORT (avoid concomitant use)

▶ Antidiabetics: progestogens antagonise hypoglycaemic effect of ANTIDIABETICS

l Antiepileptics: metabolism of progestogens accelerated by

l CARBAMAZEPINE, l ESLICARBAZEPINE, l FOSPHENYTOIN,

l OXCARBAZEPINE, l PERAMPANEL, l PHENOBARBITAL,

l PHENYTOIN, l PRIMIDONE, l RUFINAMIDE and l TOPIRAMATE

(reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF); desogestrel possibly increases plasma concentration of LAMOTRIGINE

▶ Antifungals: progestogens possibly increase plasma concentration of VORICONAZOLE; anecdotal reports of contraceptive failure and menstrual irregularities when progestogens given with GRISEOFULVIN; occasional reports of breakthrough bleeding when progestogens (used for contraception) given with TERBINAFINE

l Antivirals: plasma concentration of norethisterone increased by ATAZANAVIR; plasma concentration of drospirenone increased by BOCEPREVIR (increased risk of toxicity); contraceptive effect of progestogens possibly reduced by

l EFAVIRENZ; plasma concentration of norgestimate increased by ELVITEGRAVIR; metabolism of progestogens accelerated by l NEVIRAPINE (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

▶ Anxiolytics and Hypnotics: progestogens possibly increase plasma concentration of CHLORDIAZEPOXIDE, DIAZEPAM and NITRAZEPAM; progestogens possibly reduce plasma concentration of LORAZEPAM, OXAZEPAM and TEMAZEPAM

l Aprepitant: possible contraceptive failure of hormonal contraceptives containing progestogens when given with l APREPITANT (alternative contraception recommended)

l Bosentan: possible contraceptive failure of hormonal contraceptives containing progestogens when given with l BOSENTAN (alternative contraception recommended)

▶ Ciclosporin: progestogens possibly increase plasma concentration of CICLOSPORIN

▶ Cobicistat: plasma concentration of norgestimate increased by

COBICISTAT

Progestogens (continued)

l Cytotoxics: possible reduction in contraceptive effect of progestogens advised by manufacturer of l CRIZOTINIB and l VEMURAFENIB; possible reduced contraceptive effect of

hormonal contraceptives containing progestogens advised by manufacturer of l DABRAFENIB (alternative contraception recommended)

▶ Diuretics: risk of hyperkalaemia when drospirenone given with

POTASSIUM-SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

(monitor serum potassium during first cycle)

l Dopaminergics: progestogens increase plasma concentration of l SELEGILINE—manufacturer of selegiline advises avoid concomitant use

l Fosaprepitant: possible contraceptive failure of hormonal contraceptives containing progestogens when given with l FOSAPREPITANT (alternative contraception recommended)

▶ Lipid-regulating Drugs: plasma concentration of norethisterone increased by ATORVASTATIN; plasma concentration of active metabolite of norgestimate increased by ROSUVASTATIN; plasma concentration of norgestrel increased by ROSUVASTATIN

▶ Muscle Relaxants: progestogens possibly increase plasma concentration of TIZANIDINE (increased risk of toxicity)

▶ Sugammadex: plasma concentration of progestogens possibly reduced by SUGAMMADEX—manufacturer of sugammadex advises additional contraceptive precautions

▶ Teriflunomide: plasma concentration of levonorgestrel increased by TERIFLUNOMIDE

l Ulipristal: contraceptive effect of progestogens possibly reduced by l ULIPRISTAL

Proguanil

▶ Antacids: absorption of proguanil reduced by ORAL MAGNESIUM SALTS (as magnesium trisilicate)

▶ Anticoagulants: isolated reports that proguanil may enhance anticoagulant effect of WARFARIN

l Antimalarials: avoidance of antimalarials advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; increased antifolate effect when proguanil given with PYRIMETHAMINE

▶ Antivirals: plasma concentration of proguanil possibly affected by EFAVIRENZ

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Promazine *see* Antipsychotics Promethazine *see* Antihistamines Propafenone

▶ Aminophylline: propafenone increases plasma concentration

of AMINOPHYLLINE

▶ Anaesthetics, Local: increased myocardial depression when anti-arrhythmics given with BUPIVACAINE, LEVOBUPIVACAINE,

PRILOCAINE or ROPIVACAINE

l Anti-arrhythmics: increased myocardial depression when anti- arrhythmics given with other l ANTI-ARRHYTHMICS

l Antibacterials: metabolism of propafenone accelerated by

l RIFAMPICIN (reduced effect)

l Anticoagulants: propafenone enhances anticoagulant effect of

l COUMARINS

l Antidepressants: metabolism of propafenone possibly inhibited by FLUOXETINE and PAROXETINE; increased risk of arrhythmias when propafenone given with l TRICYCLICS

▶ Antiepileptics: metabolism of propafenone possibly accelerated by PHENOBARBITAL and PRIMIDONE

▶ Antihistamines: avoidance of propafenone advised by manufacturer of MIZOLASTINE (possible risk of ventricular arrhythmias)

l Antipsychotics: increased risk of ventricular arrhythmias when anti-arrhythmics that prolong the QT interval given with

l ANTIPSYCHOTICS that prolong the QT interval

l Antivirals: plasma concentration of propafenone possibly increased by l FOSAMPRENAVIR (increased risk of ventricular arrhythmias—avoid concomitant use); plasma concentration of propafenone increased by l RITONAVIR (increased risk of ventricular arrhythmias—avoid concomitant use); increased risk of ventricular arrhythmias when propafenone given with l SAQUINAVIR—avoid concomitant use; caution with

Propafenone

l Antivirals (continued)

Interactions | Appendix 1

propafenone advised by manufacturer of l TELAPREVIR (risk of ventricular arrhythmias)

l Beta-blockers: increased myocardial depression when anti- arrhythmics given with l BETA-BLOCKERS; propafenone increases plasma concentration of METOPROLOL and PROPRANOLOL

l Cardiac Glycosides: propafenone increases plasma concentration of l DIGOXIN (halve dose of digoxin)

▶ Ciclosporin: propafenone possibly increases plasma concentration of CICLOSPORIN

▶ Parasympathomimetics: propafenone possibly antagonises effects of NEOSTIGMINE and PYRIDOSTIGMINE

▶ Theophylline: propafenone increases plasma concentration of

THEOPHYLLINE

l Ulcer-healing Drugs: plasma concentration of propafenone increased by l CIMETIDINE

Propantheline *see* Antimuscarinics Propiverine *see* Antimuscarinics Propofol *see* Anaesthetics, General Propranolol *see* Beta-blockers Prostaglandins

▶ ACE Inhibitors: enhanced hypotensive effect when alprostadil

given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when alprostadil given with ADRENERGIC NEURONE BLOCKERS

▶ Alpha-blockers: enhanced hypotensive effect when alprostadil given with ALPHA-BLOCKERS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when alprostadil given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Beta-blockers: enhanced hypotensive effect when alprostadil given with BETA-BLOCKERS

▶ Calcium-channel Blockers: enhanced hypotensive effect when alprostadil given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when alprostadil given with CLONIDINE

▶ Diazoxide: enhanced hypotensive effect when alprostadil given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when alprostadil given with DIURETICS

▶ Methyldopa: enhanced hypotensive effect when alprostadil given with METHYLDOPA

▶ Moxonidine: enhanced hypotensive effect when alprostadil given with MOXONIDINE

▶ Nitrates: enhanced hypotensive effect when alprostadil given with NITRATES

▶ Oxytocin: prostaglandins potentiate uterotonic effect of

OXYTOCIN

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when alprostadil given with HYDRALAZINE, MINOXIDIL or SODIUM NITROPRUSSIDE

Protein Kinase Inhibitors *see* individual drugs

Proton Pump Inhibitors

▶ Antacids: absorption of lansoprazole possibly reduced by

ANTACIDS

▶ Antibacterials: plasma concentration of both drugs increased when omeprazole given with CLARITHROMYCIN

l Anticoagulants: pantoprazole might enhance the anticoagulant effect of COUMARINS; esomeprazole and omeprazole possibly enhance anticoagulant effect of l COUMARINS

▶ Antidepressants: omeprazole increases plasma concentration of ESCITALOPRAM; plasma concentration of lansoprazole possibly increased by FLUVOXAMINE; plasma concentration of omeprazole possibly reduced by ST JOHN’S WORT

l Antiepileptics: omeprazole possibly enhances effects of FOSPHENYTOIN and PHENYTOIN; esomeprazole enhances effects of l FOSPHENYTOIN and l PHENYTOIN

l Antifungals: proton pump inhibitors reduce absorption of ITRACONAZOLE and KETOCONAZOLE; esomeprazole reduces plasma concentration of l POSACONAZOLE—manufacturer of posaconazole *suspension* advises avoid concomitant use; lansoprazole, omeprazole, pantoprazole and rabeprazole

Interactions | Appendix 1

Proton Pump Inhibitors

l Antifungals (continued)

possibly reduce plasma concentration of l POSACONAZOLE— manufacturer of posaconazole *suspension* advises avoid concomitant use; plasma concentration of esomeprazole possibly increased by VORICONAZOLE; plasma concentration of omeprazole increased by VORICONAZOLE (consider reducing dose of omeprazole)

▶ Antipsychotics: omeprazole possibly reduces plasma concentration of CLOZAPINE

l Antivirals: proton pump inhibitors reduce plasma concentration of l ATAZANAVIR—avoid or adjust dose of both drugs (consult product literature); omeprazole increases plasma concentration of RALTEGRAVIR; avoidance of esomeprazole, lansoprazole, pantoprazole and rabeprazole advised by manufacturer of RILPIVIRINE (plasma concentration of rilpivirine possibly reduced); omeprazole reduces plasma concentration of l RILPIVIRINE—avoid concomitant use; esomeprazole, lansoprazole, pantoprazole and rabeprazole possibly increase plasma concentration of l SAQUINAVIR—manufacturer of saquinavir advises avoid concomitant use; omeprazole increases plasma concentration of l SAQUINAVIR—manufacturer of saquinavir advises avoid concomitant use; plasma concentration of esomeprazole and omeprazole reduced by l TIPRANAVIR

▶ Anxiolytics and Hypnotics: esomeprazole and omeprazole

possibly inhibit metabolism of DIAZEPAM (increased plasma concentration)

▶ Cardiac Glycosides: proton pump inhibitors possibly slightly increase plasma concentration of DIGOXIN

▶ Ciclosporin: omeprazole possibly affects plasma concentration of CICLOSPORIN

l Cilostazol: omeprazole increases plasma concentration of

l CILOSTAZOL (see under Cilostazol, p. 206)

l Clopidogrel: esomeprazole and omeprazole reduce antiplatelet effect of l CLOPIDOGREL; lansoprazole, pantoprazole and rabeprazole possibly reduce antiplatelet effect of CLOPIDOGREL

l Cytotoxics: proton pump inhibitors possibly reduce excretion of METHOTREXATE (increased risk of toxicity); lansoprazole reduces plasma concentration of BOSUTINIB; avoidance of proton pump inhibitors advised by manufacturer of DABRAFENIB (plasma concentration of dabrafenib possibly reduced); avoidance of esomeprazole, lansoprazole, pantoprazole and rabeprazole advised by manufacturer of

l ERLOTINIB; omeprazole reduces plasma concentration of l ERLOTINIB—manufacturer of erlotinib advises avoid concomitant use; proton pump inhibitors possibly reduce absorption of LAPATINIB; proton pump inhibitors possibly

reduce absorption of PAZOPANIB—manufacturer of pazopanib advises give at the same time as proton pump inhibitors

▶ Tacrolimus: omeprazole possibly increases plasma concentration of TACROLIMUS

▶ Ulcer-healing Drugs: absorption of lansoprazole possibly reduced by SUCRALFATE

Pseudoephedrine *see* Sympathomimetics

Pyrazinamide

▶ Sulfinpyrazone: pyrazinamide antagonises effects of

SULFINPYRAZONE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Pyridostigmine *see* Parasympathomimetics

Pyridoxine *see* Vitamins

Pyrimethamine

l Antibacterials: increased antifolate effect when pyrimethamine given with l SULFONAMIDES or l TRIMETHOPRIM

l Antiepileptics: pyrimethamine antagonises anticonvulsant effect of l FOSPHENYTOIN and l PHENYTOIN, also increased antifolate effect

l Antimalarials: avoidance of antimalarials advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; increased antifolate effect when pyrimethamine given with PROGUANIL

▶ Antivirals: increased antifolate effect when pyrimethamine given with ZIDOVUDINE

Pyrimethamine (continued)

l Cytotoxics: pyrimethamine increases antifolate effect of

l METHOTREXATE and l PEMETREXED

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Quetiapine *see* Antipsychotics

Quinagolide

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

Quinapril *see* ACE Inhibitors

Quinine

l Anti-arrhythmics: increased risk of ventricular arrhythmias when quinine given with l AMIODARONE—avoid concomitant use; quinine increases plasma concentration of l FLECAINIDE

l Antibacterials: increased risk of ventricular arrhythmias when quinine given with l MOXIFLOXACIN—avoid concomitant use; plasma concentration of quinine reduced by l RIFAMPICIN

▶ Anticoagulants: plasma concentration of both drugs increased when quinine given with WARFARIN

l Antidepressants: possible increased risk of ventricular arrhythmias when quinine given with l CITALOPRAM or l ESCITALOPRAM—avoid concomitant use

l Antimalarials: avoidance of antimalarials advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; increased risk of ventricular arrhythmias when quinine given with

l ARTEMETHER WITH LUMEFANTRINE; increased risk of convulsions when quinine given with l MEFLOQUINE (but should not prevent the use of *intravenous* quinine in severe cases)

l Antipsychotics: increased risk of ventricular arrhythmias when quinine given with l DROPERIDOL or l PIMOZIDE—avoid concomitant use; possible increased risk of ventricular arrhythmias when quinine given with l HALOPERIDOL—avoid concomitant use; possible increased risk of ventricular arrhythmias when quinine given with l RISPERIDONE

l Antivirals: plasma concentration of quinine possibly increased by l ATAZANAVIR, l DARUNAVIR, l FOSAMPRENAVIR, l INDINAVIR

and l TIPRANAVIR (increased risk of toxicity); plasma concentration of quinine increased by l RITONAVIR (increased risk of toxicity); increased risk of ventricular arrhythmias when quinine given with l SAQUINAVIR—avoid concomitant use

l Cardiac Glycosides: quinine increases plasma concentration of

l DIGOXIN

▶ Dopaminergics: quinine possibly increases plasma concentration of AMANTADINE

▶ Histamine: avoidance of antimalarials advised by manufacturer of HISTAMINE

▶ Muscle Relaxants: quinine possibly enhances effects of

SUXAMETHONIUM

▶ Ulcer-healing Drugs: metabolism of quinine inhibited by

CIMETIDINE (increased plasma concentration)

▶ Vaccines: antimalarials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Quinolones

l Aminophylline: possible increased risk of convulsions when quinolones given with l AMINOPHYLLINE; ciprofloxacin and norfloxacin increase plasma concentration of

l AMINOPHYLLINE

l Analgesics: possible increased risk of convulsions when quinolones given with l NSAIDS

▶ Antacids: absorption of ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin and ofloxacin reduced by ANTACIDS

l Anti-arrhythmics: increased risk of ventricular arrhythmias when levofloxacin or moxifloxacin given with

l AMIODARONE—avoid concomitant use; increased risk of ventricular arrhythmias when moxifloxacin given with

l DISOPYRAMIDE—avoid concomitant use

l Antibacterials: increased risk of ventricular arrhythmias when moxifloxacin given with *parenteral* l ERYTHROMYCIN—avoid concomitant use; ciprofloxacin possibly increases plasma

Quinolones

l Antibacterials (continued)

concentration of BEDAQUILINE—avoid concomitant use if ciprofloxacin given for more than 14 days; avoidance of moxifloxacin advised by manufacturer of BEDAQUILINE; increased risk of ventricular arrhythmias when moxifloxacin given with l DELAMANID; effects of nalidixic acid possibly antagonised by NITROFURANTOIN; possible increased risk of ventricular arrhythmias when moxifloxacin given with

l TELITHROMYCIN

l Anticoagulants: nalidixic acid, norfloxacin and ofloxacin enhance anticoagulant effect of l COUMARINS; ciprofloxacin and levofloxacin possibly enhance anticoagulant effect of COUMARINS; levofloxacin possibly enhances anticoagulant effect of PHENINDIONE

l Antidepressants: avoidance of moxifloxacin advised by manufacturer of l CITALOPRAM and l ESCITALOPRAM (risk of ventricular arrhythmias); ciprofloxacin inhibits metabolism of l DULOXETINE—avoid concomitant use; avoidance of ciprofloxacin advised by manufacturer of l AGOMELATINE; increased risk of ventricular arrhythmias when moxifloxacin given with l TRICYCLICS—avoid concomitant use

▶ Antidiabetics: norfloxacin possibly enhances effects of

GLIBENCLAMIDE

▶ Antiepileptics: ciprofloxacin increases or decreases plasma concentration of FOSPHENYTOIN and PHENYTOIN

l Antihistamines: increased risk of ventricular arrhythmias when moxifloxacin given with l MIZOLASTINE—avoid concomitant use

l Antimalarials: avoidance of quinolones advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE; avoidance of moxifloxacin advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when moxifloxacin given with l CHLOROQUINE, l HYDROXYCHLOROQUINE,

l MEFLOQUINE or l QUININE—avoid concomitant use

l Antipsychotics: increased risk of ventricular arrhythmias when moxifloxacin given with l BENPERIDOL—manufacturer of benperidol advises avoid concomitant use; increased risk of ventricular arrhythmias when moxifloxacin given with

l DROPERIDOL, l HALOPERIDOL, l PHENOTHIAZINES, l PIMOZIDE

or l ZUCLOPENTHIXOL—avoid concomitant use; ciprofloxacin increases plasma concentration of CLOZAPINE; ciprofloxacin possibly increases plasma concentration of OLANZAPINE

l Antivirals: manufacturer of norfloxacin advises give DIDANOSINE at least 2 hours before or after norfloxacin; increased risk of ventricular arrhythmias when moxifloxacin given with l SAQUINAVIR—avoid concomitant use

▶ Anxiolytics and Hypnotics: avoidance of ciprofloxacin advised by manufacturer of ZOLPIDEM

l Atomoxetine: increased risk of ventricular arrhythmias when moxifloxacin given with l ATOMOXETINE

l Beta-blockers: increased risk of ventricular arrhythmias when moxifloxacin given with l SOTALOL—avoid concomitant use

▶ Calcium Salts: absorption of ciprofloxacin reduced by CALCIUM SALTS

l Ciclosporin: increased risk of nephrotoxicity when quinolones

given with l CICLOSPORIN

l Clopidogrel: ciprofloxacin possibly reduces antiplatelet effect of l CLOPIDOGREL

l Cytotoxics: nalidixic acid increases risk of MELPHALAN toxicity; ciprofloxacin possibly reduces excretion of METHOTREXATE (increased risk of toxicity); possible increased risk of ventricular arrhythmias when moxifloxacin given with

l BOSUTINIB; ciprofloxacin possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; ciprofloxacin increases plasma concentration of ERLOTINIB; ciprofloxacin possibly increases the plasma concentration of l IBRUTINIB—reduce dose of ibrutinib (see under Ibrutinib,

p. 809); possible increased risk of ventricular arrhythmias when moxifloxacin given with l VANDETANIB—avoid concomitant use; increased risk of ventricular arrhythmias when levofloxacin or moxifloxacin given with l ARSENIC TRIOXIDE

Quinolones (continued)

▶ Dairy Products: absorption of ciprofloxacin and norfloxacin reduced by DAIRY PRODUCTS

Interactions | Appendix 1

▶ Dopaminergics: ciprofloxacin increases plasma concentration of RASAGILINE; ciprofloxacin inhibits metabolism of ROPINIROLE (increased plasma concentration)

▶ 5HT1-receptor Agonists: quinolones possibly inhibit metabolism of ZOLMITRIPTAN (reduce dose of zolmitriptan)

▶ Iron Salts: absorption of ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin reduced by *oral* IRON SALTS; absorption of norfloxacin reduced by *oral* IRON SALTS (give at least 2 hours apart)

▶ Lanthanum: absorption of quinolones possibly reduced by LANTHANUM (give at least 2 hours before or 4 hours after lanthanum)

l Muscle Relaxants: ciprofloxacin increases plasma concentration of l TIZANIDINE (increased risk of toxicity)— avoid concomitant use; norfloxacin possibly increases plasma concentration of TIZANIDINE (increased risk of toxicity)

▶ Mycophenolate: norfloxacin possibly reduces bioavailability of

MYCOPHENOLATE

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when moxifloxacin given with l PENTAMIDINE ISETIONATE—avoid concomitant use

l Pirfenidone: ciprofloxacin increases plasma concentration of

l PIRFENIDONE—see under Pirfenidone, p. 260

▶ Sevelamer: bioavailability of ciprofloxacin reduced by

SEVELAMER

▶ Strontium Ranelate: absorption of quinolones reduced by STRONTIUM RANELATE (manufacturer of strontium ranelate advises avoid concomitant use)

l Theophylline: possible increased risk of convulsions when quinolones given with l THEOPHYLLINE; ciprofloxacin and norfloxacin increase plasma concentration of l THEOPHYLLINE

▶ Ulcer-healing Drugs: absorption of ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin reduced by SUCRALFATE; absorption of norfloxacin reduced by SUCRALFATE (give at least 2 hours apart)

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

▶ Zinc: absorption of ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin reduced by ZINC; absorption of norfloxacin reduced by ZINC (give at least 2 hours apart)

Rabeprazole *see* Proton Pump Inhibitors

Rabies Vaccine *see* Vaccines

Raloxifene

▶ Anticoagulants: raloxifene antagonises anticoagulant effect of

COUMARINS

▶ Lipid-regulating Drugs: absorption of raloxifene reduced by COLESTYRAMINE (manufacturer of raloxifene advises avoid concomitant administration)

Raltegravir

▶ Antacids: plasma concentration of raltegravir reduced by

ALUMINIUM HYDROXIDE and ORAL MAGNESIUM SALTS—

manufacturer of raltegravir advises avoid concomitant use

l Antibacterials: plasma concentration of raltegravir reduced by

l RIFAMPICIN—consider increasing dose of raltegravir

l Antivirals: increased risk of rash when raltegravir given with DARUNAVIR; avoidance of raltegravir advised by manufacturer of l FOSAMPRENAVIR

l Orlistat: absorption of raltegravir possibly reduced by

l ORLISTAT

▶ Ulcer-healing Drugs: plasma concentration of raltegravir increased by FAMOTIDINE and OMEPRAZOLE

Raltitrexed

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Folates: manufacturer of raltitrexed advises avoid concomitant use with l FOLATES

Ramipril *see* ACE Inhibitors

Ranitidine *see* Histamine H2-antagonists

Ranolazine

l Anti-arrhythmics: manufacturer of ranolazine advises avoid concomitant use with l DISOPYRAMIDE

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Ranolazine (continued)

l Antibacterials: plasma concentration of ranolazine possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN— manufacturer of ranolazine advises avoid concomitant use; plasma concentration of ranolazine reduced by

l RIFAMPICIN—manufacturer of ranolazine advises avoid concomitant use

▶ Antidepressants: plasma concentration of ranolazine increased by PAROXETINE

l Antifungals: plasma concentration of ranolazine increased by l KETOCONAZOLE—avoid concomitant use; plasma concentration of ranolazine possibly increased by

l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE—

manufacturer of ranolazine advises avoid concomitant use

l Antivirals: plasma concentration of ranolazine possibly increased by l ATAZANAVIR, l DARUNAVIR, l FOSAMPRENAVIR, l INDINAVIR, l LOPINAVIR, l RITONAVIR, l SAQUINAVIR and

l TIPRANAVIR—manufacturer of ranolazine advises avoid concomitant use

l Beta-blockers: manufacturer of ranolazine advises avoid concomitant use with l SOTALOL

▶ Calcium-channel Blockers: plasma concentration of ranolazine increased by DILTIAZEM and VERAPAMIL (consider reducing dose of ranolazine)

▶ Cardiac Glycosides: ranolazine increases plasma concentration of DIGOXIN

▶ Ciclosporin: plasma concentration of both drugs may increase when ranolazine given with CICLOSPORIN

l Grapefruit Juice: plasma concentration of ranolazine possibly increased by l GRAPEFRUIT JUICE—manufacturer of ranolazine advises avoid concomitant use

l Lipid-regulating Drugs: ranolazine increases plasma concentration of l SIMVASTATIN (see under Simvastatin,

p. 181); separating administration from ranolazine by 12 hours advised by manufacturer of LOMITAPIDE

l Tacrolimus: ranolazine increases plasma concentration of

l TACROLIMUS

Rasagiline

NOTE Rasagiline is a MAO-B inhibitor

l Analgesics: avoid concomitant use of rasagiline with

l DEXTROMETHORPHAN; risk of CNS toxicity when rasagiline given with l PETHIDINE (avoid pethidine for 2 weeks after rasagiline)

▶ Antibacterials: plasma concentration of rasagiline increased by

CIPROFLOXACIN

l Antidepressants: after stopping rasagiline do not start

l FLUOXETINE for 2 weeks, also rasagiline should not be started until at least 5 weeks after stopping fluoxetine; after stopping rasagiline do not start l FLUVOXAMINE for 2 weeks; risk of hypertensive crisis when rasagiline given with l MAOIS, avoid MAOIs for at least 2 weeks after stopping rasagiline; increased risk of CNS toxicity when rasagiline given with

l SSRIS or l TRICYCLICS

▶ Dopaminergics: plasma concentration of rasagiline possibly reduced by ENTACAPONE

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

l Sympathomimetics: avoid concomitant use of rasagiline with

l SYMPATHOMIMETICS

Reboxetine

l Antibacterials: manufacturer of reboxetine advises avoid concomitant use with l MACROLIDES

l Antidepressants: manufacturer of reboxetine advises avoid concomitant use with l FLUVOXAMINE; increased risk of hypertension and CNS excitation when reboxetine given with l MAOIS (MAOIs should not be started until 1 week after stopping reboxetine, avoid reboxetine for 2 weeks after stopping MAOIs)

▶ Antiepileptics: plasma concentration of reboxetine possibly reduced by CARBAMAZEPINE, PHENOBARBITAL and PRIMIDONE

l Antifungals: manufacturer of reboxetine advises avoid concomitant use with l IMIDAZOLES and l TRIAZOLES

Reboxetine (continued)

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

▶ Diuretics: possible increased risk of hypokalaemia when reboxetine given with LOOP DIURETICS or THIAZIDES AND RELATED DIURETICS

▶ Ergot Alkaloids: possible risk of hypertension when reboxetine given with ERGOTAMINE

Regorafenib

▶ Analgesics: manufacturer of regorafenib advises avoid concomitant use with MEFENAMIC ACID

l Antibacterials: plasma concentration of regorafenib reduced by l RIFAMPICIN—manufacturer of regorafenib advises avoid concomitant use

l Anticoagulants: increased risk of bleeding when regorafenib given with l WARFARIN

l Antifungals: plasma concentration of regorafenib increased by

l KETOCONAZOLE—avoid concomitant use

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cytotoxics: regorafenib increases plasma concentration of

IRINOTECAN

Remifentanil *see* Opioid Analgesics Repaglinide *see* Antidiabetics Retigabine

▶ Alcohol: increased risk of blurred vision when retigabine given

with ALCOHOL

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antiepileptics: plasma concentration of retigabine possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Retinoids

l Alcohol: etretinate formed from acitretin in presence of l ALCOHOL (increased risk of teratogenicity in women of child-bearing potential)

l Antibacterials: possible increased risk of benign intracranial hypertension when retinoids given with l TETRACYCLINES (avoid concomitant use)

l Anticoagulants: acitretin possibly reduces anticoagulant effect of l COUMARINS

▶ Antiepileptics: isotretinoin possibly reduces plasma concentration of CARBAMAZEPINE

l Antifungals: plasma concentration of alitretinoin increased by KETOCONAZOLE; possible increased risk of tretinoin toxicity when given with l FLUCONAZOLE, l KETOCONAZOLE and

l VORICONAZOLE

l Cytotoxics: acitretin increases plasma concentration of

l METHOTREXATE (also increased risk of hepatotoxicity)—avoid concomitant use

▶ Lipid-regulating Drugs: alitretinoin reduces plasma concentration of SIMVASTATIN

l Vitamins: risk of hypervitaminosis A when retinoids given with l VITAMIN A—avoid concomitant use

Ribavirin

l Antivirals: effects of ribavirin possibly reduced by l ABACAVIR; increased risk of side-effects when ribavirin given with

l DIDANOSINE—avoid concomitant use; increased risk of toxicity when ribavirin given with l STAVUDINE; increased risk of anaemia when ribavirin given with l ZIDOVUDINE—avoid concomitant use

l Azathioprine: ribavirin possibly enhances myelosuppressive effects of l AZATHIOPRINE

Rifabutin *see* Rifamycins Rifampicin *see* Rifamycins Rifamycins

NOTE Interactions do not apply to rifaximin

▶ ACE Inhibitors: rifampicin reduces plasma concentration of active metabolite of IMIDAPRIL (reduced antihypertensive effect)

▶ Aliskiren: rifampicin reduces plasma concentration of

ALISKIREN

▶ Ambrisentan: rifampicin possibly increases plasma concentration of AMBRISENTAN

▶ Aminophylline: rifampicin accelerates metabolism of

AMINOPHYLLINE (reduced plasma concentration)

▶ Analgesics: rifampicin reduces plasma concentration of CELECOXIB, DICLOFENAC and ETORICOXIB; rifampicin accelerates metabolism of ALFENTANIL, CODEINE, FENTANYL, METHADONE

and MORPHINE (reduced effect); rifampicin possibly accelerates metabolism of OXYCODONE

▶ Angiotensin-II Receptor Antagonists: rifampicin reduces plasma concentration of LOSARTAN and its active metabolite

▶ Antacids: absorption of rifampicin reduced by ANTACIDS

l Anthelmintics: rifampicin reduces plasma concentration of

l PRAZIQUANTEL—avoid concomitant use

l Anti-arrhythmics: rifamycins accelerate metabolism of

l DISOPYRAMIDE (reduced plasma concentration); rifampicin reduces plasma concentration of l DRONEDARONE—avoid concomitant use; rifampicin accelerates metabolism of

l PROPAFENONE (reduced effect)

l Antibacterials: increased risk of side-effects including neutropenia when rifabutin given with l AZITHROMYCIN; rifamycins reduce plasma concentration of CLARITHROMYCIN and DAPSONE; plasma concentration of rifabutin increased by l CLARITHROMYCIN (increased risk of toxicity—reduce rifabutin dose); plasma concentration of rifabutin possibly increased by l ERYTHROMYCIN (increased risk of toxicity—reduce rifabutin dose); rifampicin possibly reduces plasma concentration of TINIDAZOLE and TRIMETHOPRIM; rifampicin reduces plasma concentration of DOXYCYCLINE—consider increasing dose of doxycycline; rifabutin possibly reduces plasma concentration of BEDAQUILINE—manufacturer of bedaquiline advises avoid concomitant use; rifampicin reduces plasma concentration of l BEDAQUILINE— manufacturer of bedaquiline advises avoid concomitant use; rifampicin accelerates metabolism of CHLORAMPHENICOL (reduced plasma concentration); rifampicin reduces plasma concentration of l DELAMANID; increased risk of hepatotoxicity when rifampicin given with l ISONIAZID; rifampicin reduces plasma concentration of LINEZOLID (possible therapeutic failure of linezolid); rifampicin reduces plasma concentration of l TELITHROMYCIN (avoid during and for 2 weeks after rifampicin)

l Anticoagulants: rifampicin possibly reduces plasma

concentration of l APIXABAN—manufacturer of apixaban advises avoid concomitant use when given for treatment of deep-vein thrombosis or pulmonary embolism; rifamycins accelerate metabolism of l COUMARINS (reduced anticoagulant effect); rifampicin reduces plasma concentration of l DABIGATRAN—manufacturer of dabigatran advises avoid concomitant use; rifampicin reduces plasma concentration of l RIVAROXABAN—manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antidiabetics: rifamycins accelerate metabolism of

l TOLBUTAMIDE (reduced effect); rifampicin reduces plasma concentration of l CANAGLIFLOZIN and NATEGLINIDE; rifampicin possibly reduces effects of LINAGLIPTIN; rifampicin possibly antagonises hypoglycaemic effect of REPAGLINIDE; rifamycins possibly accelerate metabolism of l SULFONYLUREAS (reduced effect)

l Antiepileptics: rifabutin reduces plasma concentration of l CARBAMAZEPINE; rifamycins accelerate metabolism of l FOSPHENYTOIN and l PHENYTOIN (reduced plasma

concentration); rifampicin reduces plasma concentration of l LAMOTRIGINE; plasma concentration of rifampicin possibly reduced by PHENOBARBITAL and PRIMIDONE

Rifamycins (continued)

l Antifungals: rifampicin accelerates metabolism of

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l KETOCONAZOLE (reduced plasma concentration), also plasma concentration of rifampicin may be reduced by ketoconazole; plasma concentration of rifabutin increased by

l FLUCONAZOLE (increased risk of uveitis—reduce rifabutin dose); rifampicin accelerates metabolism of l FLUCONAZOLE (reduced plasma concentration); rifabutin and rifampicin reduce plasma concentration of l ITRACONAZOLE— manufacturer of itraconazole advises avoid concomitant use; plasma concentration of rifabutin increased by

l POSACONAZOLE (also plasma concentration of posaconazole reduced); rifampicin reduces plasma concentration of

l POSACONAZOLE and l TERBINAFINE; plasma concentration of rifabutin increased by l VORICONAZOLE, also rifabutin reduces plasma concentration of voriconazole (increase dose of voriconazole and also monitor for rifabutin toxicity); rifampicin reduces plasma concentration of l VORICONAZOLE— avoid concomitant use; rifampicin initially increases and then reduces plasma concentration of CASPOFUNGIN (consider increasing dose of caspofungin); plasma concentration of rifabutin possibly increased by l TRIAZOLES (increased risk of uveitis—reduce rifabutin dose)

▶ Antihistamines: rifampicin possibly reduces effects of

FEXOFENADINE

l Antimalarials: avoidance of rifampicin advised by manufacturer of ARTENIMOL WITH PIPERAQUINE; rifampicin reduces plasma concentration of l MEFLOQUINE—avoid concomitant use; rifampicin reduces plasma concentration of l QUININE

▶ Antimuscarinics: rifampicin reduces plasma concentration of active metabolite of FESOTERODINE

l Antipsychotics: rifampicin accelerates metabolism of

l HALOPERIDOL (reduced plasma concentration); rifabutin and rifampicin possibly reduce plasma concentration of

l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); rifampicin possibly reduces plasma concentration of CLOZAPINE; rifampicin reduces plasma concentration of

l LURASIDONE—avoid concomitant use

l Antivirals: rifampicin possibly reduces plasma concentration of ABACAVIR; plasma concentration of rifabutin increased by l ATAZANAVIR, l DARUNAVIR, l FOSAMPRENAVIR and

l TIPRANAVIR (reduce dose of rifabutin); rifampicin reduces plasma concentration of l ATAZANAVIR, l DACLATASVIR,

l LOPINAVIR, l NEVIRAPINE and l RILPIVIRINE—avoid

concomitant use; avoidance of rifampicin advised by manufacturer of l BOCEPREVIR (plasma concentration of boceprevir possibly reduced); rifabutin possibly reduces plasma concentration of l DACLATASVIR and SIMEPREVIR— manufacturer of daclatasvir and simeprevir advises avoid concomitant use; rifampicin significantly reduces plasma concentration of l DARUNAVIR, l FOSAMPRENAVIR and

l TELAPREVIR—avoid concomitant use; rifampicin reduces the plasma concentration of l DOLUTEGRAVIR (see under Dolutegravir, p. 557); rifampicin reduces plasma concentration of EFAVIRENZ—increase dose of efavirenz; plasma concentration of rifabutin reduced by EFAVIRENZ— increase dose of rifabutin; avoidance of rifampicin advised by manufacturer of l ELVITEGRAVIR, ETRAVIRINE, SOFOSBUVIR and ZIDOVUDINE; rifabutin reduces plasma concentration of

l ELVITEGRAVIR also plasma concentration of active metabolite of rifabutin increased—reduce dose of rifabutin; plasma concentration of both drugs reduced when rifabutin given with l ETRAVIRINE; rifampicin accelerates metabolism of l INDINAVIR (reduced plasma concentration—avoid concomitant use); plasma concentration of rifabutin increased by l INDINAVIR, also plasma concentration of indinavir decreased (reduce dose of rifabutin and increase dose of indinavir); rifampicin reduces plasma concentration of l MARAVIROC and l RALTEGRAVIR—consider increasing dose of maraviroc and raltegravir; plasma concentration of rifabutin possibly increased by NEVIRAPINE; rifabutin decreases plasma concentration of l RILPIVIRINE (increase dose of rilpivirine—consult rilpivirine product literature);

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Rifamycins

l Antivirals (continued)

plasma concentration of rifabutin increased by l RITONAVIR (increased risk of toxicity—reduce rifabutin dose); rifampicin reduces plasma concentration of RITONAVIR; rifampicin significantly reduces plasma concentration of l SAQUINAVIR, also risk of hepatotoxicity—avoid concomitant use; plasma concentration of rifabutin increased by l SAQUINAVIR (also plasma concentration of saquinavir reduced)—reduce rifabutin dose; rifampicin reduces plasma concentration of

l SIMEPREVIR—manufacturer of simeprevir advises avoid concomitant use; avoidance of rifabutin advised by manufacturer of SOFOSBUVIR and l TELAPREVIR; rifampicin possibly reduces plasma concentration of l TIPRANAVIR— avoid concomitant use

▶ Anxiolytics and Hypnotics: rifampicin accelerates metabolism of DIAZEPAM and ZALEPLON (reduced plasma concentration); rifampicin possibly accelerates metabolism of BENZODIAZEPINES (reduced plasma concentration); rifampicin possibly accelerates metabolism of BUSPIRONE; rifampicin accelerates metabolism of ZOLPIDEM (reduced plasma concentration and reduced effect); rifampicin significantly reduces plasma concentration of ZOPICLONE

▶ Aprepitant: rifampicin reduces plasma concentration of

APREPITANT

l Atovaquone: avoidance of concomitant rifabutin advised by manufacturer of ATOVAQUONE (plasma concentration of both drugs reduced); rifampicin reduces plasma concentration of l ATOVAQUONE (and concentration of rifampicin increased)— avoid concomitant use

▶ Avanafil: rifampicin possibly reduces plasma concentration of AVANAFIL—manufacturer of avanafil advises avoid concomitant use

▶ Beta-blockers: rifampicin accelerates metabolism of BISOPROLOL and PROPRANOLOL (plasma concentration significantly reduced); rifampicin reduces plasma concentration of CARVEDILOL, CELIPROLOL and METOPROLOL; rifampicin possibly reduces plasma concentration of *oral* TIMOLOL

l Bosentan: rifampicin reduces plasma concentration of

l BOSENTAN—avoid concomitant use

l Calcium-channel Blockers: rifampicin possibly reduces plasma concentration of FELODIPINE; rifampicin possibly accelerates metabolism of l ISRADIPINE and l NICARDIPINE (possible significantly reduced plasma concentration); rifampicin accelerates metabolism of l DILTIAZEM, l NIFEDIPINE,

l NIMODIPINE and l VERAPAMIL (plasma concentration significantly reduced)

l Cannabis Extract: rifampicin reduces plasma concentration of l CANNABIS EXTRACT—manufacturer of cannabis extract advises avoid concomitant use

▶ Cardiac Glycosides: rifampicin possibly reduces plasma concentration of DIGOXIN

l Ciclosporin: rifampicin accelerates metabolism of

l CICLOSPORIN (reduced plasma concentration)

l Cobicistat: rifabutin reduces plasma concentration of

l COBICISTAT (adjust dose—consult product literature); rifampicin possibly reduces plasma concentration of

l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Corticosteroids: rifamycins accelerate metabolism of

l CORTICOSTEROIDS (reduced effect)

l Cytotoxics: rifampicin possibly reduces effects of BRENTUXIMAB VEDOTIN; rifampicin reduces plasma concentration of AFATINIB, RUXOLITINIB, SORAFENIB and l TRABECTEDIN; rifabutin

possibly decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); rifampicin decreases plasma concentration of AXITINIB (increase dose of axitinib—consult axitinib product literature); rifabutin possibly reduces plasma concentration of l BOSUTINIB, CRIZOTINIB and PONATINIB—manufacturer of bosutinib, crizotinib and ponatinib advises avoid concomitant use; rifampicin reduces plasma concentration of l BORTEZOMIB, l BOSUTINIB, l CABAZITAXEL, l CRIZOTINIB,

l PONATINIB, l REGORAFENIB and l VANDETANIB—manufacturer of bortezomib, bosutinib, cabazitaxel, crizotinib, ponatinib,

Rifamycins

l Cytotoxics (continued)

regorafenib and vandetanib advises avoid concomitant use; rifampicin reduces plasma concentration of l CABOZANTINIB, l GEFITINIB, l IBRUTINIB, l IDELALISIB, l IMATINIB and

l NILOTINIB—avoid concomitant use; avoidance of rifampicin advised by manufacturer of DABRAFENIB, l LAPATINIB and VEMURAFENIB; rifampicin accelerates metabolism of

l DASATINIB (reduced plasma concentration—avoid concomitant use); rifampicin accelerates metabolism of ERLOTINIB and SUNITINIB (reduced plasma concentration); rifampicin reduces plasma concentration of l EVEROLIMUS (avoid concomitant use or consider increasing the dose of everolimus —consult everolimus product literature); avoidance of rifabutin advised by manufacturer of

l CABAZITAXEL, l LAPATINIB and VEMURAFENIB; rifampicin possibly reduces plasma concentration of ERIBULIN and

l PAZOPANIB; rifampicin reduces plasma concentration of active metabolite of l TEMSIROLIMUS—avoid concomitant use; rifampicin possibly reduces plasma concentration of

l VINFLUNINE—manufacturer of vinflunine advises avoid concomitant use; avoidance of rifampicin advised by manufacturer of l VISMODEGIB (plasma concentration of vismodegib possibly reduced)

▶ Deferasirox: rifampicin reduces plasma concentration of

DEFERASIROX

l Diuretics: rifampicin reduces plasma concentration of

l EPLERENONE—avoid concomitant use

▶ Fosaprepitant: rifampicin reduces plasma concentration of

FOSAPREPITANT

l Hormone Antagonists: rifabutin possibly reduces plasma concentration of l ABIRATERONE—manufacturer of abiraterone advises avoid concomitant use; rifampicin reduces plasma concentration of l ABIRATERONE— manufacturer of abiraterone advises avoid concomitant use; avoidance of rifampicin advised by manufacturer of ENZALUTAMIDE; rifampicin possibly reduces plasma concentration of EXEMESTANE; rifampicin accelerates metabolism of TAMOXIFEN (reduced plasma concentration)

▶ 5HT3-receptor Antagonists: rifampicin accelerates metabolism of ONDANSETRON (reduced effect)

l Ivacaftor: rifabutin possibly reduces plasma concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use; rifampicin reduces plasma concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

▶ Leflunomide: rifampicin possibly increases plasma concentration of active metabolite of LEFLUNOMIDE

▶ Lipid-regulating Drugs: rifampicin possibly reduces plasma concentration of ATORVASTATIN and SIMVASTATIN; rifampicin accelerates metabolism of FLUVASTATIN (reduced effect)

l Macitentan: rifampicin reduces plasma concentration of

l MACITENTAN—avoid concomitant use

▶ Muscle Relaxants: rifampicin possibly reduces plasma concentration of TIZANIDINE

l Mycophenolate: rifampicin reduces plasma concentration of active metabolite of l MYCOPHENOLATE

l Nintedanib: rifampicin reduces plasma concentration of

l NINTEDANIB—avoid concomitant use

l Oestrogens: rifamycins accelerate metabolism of l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Progestogens: rifamycins accelerate metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

l Ranolazine: rifampicin reduces plasma concentration of

l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

l Roflumilast: rifampicin inhibits effects of l ROFLUMILAST

(manufacturer of roflumilast advises avoid concomitant use)

l Sirolimus: rifabutin and rifampicin reduce plasma concentration of l SIROLIMUS—avoid concomitant use

Rifamycins (continued)

l Tacrolimus: rifabutin possibly reduces plasma concentration of TACROLIMUS; rifampicin reduces plasma concentration of l TACROLIMUS

l Tadalafil: rifampicin reduces plasma concentration of

l TADALAFIL—manufacturer of tadalafil advises avoid concomitant use

▶ Teriflunomide: rifampicin reduces plasma concentration of

TERIFLUNOMIDE

▶ Theophylline: rifampicin accelerates metabolism of

THEOPHYLLINE (reduced plasma concentration)

▶ Thyroid Hormones: rifampicin accelerates metabolism of LEVOTHYROXINE (may increase requirements for levothyroxine in hypothyroidism)

▶ Tibolone: rifampicin accelerates metabolism of TIBOLONE

(reduced plasma concentration)

l Ticagrelor: rifampicin reduces plasma concentration of

l TICAGRELOR

▶ Tolvaptan: rifampicin reduces plasma concentration of

TOLVAPTAN

▶ Ulcer-healing Drugs: rifampicin accelerates metabolism of

CIMETIDINE (reduced plasma concentration)

l Ulipristal: avoidance of rifampicin advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Rilpivirine

▶ Analgesics: rilpivirine possibly reduces plasma concentration of METHADONE

▶ Antacids: manufacturer of rilpivirine advises give ANTACIDS 2 hours before or 4 hours after rilpivirine

l Antibacterials: manufacturer of rilpivirine advises avoid concomitant use with l CLARITHROMYCIN and l ERYTHROMYCIN (plasma concentration of rilpivirine possibly increased); plasma concentration of rilpivirine decreased by l RIFABUTIN (increase dose of rilpivirine—consult rilpivirine product literature); plasma concentration of rilpivirine reduced by

l RIFAMPICIN—avoid concomitant use

▶ Anticoagulants: rilpivirine possibly increases plasma concentration of DABIGATRAN

l Antidepressants: manufacturer of rilpivirine advises avoid concomitant use with l ST JOHN’S WORT (plasma concentration of rilpivirine possibly reduced)

l Antiepileptics: manufacturer of rilpivirine advises avoid concomitant use with l CARBAMAZEPINE, l FOSPHENYTOIN, l OXCARBAZEPINE, l PHENOBARBITAL, l PHENYTOIN and

l PRIMIDONE (plasma concentration of rilpivirine possibly reduced)

▶ Antivirals: manufacturer of rilpivirine advises give DIDANOSINE 2 hours before or 4 hours after rilpivirine; avoidance of rilpivirine advised by manufacturer of NEVIRAPINE

▶ Calcium Salts: manufacturer of rilpivirine advises give CALCIUM SALTS 2 hours before or 4 hours after rilpivirine

l Corticosteroids: manufacturer of rilpivirine advises avoid concomitant use with l DEXAMETHASONE (except when given as a single dose)

l Orlistat: absorption of rilpivirine possibly reduced by

l ORLISTAT

l Ulcer-healing Drugs: manufacturer of rilpivirine advises avoid concomitant use with ESOMEPRAZOLE, LANSOPRAZOLE, PANTOPRAZOLE and RABEPRAZOLE (plasma concentration of rilpivirine possibly reduced); plasma concentration of rilpivirine reduced by l OMEPRAZOLE—avoid concomitant use;

manufacturer of rilpivirine advises avoid HISTAMINE H2- ANTAGONISTS for 12 hours before or 4 hours after rilpivirine— consult product literature

Riociguat

▶ Antacids: absorption of riociguat reduced by ANTACIDS (give at least 2 hours before or 1 hour after riociguat)

▶ Antifungals: manufacturer of riociguat advises avoid concomitant use with ITRACONAZOLE, KETOCONAZOLE and VORICONAZOLE

▶ Antivirals: manufacturer of riociguat advises avoid concomitant use with RITONAVIR

Riociguat (continued)

l Avanafil: possible enhanced hypotensive effect when riociguat given with l AVANAFIL—avoid concomitant use

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▶ Bosentan: plasma concentration of riociguat reduced by

BOSENTAN

l Nitrates: possible enhanced hypotensive effect when riociguat given with l NITRATES—avoid concomitant use

l Sildenafil: enhanced hypotensive effect when riociguat given with l SILDENAFIL—avoid concomitant use

l Tadalafil: possible enhanced hypotensive effect when riociguat given with l TADALAFIL—avoid concomitant use

l Vardenafil: possible enhanced hypotensive effect when riociguat given with l VARDENAFIL—avoid concomitant use

Risedronate Sodium *see* Bisphosphonates

Risperidone *see* Antipsychotics

Ritonavir

l Alpha-blockers: ritonavir possibly increases plasma concentration of l ALFUZOSIN—avoid concomitant use

l Aminophylline: ritonavir accelerates metabolism of

l AMINOPHYLLINE (reduced plasma concentration)

l Analgesics: ritonavir possibly increases plasma concentration of NSAIDS and BUPRENORPHINE; ritonavir increases plasma concentration of l DEXTROPROPOXYPHENE and l PIROXICAM (risk of toxicity)—avoid concomitant use; ritonavir increases plasma concentration of l ALFENTANIL and l FENTANYL; ritonavir reduces plasma concentration of METHADONE; ritonavir possibly reduces plasma concentration of MORPHINE; ritonavir reduces plasma concentration of l PETHIDINE, but increases plasma concentration of toxic metabolite of pethidine (avoid concomitant use)

l Anthelmintics: ritonavir possibly reduces plasma

concentration of active metabolite of l ALBENDAZOLE— consider increasing albendazole dose when given for systemic infections

l Anti-arrhythmics: ritonavir increases plasma concentration of l AMIODARONE and l PROPAFENONE (increased risk of ventricular arrhythmias—avoid concomitant use); ritonavir possibly increases plasma concentration of l DISOPYRAMIDE (increased risk of toxicity); avoidance of ritonavir advised by manufacturer of l DRONEDARONE; ritonavir possibly increases plasma concentration of l FLECAINIDE (increased risk of ventricular arrhythmias—avoid concomitant use)

l Antibacterials: ritonavir possibly increases plasma

concentration of AZITHROMYCIN and ERYTHROMYCIN; ritonavir increases plasma concentration of l CLARITHROMYCIN (reduce dose of clarithromycin in renal impairment); ritonavir increases plasma concentration of l RIFABUTIN (increased risk of toxicity—reduce rifabutin dose); plasma concentration of ritonavir reduced by RIFAMPICIN; ritonavir possibly increases plasma concentration of BEDAQUILINE—avoid concomitant use if ritonavir given for more than 14 days; ritonavir increases plasma concentration of DELAMANID; plasma concentration of both drugs increased when ritonavir given with l FUSIDIC ACID—avoid concomitant use; avoidance of concomitant ritonavir in severe renal and hepatic impairment advised by manufacturer of l TELITHROMYCIN

l Anticoagulants: ritonavir may enhance or reduce anticoagulant

effect of l WARFARIN; avoidance of ritonavir advised by manufacturer of APIXABAN; ritonavir possibly enhances anticoagulant effect of l COUMARINS and l PHENINDIONE; ritonavir increases plasma concentration of l RIVAROXABAN— avoid concomitant use

l Antidepressants: ritonavir possibly reduces plasma concentration of PAROXETINE; ritonavir increases plasma concentration of l TRAZODONE (increased risk of toxicity); ritonavir possibly increases plasma concentration of l SSRIS and l TRICYCLICS; plasma concentration of ritonavir reduced by l ST JOHN’S WORT—avoid concomitant use

▶ Antidiabetics: ritonavir possibly increases plasma concentration of TOLBUTAMIDE

l Antiepileptics: ritonavir possibly increases plasma concentration of l CARBAMAZEPINE; plasma concentration of ritonavir possibly reduced by FOSPHENYTOIN and PHENYTOIN, also plasma concentration of fosphenytoin and phenytoin possibly affected; ritonavir possibly reduces plasma

Interactions | Appendix 1

Ritonavir

l Antiepileptics (continued)

concentration of LAMOTRIGINE, SODIUM VALPROATE and

VALPROIC ACID

l Antifungals: ritonavir increases plasma concentration of l KETOCONAZOLE (reduce dose of ketoconazole); plasma concentration of ritonavir increased by FLUCONAZOLE;

combination of ritonavir with l ITRACONAZOLE may increase plasma concentration of either drug (or both); ritonavir reduces plasma concentration of l VORICONAZOLE—avoid concomitant use

▶ Antihistamines: ritonavir possibly increases plasma concentration of NON-SEDATING ANTIHISTAMINES

l Antimalarials: caution with ritonavir advised by manufacturer of ARTEMETHER WITH LUMEFANTRINE; plasma concentration of ritonavir possibly reduced by MEFLOQUINE; ritonavir increases plasma concentration of l QUININE (increased risk of toxicity)

l Antimuscarinics: avoidance of ritonavir advised by manufacturer of DARIFENACIN and TOLTERODINE; manufacturer of fesoterodine advises dose reduction when ritonavir given with FESOTERODINE—consult fesoterodine product literature; ritonavir possibly increases plasma concentration of

l SOLIFENACIN—see under Solifenacin, p. 670

l Antipsychotics: ritonavir possibly increases plasma concentration of l ANTIPSYCHOTICS; ritonavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); manufacturer of ritonavir advises avoid concomitant use with l CLOZAPINE (increased risk of toxicity); ritonavir possibly increases plasma concentration of l LURASIDONE—avoid concomitant use; ritonavir reduces plasma concentration of OLANZAPINE—consider increasing dose of olanzapine; ritonavir increases plasma concentration of l PIMOZIDE (increased risk of ventricular arrhythmias—avoid concomitant use); ritonavir possibly increases plasma concentration of l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: plasma concentration of both drugs reduced when

ritonavir given with l BOCEPREVIR; manufacturer of ritonavir advises ritonavir and DIDANOSINE should be taken 2.5 hours apart; ritonavir increases the toxicity of l EFAVIRENZ, monitor liver function tests —manufacturer of *Atripla* ® advises avoid concomitant use with *high-dose* ritonavir; ritonavir increases plasma concentration of INDINAVIR, MARAVIROC and

l SAQUINAVIR; ritonavir increases plasma concentration of l SIMEPREVIR—manufacturer of simeprevir advises avoid concomitant use; ritonavir possibly reduces plasma concentration of TELAPREVIR

l Anxiolytics and Hypnotics: ritonavir possibly increases plasma concentration of l ANXIOLYTICS AND HYPNOTICS; ritonavir possibly increases plasma concentration of l ALPRAZOLAM, l DIAZEPAM, l FLURAZEPAM and l ZOLPIDEM (risk of extreme sedation and respiratory depression—avoid concomitant use); ritonavir possibly increases plasma concentration of

l MIDAZOLAM (risk of prolonged sedation—avoid concomitant use of *oral* midazolam); ritonavir increases plasma concentration of BUSPIRONE (increased risk of toxicity)

▶ Aprepitant: ritonavir possibly increases plasma concentration of APREPITANT

▶ Atovaquone: ritonavir possibly reduces plasma concentration of ATOVAQUONE—manufacturer of atovaquone advises avoid concomitant use

l Avanafil: ritonavir significantly increases plasma concentration of l AVANAFIL—avoid concomitant use

l Bosentan: ritonavir increases plasma concentration of

l BOSENTAN (consider reducing dose of bosentan)

▶ Bupropion: ritonavir reduces plasma concentration of

BUPROPION

l Calcium-channel Blockers: ritonavir possibly increases plasma concentration of l CALCIUM-CHANNEL BLOCKERS; avoidance of ritonavir advised by manufacturer of LERCANIDIPINE

▶ Cardiac Glycosides: ritonavir possibly increases plasma concentration of DIGOXIN

l Ciclosporin: ritonavir possibly increases plasma concentration of l CICLOSPORIN

Ritonavir (continued)

l Cilostazol: ritonavir possibly increases plasma concentration of l CILOSTAZOL (see under Cilostazol, p. 206)

l Colchicine: ritonavir possibly increases risk of l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Corticosteroids: ritonavir possibly increases plasma concentration of l CORTICOSTEROIDS—increased risk of adrenal supression; ritonavir possibly increases plasma concentration of l BUDESONIDE (including *inhaled*, *intranasal*, and *rectal* budesonide)—increased risk of adrenal suppresion; ritonavir increases plasma concentration of *inhaled* and *intranasal* l FLUTICASONE—increased risk of adrenal suppression

l Cytotoxics: ritonavir increases the plasma concentration of

AFATINIB—manufacturer of afatinib advises separating administration of ritonavir by 6 to 12 hours; ritonavir possibly increases plasma concentration of AXITINIB (reduce dose of axitinib—consult axitinib product literature); ritonavir possibly increases the plasma concentration of

l BOSUTINIB and l CABAZITAXEL—manufacturer of bosutinib and cabazitaxel advises avoid or consider reducing dose of bosutinib and cabazitaxel; ritonavir possibly increases plasma concentration of CABOZANTINIB and VINBLASTINE; ritonavir possibly increases plasma concentration of

l CRIZOTINIB, l EVEROLIMUS, NILOTINIB and l VINFLUNINE—

manufacturer of crizotinib, everolimus, nilotinib and vinflunine advises avoid concomitant use; avoidance of ritonavir advised by manufacturer of DASATINIB (plasma concentration of dasatinib possibly increased); ritonavir possibly increases the plasma concentration of l IBRUTINIB— reduce dose of ibrutinib (see under Ibrutinib, p. 809); avoidance of ritonavir advised by manufacturer of

l LAPATINIB; ritonavir possibly increases plasma concentration of l PAZOPANIB (reduce dose of pazopanib); ritonavir possibly increases plasma concentration of PONATINIB—consider reducing initial dose of ponatinib (see under Ponatinib, p. 814); manufacturer of ruxolitinib advises dose reduction when ritonavir given with l RUXOLITINIB— consult ruxolitinib product literature; ritonavir possibly increases plasma concentration of l DOCETAXEL— manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose; ritonavir increases plasma concentration of PACLITAXEL

l Dapoxetine: avoidance of ritonavir advised by manufacturer of

l DAPOXETINE (increased risk of toxicity)

l Diuretics: ritonavir increases plasma concentration of

l EPLERENONE—avoid concomitant use

l Domperidone: possible increased risk of ventricular arrhythmias when ritonavir given with l DOMPERIDONE—avoid concomitant use

l Ergot Alkaloids: increased risk of ergotism when ritonavir given with l ERGOMETRINE or l ERGOTAMINE—avoid concomitant use

▶ Fosaprepitant: ritonavir possibly increases plasma concentration of FOSAPREPITANT

l 5HT1-receptor Agonists: ritonavir increases plasma concentration of l ELETRIPTAN (risk of toxicity)—avoid concomitant use

l Ivabradine: ritonavir possibly increases plasma concentration of l IVABRADINE—avoid concomitant use

l Lipid-regulating Drugs: possible increased risk of myopathy when ritonavir given with ATORVASTATIN; possible increased risk of myopathy when ritonavir given with l ROSUVASTATIN— manufacturer of rosuvastatin advises avoid concomitant use; increased risk of myopathy when ritonavir given with

l SIMVASTATIN (avoid concomitant use); avoidance of ritonavir advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

▶ Mirabegron: when given with ritonavir avoid or reduce dose of MIRABEGRON in hepatic or renal impairment—see Mirabegron, p. 671

l Oestrogens: ritonavir accelerates metabolism of l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

Ritonavir (continued)

l Orlistat: absorption of ritonavir possibly reduced by l ORLISTAT l Ranolazine: ritonavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid

concomitant use

▶ Riociguat: avoidance of ritonavir advised by manufacturer of

RIOCIGUAT

l Sildenafil: ritonavir significantly increases plasma concentration of l SILDENAFIL—avoid concomitant use

▶ Sympathomimetics: ritonavir possibly increases plasma concentration of DEXAMFETAMINE

▶ Sympathomimetics, Beta2: manufacturer of ritonavir advises avoid concomitant use with SALMETEROL

l Tacrolimus: ritonavir possibly increases plasma concentration of l TACROLIMUS

l Tadalafil: ritonavir increases plasma concentration of l TADALAFIL—manufacturer of tadalafil advises avoid concomitant use

l Theophylline: ritonavir accelerates metabolism of

l THEOPHYLLINE (reduced plasma concentration)

l Ticagrelor: ritonavir possibly increases plasma concentration of l TICAGRELOR—manufacturer of ticagrelor advises avoid concomitant use

l Ulipristal: avoidance of ritonavir advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

l Vardenafil: ritonavir increases plasma concentration of

l VARDENAFIL—avoid concomitant use

Rituximab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Rivaroxaban

l Analgesics: increased risk of haemorrhage when anticoagulants given with *intravenous* l DICLOFENAC (avoid concomitant use, including low-dose heparins); increased risk of haemorrhage when anticoagulants given with

l KETOROLAC (avoid concomitant use, including low-dose heparins)

▶ Anti-arrhythmics: manufacturer of rivaroxaban advises avoid concomitant use with DRONEDARONE

l Antibacterials: plasma concentration of rivaroxaban reduced by l RIFAMPICIN—manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Anticoagulants: increased risk of haemorrhage when rivaroxaban given with other l ANTICOAGULANTS (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency); increased risk of haemorrhage when other anticoagulants given with l APIXABAN and l DABIGATRAN (avoid concomitant use except when switching with other anticoagulants or using heparin to maintain catheter patency)

l Antidepressants: plasma concentration of rivaroxaban possibly reduced by l ST JOHN’S WORT—manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antiepileptics: plasma concentration of rivaroxaban possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—

manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antifungals: plasma concentration of rivaroxaban increased by l KETOCONAZOLE—avoid concomitant use; manufacturer of rivaroxaban advises avoid concomitant use with ITRACONAZOLE, POSACONAZOLE and VORICONAZOLE

l Antivirals: manufacturer of rivaroxaban advises avoid concomitant use with ATAZANAVIR, DARUNAVIR, FOSAMPRENAVIR, INDINAVIR, SAQUINAVIR and TIPRANAVIR;

manufacturers advise avoid concomitant use of rivaroxaban with LOPINAVIR; plasma concentration of rivaroxaban increased by l RITONAVIR—avoid concomitant use

l Cobicistat: anticoagulant effect of rivaroxaban possibly enhanced by l COBICISTAT—avoid concomitant use

Rivastigmine *see* Parasympathomimetics

Rizatriptan *see* 5HT1-receptor Agonists (under HT)

Rocuronium *see* Muscle Relaxants

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Roflumilast

▶ Aminophylline: manufacturer of roflumilast advises avoid concomitant use with AMINOPHYLLINE

l Antibacterials: effects of roflumilast inhibited by l RIFAMPICIN

(manufacturer of roflumilast advises avoid concomitant use)

▶ Antidepressants: metabolism of roflumilast inhibited by

FLUVOXAMINE

▶ Antiepileptics: effects of roflumilast possibly inhibited by

CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN

and PRIMIDONE (manufacturer of roflumilast advises avoid concomitant use)

▶ Theophylline: manufacturer of roflumilast advises avoid concomitant use with THEOPHYLLINE

▶ Ulcer-healing Drugs: metabolism of roflumilast inhibited by

CIMETIDINE

Ropinirole

▶ Antibacterials: metabolism of ropinirole inhibited by

CIPROFLOXACIN (increased plasma concentration)

▶ Antipsychotics: manufacturer of ropinirole advises avoid concomitant use of ANTIPSYCHOTICS (antagonism of effect)

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Metoclopramide: manufacturer of ropinirole advises avoid concomitant use of METOCLOPRAMIDE (antagonism of effect)

▶ Oestrogens: plasma concentration of ropinirole increased by

OESTROGENS

Ropivacaine

▶ Anti-arrhythmics: increased myocardial depression when ropivacaine given with ANTI-ARRHYTHMICS

▶ Antidepressants: metabolism of ropivacaine inhibited by

FLUVOXAMINE—avoid prolonged administration of ropivacaine

Rosuvastatin *see* Statins Rotavirus Vaccine *see* Vaccines Rotigotine

▶ Antipsychotics: manufacturer of rotigotine advises avoid

concomitant use of ANTIPSYCHOTICS (antagonism of effect)

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

▶ Metoclopramide: manufacturer of rotigotine advises avoid concomitant use of METOCLOPRAMIDE (antagonism of effect)

Rufinamide

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antiepileptics: plasma concentration of both drugs possibly reduced when rufinamide given with CARBAMAZEPINE; plasma concentration of rufinamide possibly reduced by FOSPHENYTOIN and PHENYTOIN, also plasma concentration of fosphenytoin and phenytoin possibly increased; plasma concentration of rufinamide possibly reduced by PHENOBARBITAL and PRIMIDONE; plasma concentration of rufinamide possibly increased by SODIUM VALPROATE and VALPROIC ACID (reduce dose of rufinamide)

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Oestrogens: rufinamide accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: rufinamide accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives,

Interactions | Appendix 1

Rufinamide

l Progestogens (continued)

contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

Ruxolitinib

l Antibacterials: manufacturer of ruxolitinib advises dose reduction when ruxolitinib given with l CLARITHROMYCIN and l TELITHROMYCIN—consult ruxolitinib product literature; plasma concentration of ruxolitinib reduced by RIFAMPICIN

l Antifungals: manufacturer of ruxolitinib advises dose reduction when ruxolitinib given with l FLUCONAZOLE, l ITRACONAZOLE, l KETOCONAZOLE, l POSACONAZOLE and

l VORICONAZOLE—consult ruxolitinib product literature

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: manufacturer of ruxolitinib advises dose reduction when ruxolitinib given with l BOCEPREVIR, l INDINAVIR,

l LOPINAVIR, l RITONAVIR, l SAQUINAVIR and l TELAPREVIR—

consult ruxolitinib product literature

St John’s Wort

▶ Aminophylline: St John’s wort possibly reduces plasma concentration of AMINOPHYLLINE

▶ Analgesics: St John’s wort possibly reduces plasma concentration of METHADONE

l Anti-arrhythmics: St John’s wort possibly reduces plasma concentration of l DRONEDARONE—avoid concomitant use

l Antibacterials: St John’s wort possibly reduces plasma concentration of BEDAQUILINE—manufacturer of bedaquiline advises avoid concomitant use; St John’s wort reduces plasma concentration of l TELITHROMYCIN (avoid during and for 2 weeks after St John’s wort)

l Anticoagulants: St John’s wort possibly reduces plasma

concentration of l APIXABAN—manufacturer of apixaban advises avoid concomitant use when given for treatment of deep-vein thrombosis or pulmonary embolism; St John’s wort reduces anticoagulant effect of l COUMARINS (avoid concomitant use); St John’s wort possibly reduces plasma concentration of DABIGATRAN—manufacturer of dabigatran advises avoid concomitant use; St John’s wort possibly reduces plasma concentration of l RIVAROXABAN— manufacturer of rivaroxaban advises monitor for signs of thrombosis

l Antidepressants: possible increased serotonergic effects when

St John’s wort given with DULOXETINE or VENLAFAXINE; St John’s wort reduces plasma concentration of AMITRIPTYLINE; increased serotonergic effects when St John’s wort given with l SSRIS—avoid concomitant use

l Antiepileptics: St John’s wort possibly reduces plasma concentration of CARBAMAZEPINE; St John’s wort possibly reduces plasma concentration of l FOSPHENYTOIN,

l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE—avoid

concomitant use

l Antifungals: St John’s wort reduces plasma concentration of

l VORICONAZOLE—avoid concomitant use

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

l Antipsychotics: St John’s wort possibly reduces plasma

concentration of l ARIPIPRAZOLE (avoid concomitant use or consider increasing the dose of aripiprazole—consult aripiprazole product literature); St John’s wort possibly reduces plasma concentration of l LURASIDONE—avoid concomitant use

l Antivirals: St John’s wort reduces plasma concentration of l ATAZANAVIR, l DARUNAVIR, l EFAVIRENZ, l FOSAMPRENAVIR, l INDINAVIR, l LOPINAVIR, l NEVIRAPINE, l RITONAVIR and

l SAQUINAVIR—avoid concomitant use; St John’s wort possibly reduces plasma concentration of DACLATASVIR and

l SIMEPREVIR—manufacturer of daclatasvir and simeprevir advises avoid concomitant use; avoidance of St John’s wort advised by manufacturer of DOLUTEGRAVIR, l ELVITEGRAVIR, ETRAVIRINE, SOFOSBUVIR and l TELAPREVIR; St John’s wort

possibly reduces plasma concentration of l MARAVIROC and

l TIPRANAVIR—avoid concomitant use; avoidance of St John’s

St John’s Wort

l Antivirals (continued)

wort advised by manufacturer of l RILPIVIRINE (plasma concentration of rilpivirine possibly reduced)

▶ Anxiolytics and Hypnotics: St John’s wort possibly reduces plasma concentration of *oral* MIDAZOLAM

l Aprepitant: avoidance of St John’s wort advised by manufacturer of l APREPITANT

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

l Calcium-channel Blockers: St John’s wort possibly reduces plasma concentration of AMLODIPINE and FELODIPINE; St John’s wort reduces plasma concentration of NIFEDIPINE; St John’s wort significantly reduces plasma concentration of l VERAPAMIL

l Cannabis Extract: St John’s wort possibly reduces plasma concentration of l CANNABIS EXTRACT—manufacturer of cannabis extract advises avoid concomitant use

l Cardiac Glycosides: St John’s wort reduces plasma concentration of l DIGOXIN—avoid concomitant use

l Ciclosporin: St John’s wort reduces plasma concentration of

l CICLOSPORIN—avoid concomitant use

l Cobicistat: St John’s wort possibly reduces plasma concentration of l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use

l Cytotoxics: St John’s wort possibly reduces plasma concentration of AXITINIB—consider increasing dose of axitinib; St John’s wort possibly reduces plasma concentration of BORTEZOMIB, l BOSUTINIB, CABOZANTINIB, CRIZOTINIB, EVEROLIMUS, l IBRUTINIB, l IDELALISIB, PONATINIB

and l VINFLUNINE—manufacturer of bortezomib, bosutinib, cabozantinib, crizotinib, everolimus, ibrutinib, idelalisib, ponatinib and vinflunine advises avoid concomitant use; avoidance of St John’s wort advised by manufacturer of

l CABAZITAXEL, DABRAFENIB, GEFITINIB, l LAPATINIB and

VEMURAFENIB; St John’s wort reduces plasma concentration of l IMATINIB—avoid concomitant use; avoidance of St John’s wort advised by manufacturer of VANDETANIB and

l VISMODEGIB (plasma concentration of vandetanib and vismodegib possibly reduced); St John’s wort possibly reduces plasma concentration of ERIBULIN; St John’s wort accelerates metabolism of l IRINOTECAN (reduced plasma concentration—avoid concomitant use)

l Dapoxetine: possible increased risk of serotonergic effects when St John’s wort given with l DAPOXETINE (manufacturer of dapoxetine advises St John’s wort should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping St John’s wort)

l Diuretics: St John’s wort reduces plasma concentration of

l EPLERENONE—avoid concomitant use

▶ Fingolimod: St John’s wort possibly reduces plasma concentration of FINGOLIMOD—manufacturer of fingolimod advises avoid concomitant use

l Fosaprepitant: avoidance of St John’s wort advised by manufacturer of l FOSAPREPITANT

l Hormone Antagonists: St John’s wort possibly reduces plasma concentration of l ABIRATERONE—manufacturer of abiraterone advises avoid concomitant use

l 5HT1-receptor Agonists: increased serotonergic effects when St John’s wort given with l 5HT1 AGONISTS—avoid concomitant use

▶ Ivabradine: St John’s wort reduces plasma concentration of

IVABRADINE—avoid concomitant use

l Ivacaftor: St John’s wort possibly reduces plasma concentration of l IVACAFTOR—manufacturer of ivacaftor advises avoid concomitant use

▶ Lipid-regulating Drugs: St John’s wort reduces plasma concentration of SIMVASTATIN

▶ Macitentan: avoidance of St John’s wort advised by manufacturer of MACITENTAN

l Oestrogens: St John’s wort reduces contraceptive effect of

l OESTROGENS (avoid concomitant use)

l Progestogens: St John’s wort reduces contraceptive effect of

l PROGESTOGENS (avoid concomitant use)

l Tacrolimus: St John’s wort reduces plasma concentration of

l TACROLIMUS—avoid concomitant use

St John’s Wort (continued)

▶ Theophylline: St John’s wort possibly reduces plasma concentration of THEOPHYLLINE

▶ Ulcer-healing Drugs: St John’s wort possibly reduces plasma concentration of OMEPRAZOLE

l Ulipristal: avoidance of St John’s wort advised by manufacturer of l ULIPRISTAL (contraceptive effect of ulipristal possibly reduced)

Salbutamol *see* Sympathomimetics, Beta2 Salmeterol *see* Sympathomimetics, Beta2 Saquinavir

l Analgesics: increased risk of ventricular arrhythmias when

saquinavir given with l ALFENTANIL, l FENTANYL or

l METHADONE—avoid concomitant use

l Anti-arrhythmics: increased risk of ventricular arrhythmias when saquinavir given with l AMIODARONE, l DISOPYRAMIDE, l DRONEDARONE, l FLECAINIDE, l LIDOCAINE or

l PROPAFENONE—avoid concomitant use

l Antibacterials: plasma concentration of both drugs possibly increased when saquinavir given with l CLARITHROMYCIN (increased risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when saquinavir given with

l DAPSONE, l ERYTHROMYCIN or l MOXIFLOXACIN—avoid

concomitant use; saquinavir increases plasma concentration of l RIFABUTIN (also plasma concentration of saquinavir reduced)—reduce rifabutin dose; plasma concentration of saquinavir significantly reduced by l RIFAMPICIN, also risk of hepatotoxicity—avoid concomitant use; increased risk of ventricular arrhythmias when saquinavir given with

l DELAMANID; plasma concentration of both drugs may increase when saquinavir given with FUSIDIC ACID; avoidance of saquinavir advised by manufacturer of l TELITHROMYCIN (risk of ventricular arrhythmias)

▶ Anticoagulants: saquinavir possibly enhances anticoagulant effect of WARFARIN; avoidance of saquinavir advised by manufacturer of APIXABAN and RIVAROXABAN

l Antidepressants: increased risk of ventricular arrhythmias when saquinavir given with l TRAZODONE or l TRICYCLICS— avoid concomitant use; plasma concentration of saquinavir reduced by l ST JOHN’S WORT—avoid concomitant use

l Antiepileptics: plasma concentration of saquinavir possibly

reduced by CARBAMAZEPINE, FOSPHENYTOIN, l PHENOBARBITAL,

PHENYTOIN and l PRIMIDONE

l Antifungals: plasma concentration of saquinavir increased by

l KETOCONAZOLE—manufacturer of ketoconazole advises avoid concomitant use; plasma concentration of saquinavir possibly increased by IMIDAZOLES and TRIAZOLES

l Antihistamines: increased risk of ventricular arrhythmias when saquinavir given with l MIZOLASTINE—avoid concomitant use

l Antimalarials: caution with saquinavir advised by manufacturer of ARTEMETHER WITH LUMEFANTRINE; avoidance of saquinavir advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE (possible risk of ventricular arrhythmias); increased risk of ventricular arrhythmias when saquinavir given with l QUININE—avoid concomitant use

▶ Antimuscarinics: avoidance of saquinavir advised by manufacturer of DARIFENACIN and TOLTERODINE; manufacturer of fesoterodine advises dose reduction when saquinavir given with FESOTERODINE—consult fesoterodine product literature

l Antipsychotics: increased risk of ventricular arrhythmias when saquinavir given with l CLOZAPINE, l HALOPERIDOL or

l PHENOTHIAZINES—avoid concomitant use; saquinavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); saquinavir possibly increases plasma concentration of l LURASIDONE—avoid concomitant use; saquinavir possibly increases plasma concentration of

l PIMOZIDE (increased risk of ventricular arrhythmias—avoid concomitant use); saquinavir possibly increases plasma concentration of l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: increased risk of ventricular arrhythmias when saquinavir given with l ATAZANAVIR or l LOPINAVIR—avoid concomitant use; saquinavir reduces plasma concentration of DARUNAVIR; plasma concentration of saquinavir significantly

Saquinavir

l Antivirals (continued)

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reduced by EFAVIRENZ; plasma concentration of saquinavir increased by INDINAVIR and l RITONAVIR; saquinavir increases plasma concentration of l MARAVIROC (consider reducing dose of maraviroc); plasma concentration of saquinavir reduced by l TIPRANAVIR

l Anxiolytics and Hypnotics: saquinavir increases plasma

concentration of l MIDAZOLAM (risk of prolonged sedation— avoid concomitant use of *oral* midazolam)

l Avanafil: saquinavir possibly increases plasma concentration of l AVANAFIL—manufacturer of avanafil advises avoid concomitant use

l Beta-blockers: increased risk of ventricular arrhythmias when saquinavir given with l SOTALOL—avoid concomitant use

l Ciclosporin: plasma concentration of both drugs increased when saquinavir given with l CICLOSPORIN

▶ Corticosteroids: plasma concentration of saquinavir possibly reduced by DEXAMETHASONE

l Cytotoxics: saquinavir possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of saquinavir by 6 to 12 hours; saquinavir possibly increases plasma concentration of AXITINIB (reduce dose of axitinib—consult axitinib product literature); saquinavir possibly increases the plasma concentration of l BOSUTINIB and l CABAZITAXEL— manufacturer of bosutinib and cabazitaxel advises avoid or consider reducing dose of bosutinib and cabazitaxel; saquinavir possibly increases plasma concentration of

l CRIZOTINIB and l EVEROLIMUS—manufacturer of crizotinib and everolimus advises avoid concomitant use; saquinavir possibly increases the plasma concentration of l IBRUTINIB— reduce dose of ibrutinib (see under Ibrutinib, p. 809); avoidance of saquinavir advised by manufacturer of

l LAPATINIB; increased risk of ventricular arrhythmias when saquinavir given with l PAZOPANIB—avoid concomitant use; saquinavir possibly increases plasma concentration of PONATINIB—consider reducing initial dose of ponatinib (see under Ponatinib, p. 814); manufacturer of ruxolitinib advises dose reduction when saquinavir given with l RUXOLITINIB— consult ruxolitinib product literature; saquinavir possibly increases plasma concentration of l DOCETAXEL— manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose

l Dapoxetine: avoidance of saquinavir advised by manufacturer

of l DAPOXETINE (increased risk of toxicity)

▶ Diuretics: saquinavir increases plasma concentration of

EPLERENONE (reduce dose of eplerenone)

l Domperidone: possible increased risk of ventricular arrhythmias when saquinavir given with l DOMPERIDONE— avoid concomitant use

l Ergot Alkaloids: increased risk of ergotism when saquinavir given with l ERGOTAMINE—avoid concomitant use

l Lipid-regulating Drugs: possible increased risk of myopathy when saquinavir given with ATORVASTATIN; possible increased risk of myopathy when saquinavir given with

l ROSUVASTATIN—manufacturer of rosuvastatin advises avoid concomitant use; increased risk of myopathy when saquinavir given with l SIMVASTATIN (avoid concomitant use); avoidance of saquinavir advised by manufacturer of

l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

l Orlistat: absorption of saquinavir possibly reduced by

l ORLISTAT

l Pentamidine Isetionate: increased risk of ventricular arrhythmias when saquinavir given with l PENTAMIDINE ISETIONATE—avoid concomitant use

l Ranolazine: saquinavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

l Sildenafil: increased risk of ventricular arrhythmias when saquinavir given with l SILDENAFIL—avoid concomitant use

l Tacrolimus: saquinavir increases plasma concentration of

l TACROLIMUS (consider reducing dose of tacrolimus)

l Tadalafil: increased risk of ventricular arrhythmias when saquinavir given with l TADALAFIL—avoid concomitant use

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Saquinavir (continued)

l Ulcer-healing Drugs: plasma concentration of saquinavir possibly increased by CIMETIDINE; plasma concentration of saquinavir possibly increased by l ESOMEPRAZOLE,

l LANSOPRAZOLE, l PANTOPRAZOLE and l RABEPRAZOLE—

manufacturer of saquinavir advises avoid concomitant use; plasma concentration of saquinavir increased by

l OMEPRAZOLE—manufacturer of saquinavir advises avoid concomitant use

l Vardenafil: increased risk of ventricular arrhythmias when saquinavir given with l VARDENAFIL—avoid concomitant use

Saxagliptin *see* Antidiabetics

Selegiline

NOTE Selegiline is a MAO-B inhibitor

l Analgesics: hyperpyrexia and CNS toxicity reported when selegiline given with l PETHIDINE (avoid concomitant use); manufacturer of selegiline advises avoid concomitant use with OPIOID ANALGESICS

l Antidepressants: manufacturer of selegiline advises avoid concomitant use with CITALOPRAM and ESCITALOPRAM; increased risk of hypertension and CNS excitation when selegiline given with l FLUOXETINE (selegiline should not be started until 5 weeks after stopping fluoxetine, avoid fluoxetine for 2 weeks after stopping selegiline); increased risk of hypertension and CNS excitation when selegiline given with l FLUVOXAMINE, l SERTRALINE or l VENLAFAXINE

(selegiline should not be started until 1 week after stopping fluvoxamine, sertraline or venlafaxine, avoid fluvoxamine, sertraline or venlafaxine for 2 weeks after stopping selegiline); increased risk of hypertension and CNS excitation when selegiline given with l PAROXETINE (selegiline should not be started until 2 weeks after stopping paroxetine, avoid paroxetine for 2 weeks after stopping selegiline); enhanced hypotensive effect when selegiline given with l MAOIS— manufacturer of selegiline advises avoid concomitant use; avoid concomitant use of selegiline with l MOCLOBEMIDE; CNS toxicity reported when selegiline given with l TRICYCLICS

▶ Dopaminergics: selegiline enhances effects and increases toxicity of CO-BENELDOPA, CO-CARELDOPA or LEVODOPA (reduce dose of co-beneldopa, co-careldopa or levodopa); max. dose of 10 mg selegiline advised by manufacturer of ENTACAPONE if used concomitantly

▶ 5HT1-receptor Agonists: manufacturer of selegiline advises avoid concomitant use with 5HT1 AGONISTS

▶ Memantine: effects of dopaminergics and selegiline possibly

enhanced by MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

l Oestrogens: plasma concentration of selegiline increased by l OESTROGENS—manufacturer of selegiline advises avoid concomitant use

l Progestogens: plasma concentration of selegiline increased by l PROGESTOGENS—manufacturer of selegiline advises avoid concomitant use

l Sympathomimetics: manufacturer of selegiline advises avoid concomitant use with SYMPATHOMIMETICS; risk of hypertensive crisis when selegiline given with l DOPAMINE

Selenium

▶ Eltrombopag: selenium possibly reduces absorption of

ELTROMBOPAG (give at least 4 hours apart)

▶ Vitamins: absorption of selenium possibly reduced by

ASCORBIC ACID (give at least 4 hours apart) Sertraline *see* Antidepressants, SSRI Sevelamer

▶ Antibacterials: sevelamer reduces bioavailability of

CIPROFLOXACIN

▶ Ciclosporin: sevelamer possibly reduces plasma concentration of CICLOSPORIN

▶ Mycophenolate: sevelamer possibly reduces plasma concentration of MYCOPHENOLATE

▶ Tacrolimus: sevelamer possibly reduces plasma concentration of TACROLIMUS

▶ Thyroid Hormones: sevelamer possibly reduces absorption of

LEVOTHYROXINE

Sevelamer (continued)

▶ Vitamins: sevelamer reduces absorption of CALCITRIOL (give at least 1 hour before or 3 hours after sevelamer)

Sevoflurane *see* Anaesthetics, General

Sildenafil

l Alpha-blockers: enhanced hypotensive effect when sildenafil given with l ALPHA-BLOCKERS (avoid alpha-blockers for 4 hours after sildenafil)—when patient is stable on the alpha blocker initiate sildenafil at the lowest possible dose

▶ Anti-arrhythmics: avoidance of sildenafil advised by manufacturer of DISOPYRAMIDE (risk of ventricular arrhythmias)

l Antibacterials: plasma concentration of sildenafil increased by l CLARITHROMYCIN—consider reducing initial dose of sildenafil for erectile dysfunction or reduce sildenafil dose frequency to once daily for pulmonary hypertension; plasma concentration of sildenafil increased by ERYTHROMYCIN— reduce initial dose of sildenafil for erectile dysfunction or reduce sildenafil dose frequency to twice daily for pulmonary hypertension; plasma concentration of sildenafil possibly increased by l TELITHROMYCIN—consider reducing initial dose of sildenafil for erectile dysfunction or reduce sildenafil dose frequency to once daily for pulmonary hypertension

l Antifungals: plasma concentration of sildenafil increased by

l KETOCONAZOLE—reduce initial dose of sildenafil for erectile dysfunction and avoid concomitant use of sildenafil for pulmonary hypertension; plasma concentration of sildenafil increased by ITRACONAZOLE—reduce initial dose of sildenafil

l Antivirals: side-effects of sildenafil possibly increased by

l ATAZANAVIR; plasma concentration of sildenafil reduced by ETRAVIRINE; plasma concentration of sildenafil possibly increased by FOSAMPRENAVIR; plasma concentration of sildenafil increased by l INDINAVIR—reduce initial dose of sildenafil; plasma concentration of sildenafil significantly increased by l RITONAVIR—avoid concomitant use; increased risk of ventricular arrhythmias when sildenafil given with

l SAQUINAVIR—avoid concomitant use; avoidance of sildenafil advised by manufacturer of l TELAPREVIR; avoidance of sildenafil for pulmonary arterial hypertension advised by manufacturer of TIPRANAVIR

▶ Bosentan: plasma concentration of sildenafil reduced by

BOSENTAN, also plasma concentration of bosentan increased

▶ Calcium-channel Blockers: enhanced hypotensive effect when sildenafil given with AMLODIPINE

l Cobicistat: plasma concentration of sildenafil possibly increased by l COBICISTAT—manufacturer of cobicistat advises avoid concomitant use of sildenafil for pulmonary arterial hypertension or reduce dose of sildenafil for erectile dysfunction—consult cobicistat product literature

▶ Cytotoxics: avoidance of sildenafil for pulmonary arterial hypertension advised by manufacturer of IDELALISIB

▶ Dapoxetine: avoidance of sildenafil advised by manufacturer of DAPOXETINE

▶ Grapefruit Juice: plasma concentration of sildenafil possibly increased by GRAPEFRUIT JUICE

l Nicorandil: sildenafil significantly enhances hypotensive effect of l NICORANDIL (avoid concomitant use)

l Nitrates: sildenafil significantly enhances hypotensive effect of l NITRATES (avoid concomitant use)

l Riociguat: enhanced hypotensive effect when sildenafil given with l RIOCIGUAT—avoid concomitant use

▶ Ulcer-healing Drugs: plasma concentration of sildenafil increased by CIMETIDINE—consider reducing dose of sildenafil for erectile dysfunction

Siltuximab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Simeprevir

l Anti-arrhythmics: possible increased risk of bradycardia when simeprevir (with sofosbuvir) given with l AMIODARONE—see under Amiodarone, p. 88

l Antibacterials: plasma concentration of simeprevir possibly increased by l CLARITHROMYCIN and l TELITHROMYCIN—

Simeprevir

l Antibacterials (continued)

manufacturer of simeprevir advises avoid concomitant use; plasma concentration of both drugs increased when simeprevir given with l ERYTHROMYCIN—manufacturer of simeprevir advises avoid concomitant use; plasma concentration of simeprevir possibly reduced by RIFABUTIN— manufacturer of simeprevir advises avoid concomitant use; plasma concentration of simeprevir reduced by

l RIFAMPICIN—manufacturer of simeprevir advises avoid concomitant use

l Antidepressants: plasma concentration of simeprevir possibly reduced by l ST JOHN’S WORT—manufacturer of simeprevir advises avoid concomitant use

l Antiepileptics: plasma concentration of simeprevir possibly reduced by l CARBAMAZEPINE, l FOSPHENYTOIN,

l OXCARBAZEPINE, l PHENOBARBITAL, l PHENYTOIN and

l PRIMIDONE—manufacturer of simeprevir advises avoid concomitant use

l Antifungals: manufacturer of simeprevir advises avoid concomitant use with l KETOCONAZOLE; plasma concentration of simeprevir possibly increased by l FLUCONAZOLE,

l ITRACONAZOLE, l POSACONAZOLE and l VORICONAZOLE—

manufacturer of simeprevir advises avoid concomitant use

l Antivirals: plasma concentration of both drugs increased when simeprevir given with l DARUNAVIR—manufacturer of simeprevir advises avoid concomitant use; plasma concentration of simeprevir reduced by EFAVIRENZ; manufacturer of simeprevir advises avoid concomitant use with ETRAVIRINE; plasma concentration of simeprevir possibly reduced by l NEVIRAPINE—manufacturer of simeprevir advises avoid concomitant use; plasma concentration of simeprevir increased by l RITONAVIR—manufacturer of simeprevir advises avoid concomitant use

▶ Anxiolytics and Hypnotics: simeprevir increases plasma concentration of *oral* MIDAZOLAM

▶ Cardiac Glycosides: simeprevir increases plasma concentration of DIGOXIN

l Cobicistat: plasma concentration of simeprevir possibly increased by l COBICISTAT—manufacturer of simeprevir advises avoid concomitant use

▶ Corticosteroids: plasma concentration of simeprevir possibly reduced by DEXAMETHASONE—manufacturer of simeprevir advises avoid concomitant use

▶ Lipid-regulating Drugs: simeprevir increases plasma concentration of ATORVASTATIN, ROSUVASTATIN and SIMVASTATIN (consider reducing dose of atorvastatin, rosuvastatin and simvastatin)

Simvastatin *see* Statins

Sirolimus

▶ Anti-arrhythmics: caution with sirolimus advised by manufacturer of DRONEDARONE

l Antibacterials: plasma concentration of sirolimus increased by l CLARITHROMYCIN and l TELITHROMYCIN—avoid concomitant use; plasma concentration of both drugs increased when sirolimus given with l ERYTHROMYCIN; plasma concentration of sirolimus reduced by l RIFABUTIN and l RIFAMPICIN—avoid concomitant use

l Antifungals: plasma concentration of sirolimus increased by

l ITRACONAZOLE, l KETOCONAZOLE and l VORICONAZOLE—avoid

concomitant use; plasma concentration of sirolimus increased by MICAFUNGIN and l MICONAZOLE; plasma concentration of sirolimus possibly increased by FLUCONAZOLE and POSACONAZOLE

l Antivirals: plasma concentration of sirolimus possibly increased by l ATAZANAVIR and LOPINAVIR; plasma concentration of sirolimus increased by l BOCEPREVIR (increased risk of toxicity—reduce sirolimus dose); plasma concentration of both drugs increased when sirolimus given with l TELAPREVIR (reduce dose of sirolimus)

l Calcium-channel Blockers: plasma concentration of sirolimus possibly increased by NICARDIPINE; plasma concentration of sirolimus increased by l DILTIAZEM; plasma concentration of both drugs increased when sirolimus given with l VERAPAMIL

Sirolimus (continued)

▶ Ciclosporin: plasma concentration of sirolimus increased by

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CICLOSPORIN

l Cytotoxics: caution with sirolimus advised by manufacturer of

l CRIZOTINIB

l Grapefruit Juice: plasma concentration of sirolimus increased by l GRAPEFRUIT JUICE—avoid concomitant use

Sitagliptin *see* Antidiabetics Smallpox Vaccine *see* Vaccines Sodium Aurothiomalate

l ACE Inhibitors: flushing and hypotension reported when

sodium aurothiomalate given with l ACE INHIBITORS

▶ Penicillamine: avoidance of sodium aurothiomalate advised by manufacturer of PENICILLAMINE (increased risk of toxicity)

Sodium Benzoate

▶ Antiepileptics: effects of sodium benzoate possibly reduced by

SODIUM VALPROATE and VALPROIC ACID

▶ Antipsychotics: effects of sodium benzoate possibly reduced by

HALOPERIDOL

▶ Corticosteroids: effects of sodium benzoate possibly reduced by CORTICOSTEROIDS

Sodium Bicarbonate *see* Antacids

Sodium Citrate

▶ Antibacterials: avoid concomitant use of sodium citrate with

METHENAMINE

▶ Ulcer-healing Drugs: avoidance of sodium citrate advised by manufacturer of SUCRALFATE

Sodium Clodronate *see* Bisphosphonates

Sodium Ferredate *see* Iron salts

Sodium Nitroprusside *see* Vasodilator Antihypertensives

Sodium Oxybate

l Analgesics: effects of sodium oxybate enhanced by l OPIOID ANALGESICS (avoid concomitant use)

▶ Antidepressants: increased risk of side-effects when sodium oxybate given with TRICYCLICS

l Antiepileptics: manufacturer of sodium oxybate advises avoid concomitant use with PHENOBARBITAL and PRIMIDONE; plasma concentration of sodium oxybate increased by l SODIUM VALPROATE and l VALPROIC ACID (see under Sodium Oxybate, p. 425)

▶ Antipsychotics: effects of sodium oxybate possibly enhanced by ANTIPSYCHOTICS

l Anxiolytics and Hypnotics: effects of sodium oxybate enhanced by l BENZODIAZEPINES (avoid concomitant use)

Sodium Phenylbutyrate

▶ Antiepileptics: effects of sodium phenylbutyrate possibly reduced by SODIUM VALPROATE and VALPROIC ACID

▶ Antipsychotics: effects of sodium phenylbutyrate possibly reduced by HALOPERIDOL

▶ Corticosteroids: effects of sodium phenylbutyrate possibly reduced by CORTICOSTEROIDS

Sodium Stibogluconate

l Antifungals: possible increased risk of arrhythmias when sodium stibogluconate given before l AMPHOTERICIN— manufacturer of sodium stibogluconate advises giving 14 days apart

Sodium Valproate

▶ Analgesics: effects of sodium valproate enhanced by ASPIRIN

l Antibacterials: metabolism of sodium valproate possibly inhibited by ERYTHROMYCIN (increased plasma concentration); avoidance of sodium valproate advised by manufacturer of

l PIVMECILLINAM; plasma concentration of sodium valproate reduced by l CARBAPENEMS—avoid concomitant use

▶ Anticoagulants: sodium valproate possibly enhances anticoagulant effect of COUMARINS

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antiepileptics: plasma concentration of sodium valproate reduced by CARBAMAZEPINE, also plasma concentration of active metabolite of carbamazepine increased; sodium valproate possibly increases plasma concentration of ETHOSUXIMIDE; sodium valproate increases or possibly

Interactions | Appendix 1

Sodium Valproate

l Antiepileptics (continued)

decreases plasma concentration of FOSPHENYTOIN and PHENYTOIN, also plasma concentration of sodium valproate reduced; sodium valproate increases plasma concentration of l LAMOTRIGINE (increased risk of toxicity—reduce lamotrigine dose); sodium valproate sometimes reduces plasma concentration of an active metabolite of OXCARBAZEPINE; sodium valproate increases plasma concentration of PHENOBARBITAL and PRIMIDONE (also plasma concentration of sodium valproate reduced); sodium valproate possibly increases plasma concentration of RUFINAMIDE (reduce dose of rufinamide); hyperammonaemia and CNS toxicity reported when sodium valproate given with TOPIRAMATE

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered); sodium valproate possibly increases or decreases plasma concentration of CLOZAPINE; increased risk of side- effects including neutropenia when sodium valproate given with l OLANZAPINE

▶ Antivirals: plasma concentration of sodium valproate possibly reduced by RITONAVIR; sodium valproate possibly increases plasma concentration of ZIDOVUDINE (increased risk of toxicity)

▶ Anxiolytics and Hypnotics: plasma concentration of sodium valproate possibly increased by CLOBAZAM; increased risk of side-effects when sodium valproate given with CLONAZEPAM; sodium valproate possibly increases plasma concentration of DIAZEPAM and LORAZEPAM

▶ Bupropion: sodium valproate inhibits the metabolism of

BUPROPION

▶ Cytotoxics: sodium valproate increases plasma concentration of TEMOZOLOMIDE

▶ Lipid-regulating Drugs: absorption of sodium valproate possibly reduced by COLESTYRAMINE

▶ Oestrogens: plasma concentration of sodium valproate possibly reduced by ETHINYLESTRADIOL

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

▶ Sodium Benzoate: sodium valproate possibly reduces effects of

SODIUM BENZOATE

l Sodium Oxybate: sodium valproate increases the plasma concentration of l SODIUM OXYBATE (see under Sodium Oxybate, p. 425)

▶ Sodium Phenylbutyrate: sodium valproate possibly reduces effects of SODIUM PHENYLBUTYRATE

l Ulcer-healing Drugs: metabolism of sodium valproate inhibited by l CIMETIDINE (increased plasma concentration)

Sofosbuvir

l Anti-arrhythmics: possible increased risk of bradycardia when sofosbuvir given with l AMIODARONE—see under Amiodarone,

p. 88

▶ Antibacterials: manufacturer of sofosbuvir advises avoid concomitant use with RIFABUTIN and RIFAMPICIN

▶ Antidepressants: manufacturer of sofosbuvir advises avoid concomitant use with ST JOHN’S WORT

▶ Antiepileptics: manufacturer of sofosbuvir advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN, OXCARBAZEPINE, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

Solifenacin *see* Antimuscarinics

Somatropin

▶ Corticosteroids: growth-promoting effect of somatropin may be inhibited by CORTICOSTEROIDS

▶ Oestrogens: increased doses of somatropin may be needed when given with OESTROGENS (when used as oral replacement therapy)

Sorafenib

▶ Antibacterials: bioavailability of sorafenib reduced by NEOMYCIN; plasma concentration of sorafenib reduced by RIFAMPICIN

l Anticoagulants: sorafenib possibly enhances anticoagulant

effect of l COUMARINS

Sorafenib (continued)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of sorafenib advised by manufacturer of

l BOCEPREVIR

▶ Cytotoxics: sorafenib increases plasma concentration of DOCETAXEL and DOXORUBICIN; sorafenib possibly increases plasma concentration of IRINOTECAN

Sotalol *see* Beta-blockers Spironolactone *see* Diuretics Statins

▶ Antacids: absorption of rosuvastatin reduced by ANTACIDS

l Anti-arrhythmics: increased risk of myopathy when simvastatin given with l AMIODARONE (see under Simvastatin, p. 181); plasma concentration of rosuvastatin increased by

l DRONEDARONE—adjust dose of rosuvastatin (consult product literature); increased risk of myopathy when simvastatin given with l DRONEDARONE; plasma concentration of atorvastatin possibly increased by DRONEDARONE

l Antibacterials: plasma concentration of atorvastatin and pravastatin increased by l CLARITHROMYCIN; increased risk of myopathy when simvastatin given with l CLARITHROMYCIN,

l ERYTHROMYCIN or l TELITHROMYCIN (avoid concomitant use); plasma concentration of rosuvastatin reduced by ERYTHROMYCIN; possible increased risk of myopathy when atorvastatin given with ERYTHROMYCIN; plasma concentration of pravastatin increased by ERYTHROMYCIN; plasma concentration of atorvastatin and simvastatin possibly reduced by RIFAMPICIN; metabolism of fluvastatin accelerated by RIFAMPICIN (reduced effect); increased risk of myopathy when statins given with l DAPTOMYCIN (preferably avoid concomitant use); risk of myopathy and rhabdomyolysis when statins given with l FUSIDIC ACID—avoid concomitant use and for 7 days after last fusidic acid dose; increased risk of myopathy when atorvastatin given with l TELITHROMYCIN (avoid concomitant use); possible increased risk of myopathy when pravastatin given with TELITHROMYCIN

l Anticoagulants: atorvastatin may transiently reduce anticoagulant effect of WARFARIN; rosuvastatin possibly enhances anticoagulant effect of l COUMARINS and

l PHENINDIONE; simvastatin can enhance the anticoagulant effect of COUMARINS; fluvastatin enhances anticoagulant effect of l COUMARINS

▶ Antidepressants: plasma concentration of simvastatin reduced by ST JOHN’S WORT

▶ Antidiabetics: fluvastatin possibly increases plasma concentration of GLIBENCLAMIDE

l Antiepileptics: plasma concentration of simvastatin reduced by l CARBAMAZEPINE and ESLICARBAZEPINE—consider increasing dose of simvastatin; plasma concentration of rosuvastatin reduced by ESLICARBAZEPINE; combination of fluvastatin with FOSPHENYTOIN or PHENYTOIN may increase plasma concentration of either drug (or both)

l Antifungals: possible increased risk of myopathy when atorvastatin given with l KETOCONAZOLE—manufacturer of ketoconazole advises avoid concomitant use; increased risk of myopathy when simvastatin given with l ITRACONAZOLE,

l KETOCONAZOLE or l POSACONAZOLE (avoid concomitant use); possible increased risk of myopathy when simvastatin given with l FLUCONAZOLE or l MICONAZOLE; possible increased risk of myopathy when atorvastatin given with l FLUCONAZOLE or IMIDAZOLES; plasma concentration of fluvastatin increased by FLUCONAZOLE—possible increased risk of myopathy; plasma concentration of rosuvastatin increased by l ITRACONAZOLE— adjust dose of rosuvastatin (consult product literature); increased risk of myopathy when atorvastatin given with

l ITRACONAZOLE, l POSACONAZOLE or l VORICONAZOLE;

increased risk of myopathy when simvastatin given with

l VORICONAZOLE

l Antivirals: possible increased risk of myopathy when atorvastatin or pravastatin given with l ATAZANAVIR; plasma concentration of rosuvastatin increased by l ATAZANAVIR,

l DARUNAVIR, l LOPINAVIR and l TIPRANAVIR—adjust dose of rosuvastatin (consult product literature); increased risk of myopathy when simvastatin given with l ATAZANAVIR,

Statins

l Antivirals (continued)

l INDINAVIR, l RITONAVIR or l SAQUINAVIR (avoid concomitant use); plasma concentration of pravastatin increased by BOCEPREVIR; plasma concentration of atorvastatin increased by BOCEPREVIR (reduce dose of atorvastatin); manufacturers advise avoid concomitant use of simvastatin with

l BOCEPREVIR and l TELAPREVIR; plasma concentration of rosuvastatin increased by DACLATASVIR; plasma concentration of pravastatin possibly increased by DARUNAVIR; possible increased risk of myopathy when atorvastatin given with DARUNAVIR, FOSAMPRENAVIR, INDINAVIR, LOPINAVIR, RITONAVIR

or SAQUINAVIR; plasma concentration of atorvastatin, pravastatin and simvastatin reduced by EFAVIRENZ; plasma concentration of atorvastatin possibly reduced by ETRAVIRINE; possible increased risk of myopathy when rosuvastatin given with l FOSAMPRENAVIR, l INDINAVIR, l RITONAVIR and

l SAQUINAVIR—manufacturer of rosuvastatin advises avoid concomitant use; possible increased risk of myopathy when simvastatin given with l FOSAMPRENAVIR or l LOPINAVIR— avoid concomitant use; plasma concentration of atorvastatin, rosuvastatin and simvastatin increased by SIMEPREVIR (consider reducing dose of atorvastatin, rosuvastatin and simvastatin); avoidance of atorvastatin advised by manufacturer of l TELAPREVIR; plasma concentration of simvastatin possibly increased by l TIPRANAVIR—avoid concomitant use; increased risk of myopathy when atorvastatin given with l TIPRANAVIR (see under Atorvastatin, p. 179)

▶ Anxiolytics and Hypnotics: atorvastatin possibly increases plasma concentration of MIDAZOLAM

▶ Bosentan: plasma concentration of simvastatin reduced by

BOSENTAN

l Calcium-channel Blockers: possible increased risk of myopathy when simvastatin given with l AMLODIPINE and l DILTIAZEM (see under Simvastatin, p. 181); plasma concentration of atorvastatin increased by DILTIAZEM—possible increased risk of myopathy; increased risk of myopathy when simvastatin given with l VERAPAMIL (see under Simvastatin, p. 181); atorvastatin increases plasma concentration of l VERAPAMIL, also possible increased risk of myopathy (consider reducing dose of atorvastatin)

▶ Cardiac Glycosides: atorvastatin possibly increases plasma concentration of DIGOXIN

l Ciclosporin: increased risk of myopathy when rosuvastatin or simvastatin given with l CICLOSPORIN (avoid concomitant use); increased risk of myopathy when atorvastatin given with l CICLOSPORIN (see under Atorvastatin, p. 179); increased risk of myopathy when fluvastatin or pravastatin given with l CICLOSPORIN

l Clopidogrel: plasma concentration of rosuvastatin increased by l CLOPIDOGREL—adjust dose of rosuvastatin (consult product literature)

l Cobicistat: plasma concentration of atorvastatin possibly increased by COBICISTAT—manufacturer of cobicistat advises reduce dose of atorvastatin; avoidance of simvastatin advised by manufacturer of l COBICISTAT

l Colchicine: possible increased risk of myopathy when statins given with l COLCHICINE

▶ Cytotoxics: plasma concentration of simvastatin possibly increased by DASATINIB; avoidance of simvastatin advised by manufacturer of IDELALISIB; plasma concentration of simvastatin increased by IMATINIB

l Eltrombopag: plasma concentration of rosuvastatin increased by l ELTROMBOPAG—adjust dose of rosuvastatin (consult product literature)

l Grapefruit Juice: plasma concentration of atorvastatin possibly increased by GRAPEFRUIT JUICE; plasma concentration of simvastatin increased by l GRAPEFRUIT JUICE—avoid concomitant use

l Hormone Antagonists: possible increased risk of myopathy when simvastatin given with l DANAZOL—avoid concomitant use

l Lipid-regulating Drugs: possible increased risk of myopathy when simvastatin given with l BEZAFIBRATE (see under Simvastatin, p. 181); possible increased risk of myopathy

Statins

l Lipid-regulating Drugs (continued)

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when simvastatin given with l CIPROFIBRATE (see under Simvastatin, p. 181); when given with statins reduce maximum dose of FENOFIBRATE—see under Fenofibrate,

p. 175; increased risk of myopathy when atorvastatin, fluvastatin or pravastatin given with l GEMFIBROZIL (preferably avoid concomitant use); increased risk of myopathy when simvastatin given with l GEMFIBROZIL (avoid concomitant use); plasma concentration of rosuvastatin increased by l EZETIMIBE—adjust dose of rosuvastatin (consult product literature); increased risk of myopathy when statins given with l FIBRATES; increased risk of myopathy when rosuvastatin given with l FIBRATES (see under Rosuvastatin, p. 180); plasma concentration of simvastatin increased by l LOMITAPIDE (see under Simvastatin, p. 181); plasma concentration of atorvastatin increased by LOMITAPIDE—manufacturer of lomitapide advises reduce dose of atorvastatin by half or separate administration by 12 hours; increased risk of myopathy when statins given with

l NICOTINIC ACID (applies to lipid regulating doses of nicotinic acid)

▶ Oestrogens: atorvastatin and rosuvastatin increase plasma concentration of ETHINYLESTRADIOL

▶ Progestogens: atorvastatin increases plasma concentration of NORETHISTERONE; rosuvastatin increases plasma concentration of active metabolite of NORGESTIMATE; rosuvastatin increases plasma concentration of NORGESTREL

l Ranolazine: plasma concentration of simvastatin increased by

l RANOLAZINE (see under Simvastatin, p. 181)

▶ Retinoids: plasma concentration of simvastatin reduced by

ALITRETINOIN

l Teriflunomide: plasma concentration of rosuvastatin increased by l TERIFLUNOMIDE (consider reducing dose of rosuvastatin)

l Ticagrelor: plasma concentration of simvastatin increased by

l TICAGRELOR (increased risk of toxicity)

Stavudine

l Antivirals: increased risk of side-effects when stavudine given with l DIDANOSINE; increased risk of toxicity when stavudine given with l RIBAVIRIN; effects of stavudine possibly inhibited by l ZIDOVUDINE (manufacturers advise avoid concomitant use)

l Cytotoxics: effects of stavudine possibly inhibited by DOXORUBICIN; increased risk of toxicity when stavudine given with l HYDROXYCARBAMIDE—avoid concomitant use

l Orlistat: absorption of stavudine possibly reduced by

l ORLISTAT

Stiripentol

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antiepileptics: stiripentol increases plasma concentration of

l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

▶ Anxiolytics and Hypnotics: stiripentol increases plasma concentration of CLOBAZAM

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Streptomycin *see* Aminoglycosides

Strontium Ranelate

▶ Antibacterials: strontium ranelate reduces absorption of QUINOLONES and TETRACYCLINES (manufacturer of strontium ranelate advises avoid concomitant use)

Sucralfate

▶ Aminophylline: sucralfate possibly reduces absorption of

AMINOPHYLLINE (give at least 2 hours apart)

▶ Antibacterials: sucralfate reduces absorption of CIPROFLOXACIN, LEVOFLOXACIN, MOXIFLOXACIN, OFLOXACIN and TETRACYCLINES;

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Sucralfate

Antibacterials (continued)

sucralfate reduces absorption of NORFLOXACIN (give at least 2 hours apart)

l Anticoagulants: sucralfate possibly reduces absorption of

l COUMARINS (reduced anticoagulant effect)

l Antiepileptics: sucralfate reduces absorption of l FOSPHENYTOIN

and l PHENYTOIN

▶ Antifungals: sucralfate reduces absorption of KETOCONAZOLE

▶ Antipsychotics: sucralfate reduces absorption of SULPIRIDE

▶ Cardiac Glycosides: sucralfate possibly reduces absorption of

CARDIAC GLYCOSIDES

▶ Potassium Salts: manufacturer of sucralfate advises avoid concomitant use with POTASSIUM CITRATE

▶ Sodium Citrate: manufacturer of sucralfate advises avoid concomitant use with SODIUM CITRATE

▶ Theophylline: sucralfate possibly reduces absorption of

THEOPHYLLINE (give at least 2 hours apart)

▶ Thyroid Hormones: sucralfate reduces absorption of

LEVOTHYROXINE

▶ Ulcer-healing Drugs: sucralfate possibly reduces absorption of

LANSOPRAZOLE

Sugammadex

▶ Antibacterials: response to sugammadex possibly reduced by

FUSIDIC ACID

▶ Progestogens: sugammadex possibly reduces plasma concentration of PROGESTOGENS—manufacturer of sugammadex advises additional contraceptive precautions

Sulfadiazine *see* Sulfonamides Sulfadoxine *see* Sulfonamides Sulfamethoxazole *see* Sulfonamides Sulfasalazine

▶ Cardiac Glycosides: sulfasalazine possibly reduces absorption of DIGOXIN

▶ Folates: sulfasalazine possibly reduces absorption of FOLIC ACID

Sulfinpyrazone

▶ Aminophylline: sulfinpyrazone reduces plasma concentration of AMINOPHYLLINE

▶ Analgesics: effects of sulfinpyrazone antagonised by ASPIRIN

▶ Antibacterials: sulfinpyrazone reduces excretion of NITROFURANTOIN (increased risk of toxicity); sulfinpyrazone reduces excretion of PENICILLINS; effects of sulfinpyrazone antagonised by PYRAZINAMIDE

l Anticoagulants: increased risk of bleeding when sulfinpyrazone given with APIXABAN; sulfinpyrazone enhances anticoagulant effect of l COUMARINS; possible increased risk of bleeding when sulfinpyrazone given with l DABIGATRAN

l Antidiabetics: sulfinpyrazone enhances effects of

l SULFONYLUREAS

l Antiepileptics: sulfinpyrazone increases plasma concentration of l FOSPHENYTOIN and l PHENYTOIN

▶ Calcium-channel Blockers: sulfinpyrazone reduces plasma concentration of VERAPAMIL

l Ciclosporin: sulfinpyrazone reduces plasma concentration of

l CICLOSPORIN

▶ Theophylline: sulfinpyrazone reduces plasma concentration of

THEOPHYLLINE

Sulfonamides

▶ Anaesthetics, General: sulfonamides enhance effects of

THIOPENTAL

l Anaesthetics, Local: effects of sulfonamides possibly inhibited by l CHLOROPROCAINE (manufacturer of chloroprocaine advises avoid concomitant use); increased risk of methaemoglobinaemia when sulfonamides given with PRILOCAINE

▶ Anti-arrhythmics: possible increased risk of ventricular arrhythmias when sulfamethoxazole (as co-trimoxazole) given with AMIODARONE—manufacturer of amiodarone advises avoid concomitant use of co-trimoxazole

l Antibacterials: increased risk of crystalluria when sulfonamides given with l METHENAMINE

Sulfonamides (continued)

l Anticoagulants: sulfonamides enhance anticoagulant effect of l COUMARINS; sulfonamides possibly inhibit metabolism of PHENINDIONE

▶ Antidiabetics: sulfonamides rarely enhance the effects of

SULFONYLUREAS

▶ Antiepileptics: sulfonamides possibly increase plasma concentration of FOSPHENYTOIN and PHENYTOIN

l Antimalarials: increased antifolate effect when sulfonamides given with l PYRIMETHAMINE

l Antipsychotics: avoid concomitant use of sulfonamides with

l CLOZAPINE (increased risk of agranulocytosis)

l Azathioprine: increased risk of haematological toxicity when sulfamethoxazole (as co-trimoxazole) given with

l AZATHIOPRINE

l Ciclosporin: increased risk of nephrotoxicity when sulfonamides given with l CICLOSPORIN; sulfadiazine possibly reduces plasma concentration of l CICLOSPORIN

l Cytotoxics: increased risk of haematological toxicity when sulfamethoxazole (as co-trimoxazole) given with

l MERCAPTOPURINE or l METHOTREXATE; sulfonamides increase risk of METHOTREXATE toxicity

▶ Potassium Aminobenzoate: effects of sulfonamides inhibited by

POTASSIUM AMINOBENZOATE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Sulfonylureas *see* Antidiabetics

Sulindac *see* NSAIDs

Sulpiride *see* Antipsychotics

Sumatriptan *see* 5HT1-receptor Agonists (under HT)

Sunitinib

▶ Antibacterials: metabolism of sunitinib accelerated by

RIFAMPICIN (reduced plasma concentration)

▶ Antifungals: metabolism of sunitinib inhibited by

KETOCONAZOLE (increased plasma concentration)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: avoidance of sunitinib advised by manufacturer of

l BOCEPREVIR

Suxamethonium *see* Muscle Relaxants

Sympathomimetics

l Adrenergic Neurone Blockers: ephedrine, isometheptene, metaraminol, methylphenidate, noradrenaline (norepinephrine), oxymetazoline, phenylephrine, pseudoephedrine and xylometazoline antagonise hypotensive effect of l ADRENERGIC NEURONE BLOCKERS; dexamfetamine and lisdexamfetamine antagonise hypotensive effect of l GUANETHIDINE; increased risk of hypertension when adrenaline (epinephrine) given with l GUANETHIDINE

▶ Alcohol: effects of methylphenidate possibly enhanced by

ALCOHOL

▶ Alpha2-adrenoceptor Stimulants: avoidance of sympathomimetics advised by manufacturer of APRACLONIDINE

l Alpha-blockers: avoid concomitant use of adrenaline

(epinephrine) or dopamine with l TOLAZOLINE

▶ Aminophylline: avoidance of ephedrine in children advised by manufacturer of AMINOPHYLLINE

l Anaesthetics, General: avoidance of sympathomimetics advised by manufacturer of l ISOFLURANE (risk of ventricular arrhythmias); increased risk of arrhythmias when adrenaline (epinephrine) or noradrenaline (norepinephrine) given with l VOLATILE LIQUID GENERAL ANAESTHETICS; increased risk of hypertension when methylphenidate given with l VOLATILE LIQUID GENERAL ANAESTHETICS

▶ Antacids: absorption of pseudoephedrine possibly increased by ALUMINIUM HYDROXIDE

l Anticoagulants: methylphenidate possibly enhances anticoagulant effect of l COUMARINS

l Antidepressants: risk of hypertensive crisis when adrenaline (epinephrine), dobutamine, dopamine, noradrenaline (norepinephrine) or xylometazoline given with l MAOIS; risk of hypertensive crisis when dexamfetamine, ephedrine, isometheptene, lisdexamfetamine, metaraminol,

Sympathomimetics

l Antidepressants (continued)

methylphenidate, phenylephrine or pseudoephedrine given with l MAOIS, avoid dexamfetamine, ephedrine, isometheptene, lisdexamfetamine, metaraminol, methylphenidate, phenylephrine or pseudoephedrine for at least 2 weeks after stopping MAOIs; risk of hypertensive crisis when oxymetazoline given with l MAOIS, some manufacturers advise avoid oxymetazoline for at least 2 weeks after stopping MAOIs; risk of hypertensive crisis when sympathomimetics given with l MOCLOBEMIDE; methylphenidate possibly inhibits metabolism of SSRIS and TRICYCLICS; increased risk of hypertension and arrhythmias when adrenaline (epinephrine) given with l TRICYCLICS (but local anaesthetics with adrenaline appear to be safe); increased risk of hypertension and arrhythmias when noradrenaline (norepinephrine) or phenylephrine given with l TRICYCLICS

▶ Antiepileptics: methylphenidate increases plasma concentration of FOSPHENYTOIN and PHENYTOIN; methylphenidate possibly increases plasma concentration of PHENOBARBITAL and PRIMIDONE

▶ Antipsychotics: hypertensive effect of sympathomimetics antagonised by ANTIPSYCHOTICS; effects of lisdexamfetamine possibly reduced by CHLORPROMAZINE; dexamfetamine possibly antagonises antipsychotic effects of CHLORPROMAZINE; methylphenidate possibly increases side- effects of RISPERIDONE

▶ Antivirals: plasma concentration of dexamfetamine possibly increased by RITONAVIR

l Beta-blockers: increased risk of severe hypertension and bradycardia when adrenaline (epinephrine) given with non- cardioselective l BETA-BLOCKERS, also response to adrenaline (epinephrine) may be reduced; increased risk of severe hypertension and bradycardia when dobutamine given with non-cardioselective l BETA-BLOCKERS; possible increased risk of severe hypertension and bradycardia when noradrenaline (norepinephrine) given with non-cardioselective l BETA- BLOCKERS

l Clonidine: possible risk of hypertension when adrenaline

(epinephrine) or noradrenaline (norepinephrine) given with CLONIDINE; serious adverse events reported with concomitant use of methylphenidate and l CLONIDINE (causality not established)

▶ Corticosteroids: ephedrine accelerates metabolism of

DEXAMETHASONE

l Dopaminergics: risk of toxicity when isometheptene given with l BROMOCRIPTINE; effects of adrenaline (epinephrine), dobutamine, dopamine and noradrenaline (norepinephrine) possibly enhanced by ENTACAPONE; avoid concomitant use of sympathomimetics with l RASAGILINE; avoidance of sympathomimetics advised by manufacturer of SELEGILINE; risk of hypertensive crisis when dopamine given with

l SELEGILINE

▶ Doxapram: increased risk of hypertension when sympathomimetics given with DOXAPRAM

▶ Ergot Alkaloids: increased risk of ergotism when sympathomimetics given with ERGOTAMINE

▶ Oxytocin: risk of hypertension when vasoconstrictor sympathomimetics given with OXYTOCIN (due to enhanced vasopressor effect)

l Sympathomimetics: effects of adrenaline (epinephrine) possibly enhanced by l DOPEXAMINE; dopexamine possibly enhances effects of l NORADRENALINE (NOREPINEPHRINE)

▶ Theophylline: avoidance of ephedrine in children advised by manufacturer of THEOPHYLLINE

▶ Ulcer-healing Drugs: metabolism of dobutamine possibly inhibited by CIMETIDINE

Sympathomimetics, Beta2

▶ Aminophylline: increased risk of hypokalaemia when high doses of beta2 sympathomimetics given with AMINOPHYLLINE

l Antifungals: plasma concentration of olodaterol increased by

KETOCONAZOLE; metabolism of salmeterol inhibited by

l KETOCONAZOLE (increased plasma concentration)

l Antivirals: avoidance of salmeterol advised by manufacturer of

LOPINAVIR, RITONAVIR and TIPRANAVIR; avoidance of

Sympathomimetics, Beta2

l Antivirals (continued)

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salmeterol advised by manufacturer of l TELAPREVIR (risk of ventricular arrhythmias)

▶ Atomoxetine: Increased risk of cardiovascular side-effects when *parenteral* salbutamol given with ATOMOXETINE

▶ Cardiac Glycosides: salbutamol possibly reduces plasma concentration of DIGOXIN

▶ Cobicistat: avoidance of salmeterol advised by manufacturer of

COBICISTAT

▶ Corticosteroids: increased risk of hypokalaemia when high doses of beta2 sympathomimetics given with CORTICOSTEROIDS

▶ Cytotoxics: avoidance of salmeterol advised by manufacturer of IDELALISIB

▶ Diuretics: increased risk of hypokalaemia when high doses of beta2 sympathomimetics given with ACETAZOLAMIDE, LOOP DIURETICS or THIAZIDES AND RELATED DIURETICS

l Methyldopa: acute hypotension reported when *infusion* of salbutamol given with l METHYLDOPA

▶ Muscle Relaxants: bambuterol enhances effects of

SUXAMETHONIUM

▶ Theophylline: increased risk of hypokalaemia when high doses of beta2 sympathomimetics given with THEOPHYLLINE

Tacrolimus

NOTE Interactions do not generally apply to tacrolimus used topically; risk of facial flushing and skin irritation with topical tacrolimus on consumption of alcohol

l Analgesics: possible increased risk of nephrotoxicity when tacrolimus given with NSAIDS; increased risk of nephrotoxicity when tacrolimus given with l IBUPROFEN

▶ Angiotensin-II Receptor Antagonists: increased risk of hyperkalaemia when tacrolimus given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Anti-arrhythmics: caution with tacrolimus advised by manufacturer of DRONEDARONE

l Antibacterials: plasma concentration of tacrolimus increased by l CLARITHROMYCIN and l ERYTHROMYCIN; plasma concentration of tacrolimus possibly reduced by RIFABUTIN; plasma concentration of tacrolimus reduced by l RIFAMPICIN; increased risk of nephrotoxicity when tacrolimus given with l AMINOGLYCOSIDES; plasma concentration of tacrolimus possibly increased by l CHLORAMPHENICOL and

l TELITHROMYCIN; possible increased risk of nephrotoxicity when tacrolimus given with VANCOMYCIN

l Anticoagulants: tacrolimus possibly increases plasma concentration of l DABIGATRAN—manufacturer of dabigatran advises avoid concomitant use

l Antidepressants: plasma concentration of tacrolimus reduced

by l ST JOHN’S WORT—avoid concomitant use

l Antiepileptics: plasma concentration of tacrolimus reduced by FOSPHENYTOIN and PHENYTOIN, also plasma concentration of fosphenytoin and phenytoin possibly increased; plasma concentration of tacrolimus reduced by l PHENOBARBITAL and l PRIMIDONE

l Antifungals: plasma concentration of tacrolimus increased by

l FLUCONAZOLE, l ITRACONAZOLE, l KETOCONAZOLE,

l POSACONAZOLE and l VORICONAZOLE (consider reducing dose of tacrolimus); plasma concentration of tacrolimus possibly increased by l MICONAZOLE *oral gel*; increased risk of nephrotoxicity when tacrolimus given with l AMPHOTERICIN; plasma concentration of tacrolimus reduced by

l CASPOFUNGIN

l Antipsychotics: avoidance of tacrolimus advised by manufacturer of l DROPERIDOL (risk of ventricular arrhythmias)

l Antivirals: possible increased risk of nephrotoxicity when tacrolimus given with ACICLOVIR, GANCICLOVIR, VALACICLOVIR or VALGANCICLOVIR; plasma concentration of tacrolimus possibly increased by l ATAZANAVIR and l RITONAVIR; plasma concentration of tacrolimus increased by l BOCEPREVIR (reduce dose of tacrolimus); plasma concentration of tacrolimus possibly affected by l EFAVIRENZ; plasma concentration of tacrolimus increased by l FOSAMPRENAVIR; plasma concentration of tacrolimus increased by

l SAQUINAVIR (consider reducing dose of tacrolimus); plasma

Interactions | Appendix 1

Tacrolimus

l Antivirals (continued)

concentration of both drugs increased when tacrolimus given with l TELAPREVIR (reduce dose of tacrolimus)

l Calcium-channel Blockers: plasma concentration of tacrolimus possibly increased by FELODIPINE and VERAPAMIL; plasma concentration of tacrolimus increased by l DILTIAZEM,

NICARDIPINE and l NIFEDIPINE

l Ciclosporin: tacrolimus increases plasma concentration of l CICLOSPORIN (increased risk of nephrotoxicity)—avoid concomitant use

▶ Colestilan: manufacturer of colestilan advises give tacrolimus at least 1 hour before or 3 hours after COLESTILAN

l Cytotoxics: tacrolimus possibly increases the plasma concentration of AFATINIB—manufacturer of afatinib advises separating administration of tacrolimus by 6 to 12 hours; caution with tacrolimus advised by manufacturer of

l CRIZOTINIB; plasma concentration of tacrolimus increased by IMATINIB

▶ Dexrazoxane: increased risk of immunosupression with tacrolimus advised by manufacturer of DEXRAZOXANE

l Diuretics: increased risk of hyperkalaemia when tacrolimus given with l POTASSIUM-SPARING DIURETICS AND ALDOSTERONE ANTAGONISTS

l Grapefruit Juice: plasma concentration of tacrolimus increased

by l GRAPEFRUIT JUICE

▶ Hormone Antagonists: plasma concentration of tacrolimus possibly increased by DANAZOL

▶ Lipid-regulating Drugs: separating administration from tacrolimus by 12 hours advised by manufacturer of LOMITAPIDE

▶ Mifamurtide: avoidance of tacrolimus advised by manufacturer of MIFAMURTIDE

▶ Oestrogens: plasma concentration of tacrolimus possibly increased by ETHINYLESTRADIOL

l Potassium Salts: increased risk of hyperkalaemia when tacrolimus given with l POTASSIUM SALTS

l Ranolazine: plasma concentration of tacrolimus increased by

l RANOLAZINE

▶ Sevelamer: plasma concentration of tacrolimus possibly reduced by SEVELAMER

▶ Ulcer-healing Drugs: plasma concentration of tacrolimus possibly increased by OMEPRAZOLE

Tadalafil

l Alpha-blockers: enhanced hypotensive effect when tadalafil given with l DOXAZOSIN—manufacturer of tadalafil advises avoid concomitant use; enhanced hypotensive effect when tadalafil given with l ALPHA-BLOCKERS—when patient is stable on the alpha blocker initiate tadalafil at the lowest possible dose

▶ Anti-arrhythmics: avoidance of tadalafil advised by manufacturer of DISOPYRAMIDE (risk of ventricular arrhythmias)

l Antibacterials: plasma concentration of tadalafil possibly increased by CLARITHROMYCIN and ERYTHROMYCIN; plasma concentration of tadalafil reduced by l RIFAMPICIN— manufacturer of tadalafil advises avoid concomitant use

l Antifungals: tadalafil concentration is increased by

l KETOCONAZOLE—avoid concomitant use of tadalafil for pulmonary hypertension; plasma concentration of tadalafil possibly increased by ITRACONAZOLE

l Antivirals: plasma concentration of tadalafil possibly increased by FOSAMPRENAVIR and INDINAVIR; plasma concentration of tadalafil increased by l RITONAVIR— manufacturer of tadalafil advises avoid concomitant use; increased risk of ventricular arrhythmias when tadalafil given with l SAQUINAVIR—avoid concomitant use; avoidance of high doses of tadalafil advised by manufacturer of l TELAPREVIR— consult product literature

▶ Bosentan: plasma concentration of tadalafil reduced by

BOSENTAN

l Cobicistat: plasma concentration of tadalafil possibly increased by l COBICISTAT—manufacturer of cobicistat advises reduce dose of tadalafil (consult cobicistat product literature)

▶ Dapoxetine: avoidance of tadalafil advised by manufacturer of

DAPOXETINE

Tadalafil (continued)

▶ Grapefruit Juice: plasma concentration of tadalafil possibly increased by GRAPEFRUIT JUICE

l Nicorandil: tadalafil significantly enhances hypotensive effect of l NICORANDIL (avoid concomitant use)

l Nitrates: tadalafil significantly enhances hypotensive effect of

l NITRATES (avoid concomitant use)

l Riociguat: possible enhanced hypotensive effect when tadalafil given with l RIOCIGUAT—avoid concomitant use

Tamoxifen

▶ Antibacterials: metabolism of tamoxifen accelerated by

RIFAMPICIN (reduced plasma concentration)

l Anticoagulants: tamoxifen enhances anticoagulant effect of

l COUMARINS

l Antidepressants: metabolism of tamoxifen to active metabolite possibly inhibited by l FLUOXETINE and l PAROXETINE (avoid concomitant use)

l Antipsychotics: avoidance of tamoxifen advised by manufacturer of l DROPERIDOL (risk of ventricular arrhythmias)

l Bupropion: metabolism of tamoxifen to active metabolite possibly inhibited by l BUPROPION (avoid concomitant use)

l Cinacalcet: metabolism of tamoxifen to active metabolite possibly inhibited by l CINACALCET (avoid concomitant use)

Tamsulosin *see* Alpha-blockers

Tapentadol *see* Opioid Analgesics

Taxanes *see* Cabazitaxel, Docetaxel, and Paclitaxel

Tegafur

▶ Antibacterials: metabolism of tegafur inhibited by

METRONIDAZOLE (increased toxicity)

l Anticoagulants: tegafur enhances anticoagulant effect of

l COUMARINS

▶ Antiepileptics: tegafur possibly inhibits metabolism of

FOSPHENYTOIN and PHENYTOIN (increased risk of toxicity)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Filgrastim: neutropenia possibly exacerbated when tegafur given with FILGRASTIM

l Folates: toxicity of tegafur increased by l FOLIC ACID—avoid concomitant use

▶ Lipegfilgrastim: neutropenia possibly exacerbated when tegafur given with LIPEGFILGRASTIM

▶ Pegfilgrastim: neutropenia possibly exacerbated when tegafur given with PEGFILGRASTIM

▶ Ulcer-healing Drugs: metabolism of tegafur inhibited by

CIMETIDINE (increased plasma concentration)

Teicoplanin

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Telaprevir

l Alpha-blockers: manufacturer of telaprevir advises avoid concomitant use with l ALFUZOSIN

l Analgesics: manufacturer of telaprevir advises caution with

l METHADONE (risk of ventricular arrhythmias)

l Anti-arrhythmics: manufacturer of telaprevir advises avoid concomitant use with l AMIODARONE and l DISOPYRAMIDE (risk of ventricular arrhythmias); manufacturer of telaprevir advises caution with l FLECAINIDE and l PROPAFENONE (risk of ventricular arrhythmias); manufacturer of telaprevir advises caution with *intravenous* LIDOCAINE

l Antibacterials: plasma concentration of both drugs possibly increased when telaprevir given with l CLARITHROMYCIN,

l ERYTHROMYCIN and l TELITHROMYCIN (increased risk of ventricular arrhythmias); manufacturer of telaprevir advises avoid concomitant use with l RIFABUTIN; plasma concentration of telaprevir significantly reduced by

l RIFAMPICIN—avoid concomitant use

l Anticoagulants: telaprevir possibly affects plasma concentration of l WARFARIN; avoidance of telaprevir advised by manufacturer of APIXABAN; telaprevir possibly increases plasma concentration of DABIGATRAN

l Antidepressants: telaprevir possibly increases plasma concentration of TRAZODONE; manufacturer of telaprevir advises avoid concomitant use with l ST JOHN’S WORT

Telaprevir (continued)

▶ Antidiabetics: telaprevir increases plasma concentration of

METFORMIN (consider reducing dose of metformin)

l Antiepileptics: manufacturer of telaprevir advises avoid concomitant use with l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE

l Antifungals: plasma concentration of both drugs possibly increased when telaprevir given with KETOCONAZOLE (increased risk of ventricular arrhythmias)—reduce dose of ketoconazole; telaprevir possibly increases plasma concentration of ITRACONAZOLE; telaprevir possibly increases plasma concentration of l POSACONAZOLE (increased risk of ventricular arrhythmias); telaprevir possibly affects plasma concentration of l VORICONAZOLE (possible increased risk of ventricular arrhythmias)

l Antipsychotics: telaprevir possibly increases plasma concentration of l LURASIDONE—avoid concomitant use; manufacturer of telaprevir advises avoid concomitant use with l PIMOZIDE; telaprevir possibly increases plasma concentration of l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: plasma concentration of telaprevir possibly reduced by ATAZANAVIR, also plasma concentration of atazanavir possibly increased; telaprevir increases the plasma concentration of l DACLATASVIR—reduce dose of daclatasvir (see under Daclatasvir, p. 544); avoid concomitant use of telaprevir with l DARUNAVIR; plasma concentration of telaprevir reduced by l EFAVIRENZ—increase dose of telaprevir; manufacturers advise avoid concomitant use of telaprevir with l FOSAMPRENAVIR and l LOPINAVIR; telaprevir increases plasma concentration of MARAVIROC (consider reducing dose of maraviroc); plasma concentration of telaprevir possibly reduced by NEVIRAPINE—consider increasing dose of telaprevir; plasma concentration of telaprevir possibly reduced by RITONAVIR; telaprevir increases plasma concentration of TENOFOVIR; avoidance of telaprevir advised by manufacturer of TIPRANAVIR

l Anxiolytics and Hypnotics: telaprevir possibly increases plasma

concentration of l MIDAZOLAM (risk of prolonged sedation— avoid concomitant use of *oral* midazolam)

l Beta-blockers: manufacturer of telaprevir advises avoid concomitant use with l SOTALOL (risk of ventricular arrhythmias)

▶ Bosentan: plasma concentration of telaprevir possibly reduced by BOSENTAN, also plasma concentration of bosentan possibly increased

▶ Calcium-channel Blockers: telaprevir increases plasma concentration of AMLODIPINE (consider reducing dose of amlodipine); manufacturer of telaprevir advises caution with DILTIAZEM, FELODIPINE, NICARDIPINE, NIFEDIPINE and VERAPAMIL

▶ Cardiac Glycosides: telaprevir increases plasma concentration of DIGOXIN

l Ciclosporin: plasma concentration of both drugs increased when telaprevir given with l CICLOSPORIN (reduce dose of ciclosporin)

l Cilostazol: telaprevir possibly increases plasma concentration of l CILOSTAZOL (see under Cilostazol, p. 206)

l Colchicine: telaprevir possibly increases risk of l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

▶ Corticosteroids: telaprevir possibly increases plasma concentration of *inhaled* and *intranasal* BUDESONIDE and FLUTICASONE; plasma concentration of telaprevir possibly reduced by DEXAMETHASONE

l Cytotoxics: telaprevir possibly increases the plasma concentration of l BOSUTINIB—manufacturer of bosutinib advises avoid or consider reducing dose of bosutinib; manufacturer of ruxolitinib advises dose reduction when telaprevir given with l RUXOLITINIB—consult ruxolitinib product literature

l Domperidone: possible increased risk of ventricular

arrhythmias when telaprevir given with l DOMPERIDONE—

avoid concomitant use

l Ergot Alkaloids: manufacturer of telaprevir advises avoid concomitant use with l ERGOT ALKALOIDS

Telaprevir (continued)

l Lipid-regulating Drugs: manufacturer of telaprevir advises avoid concomitant use with l ATORVASTATIN; manufacturers advise avoid concomitant use of telaprevir with

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l SIMVASTATIN; avoidance of telaprevir advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

l Oestrogens: telaprevir possibly reduces plasma concentration of l ETHINYLESTRADIOL—manufacturer of telaprevir advises additional contraceptive precautions

l Sildenafil: manufacturer of telaprevir advises avoid concomitant use with l SILDENAFIL

l Sirolimus: plasma concentration of both drugs increased when telaprevir given with l SIROLIMUS (reduce dose of sirolimus)

l Sympathomimetics, Beta2: manufacturer of telaprevir advises avoid concomitant use with l SALMETEROL (risk of ventricular arrhythmias)

l Tacrolimus: plasma concentration of both drugs increased when telaprevir given with l TACROLIMUS (reduce dose of tacrolimus)

l Tadalafil: manufacturer of telaprevir advises avoid concomitant use with high doses of l TADALAFIL—consult product literature

l Vardenafil: manufacturer of telaprevir advises avoid concomitant use with l VARDENAFIL

Telavancin

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Telbivudine

l Interferons: increased risk of peripheral neuropathy when telbivudine given with l INTERFERON ALFA and

l PEGINTERFERON ALFA

Telithromycin

l Analgesics: possible increased risk of ventricular arrhythmias when telithromycin given with l METHADONE; telithromycin inhibits the metabolism of OXYCODONE

l Anti-arrhythmics: possible increased risk of ventricular arrhythmias when telithromycin given with l AMIODARONE and l DISOPYRAMIDE; increased risk of ventricular arrhythmias when telithromycin given with l DRONEDARONE—avoid concomitant use

l Antibacterials: possible increased risk of ventricular arrhythmias when telithromycin given with l MOXIFLOXACIN; plasma concentration of telithromycin reduced by

l RIFAMPICIN (avoid during and for 2 weeks after rifampicin)

▶ Anticoagulants: avoidance of telithromycin advised by manufacturer of APIXABAN

l Antidepressants: possible increased risk of ventricular arrhythmias when telithromycin given with l CITALOPRAM and l TRICYCLICS; plasma concentration of telithromycin reduced by l ST JOHN’S WORT (avoid during and for 2 weeks after St John’s wort)

l Antiepileptics: plasma concentration of telithromycin reduced by l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL,

l PHENYTOIN and l PRIMIDONE (avoid during and for 2 weeks after carbamazepine, fosphenytoin, phenobarbital, phenytoin and primidone)

l Antifungals: plasma concentration of telithromycin increased by l KETOCONAZOLE—avoid in severe renal and hepatic impairment

▶ Antimuscarinics: manufacturer of fesoterodine advises dose reduction when telithromycin given with FESOTERODINE— consult fesoterodine product literature

l Antipsychotics: possible increased risk of ventricular arrhythmias when telithromycin given with

l CHLORPROMAZINE; telithromycin possibly increases plasma concentration of l LURASIDONE—avoid concomitant use; increased risk of ventricular arrhythmias when telithromycin given with l PIMOZIDE—avoid concomitant use; telithromycin possibly increases plasma concentration of QUETIAPINE

l Antivirals: manufacturer of telithromycin advises avoid concomitant use with l ATAZANAVIR, l FOSAMPRENAVIR,

l INDINAVIR, l LOPINAVIR, l RITONAVIR and l TIPRANAVIR in

severe renal and hepatic impairment; telithromycin possibly increases the plasma concentration of l DACLATASVIR—reduce

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Telithromycin

l Antivirals (continued)

dose of daclatasvir (see under Daclatasvir, p. 544); telithromycin possibly increases plasma concentration of l MARAVIROC (consider reducing dose of maraviroc);

manufacturer of telithromycin advises avoid concomitant use with l SAQUINAVIR (risk of ventricular arrhythmias); telithromycin possibly increases plasma concentration of

l SIMEPREVIR—manufacturer of simeprevir advises avoid concomitant use; plasma concentration of both drugs possibly increased when telithromycin given with

l TELAPREVIR (increased risk of ventricular arrhythmias)

l Anxiolytics and Hypnotics: telithromycin inhibits metabolism of l MIDAZOLAM (increased plasma concentration with increased sedation)

▶ Aprepitant: telithromycin possibly increases plasma concentration of APREPITANT

l Avanafil: telithromycin possibly increases plasma concentration of l AVANAFIL—manufacturer of avanafil advises avoid concomitant use

l Calcium-channel Blockers: telithromycin possibly inhibits metabolism of l CALCIUM-CHANNEL BLOCKERS (increased risk of side-effects)

▶ Cardiac Glycosides: telithromycin possibly increases plasma concentration of DIGOXIN

l Ciclosporin: telithromycin possibly increases plasma concentration of l CICLOSPORIN

l Colchicine: telithromycin possibly increases risk of

l COLCHICINE toxicity—suspend or reduce dose of colchicine (avoid concomitant use in hepatic or renal impairment)

l Cytotoxics: telithromycin possibly increases plasma concentration of AXITINIB (reduce dose of axitinib—consult axitinib product literature); telithromycin possibly increases the plasma concentration of l BOSUTINIB and l CABAZITAXEL— manufacturer of bosutinib and cabazitaxel advises avoid or consider reducing dose of bosutinib and cabazitaxel; telithromycin possibly increases plasma concentration of

l CRIZOTINIB and l EVEROLIMUS—manufacturer of crizotinib and everolimus advises avoid concomitant use; avoidance of telithromycin advised by manufacturer of DASATINIB (plasma concentration of dasatinib possibly increased); telithromycin possibly increases the plasma concentration of l IBRUTINIB— reduce dose of ibrutinib (see under Ibrutinib, p. 809); avoidance of telithromycin advised by manufacturer of

l LAPATINIB and l NILOTINIB; telithromycin possibly increases plasma concentration of l PAZOPANIB (reduce dose of pazopanib); telithromycin possibly increases plasma concentration of PONATINIB—consider reducing initial dose of ponatinib (see under Ponatinib, p. 814); manufacturer of ruxolitinib advises dose reduction when telithromycin given with l RUXOLITINIB—consult ruxolitinib product literature; telithromycin possibly increases plasma concentration of

l DOCETAXEL—manufacturer of docetaxel advises avoid concomitant use or consider reducing docetaxel dose

l Dapoxetine: avoidance of telithromycin advised by manufacturer of l DAPOXETINE (increased risk of toxicity)

l Diuretics: telithromycin increases plasma concentration of

l EPLERENONE—avoid concomitant use

l Domperidone: possible increased risk of ventricular arrhythmias when telithromycin given with l DOMPERIDONE— avoid concomitant use

l Ergot Alkaloids: increased risk of ergotism when telithromycin given with l ERGOTAMINE—avoid concomitant use

▶ Fosaprepitant: telithromycin possibly increases plasma concentration of FOSAPREPITANT

l Ivabradine: telithromycin possibly increases plasma concentration of l IVABRADINE—avoid concomitant use

l Ivacaftor: telithromycin possibly increases plasma concentration of l IVACAFTOR (see under Ivacaftor, p. 257)

l Lipid-regulating Drugs: increased risk of myopathy when telithromycin given with l ATORVASTATIN or l SIMVASTATIN (avoid concomitant use); possible increased risk of myopathy when telithromycin given with PRAVASTATIN; avoidance of telithromycin advised by manufacturer of l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

Telithromycin (continued)

l Pentamidine Isetionate: possible increased risk of ventricular arrhythmias when telithromycin given with *parenteral*

l PENTAMIDINE ISETIONATE

l Ranolazine: telithromycin possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

l Sildenafil: telithromycin possibly increases plasma concentration of l SILDENAFIL—consider reducing initial dose of sildenafil for erectile dysfunction or reduce sildenafil dose frequency to once daily for pulmonary hypertension

l Sirolimus: telithromycin increases plasma concentration of

l SIROLIMUS—avoid concomitant use

l Tacrolimus: telithromycin possibly increases plasma concentration of l TACROLIMUS

▶ Ulipristal: avoidance of telithromycin advised by manufacturer of *low-dose* ULIPRISTAL

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Telmisartan *see* Angiotensin-II Receptor Antagonists

Temazepam *see* Anxiolytics and Hypnotics

Temocillin *see* Penicillins

Temoporfin

l Cytotoxics: increased skin photosensitivity when temoporfin given with *topical* l FLUOROURACIL

Temozolomide

▶ Antiepileptics: plasma concentration of temozolomide increased by SODIUM VALPROATE and VALPROIC ACID

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Temsirolimus

NOTE The main active metabolite of temsirolimus is sirolimus—*see also* interactions of sirolimus and consult product literature

l Antibacterials: plasma concentration of active metabolite of temsirolimus reduced by l RIFAMPICIN—avoid concomitant use

l Antifungals: plasma concentration of active metabolite of temsirolimus increased by l KETOCONAZOLE—avoid concomitant use; manufacturer of temsirolimus advises avoid concomitant use with l ITRACONAZOLE (plasma concentration of temsirolimus possibly increased)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Tenofovir

l Antivirals: manufacturer of tenofovir advises avoid concomitant use with ADEFOVIR; tenofovir reduces plasma concentration of ATAZANAVIR, also plasma concentration of tenofovir possibly increased; tenofovir increases plasma concentration of l DIDANOSINE (increased risk of toxicity)— avoid concomitant use; plasma concentration of tenofovir increased by LOPINAVIR and TELAPREVIR

l Orlistat: absorption of tenofovir possibly reduced by

l ORLISTAT

Tenoxicam *see* NSAIDs Terazosin *see* Alpha-blockers Terbinafine

l Antibacterials: plasma concentration of terbinafine reduced by

l RIFAMPICIN

▶ Antidepressants: terbinafine possibly increases plasma concentration of PAROXETINE and TRICYCLICS

▶ Antifungals: terbinafine increases plasma concentration of

FLUCONAZOLE

▶ Ciclosporin: terbinafine possibly reduces plasma concentration of CICLOSPORIN

▶ Oestrogens: occasional reports of breakthrough bleeding when terbinafine given with OESTROGENS (when used for contraception)

▶ Progestogens: occasional reports of breakthrough bleeding when terbinafine given with PROGESTOGENS (when used for contraception)

▶ Ulcer-healing Drugs: plasma concentration of terbinafine increased by CIMETIDINE

Terbutaline *see* Sympathomimetics, Beta2

Teriflunomide

▶ Antibacterials: teriflunomide increases plasma concentration of CEFACLOR; plasma concentration of teriflunomide reduced by RIFAMPICIN

▶ Antidiabetics: teriflunomide increases plasma concentration of

REPAGLINIDE

l Lipid-regulating Drugs: the effect of teriflunomide is significantly decreased by COLESTYRAMINE (enhanced elimination)—avoid unless drug elimination desired; teriflunomide increases plasma concentration of

l ROSUVASTATIN (consider reducing dose of rosuvastatin)

▶ Oestrogens: teriflunomide increases plasma concentration of

ETHINYLESTRADIOL

▶ Progestogens: teriflunomide increases plasma concentration of LEVONORGESTREL

l Vaccines: risk of generalised infections when teriflunomide given with live l VACCINES—avoid concomitant use

Testolactone

l Anticoagulants: testolactone enhances anticoagulant effect of

l COUMARINS and l PHENINDIONE

Testosterone

l Anticoagulants: testosterone enhances anticoagulant effect of

l COUMARINS and l PHENINDIONE

▶ Antidiabetics: testosterone possibly enhances hypoglycaemic effect of ANTIDIABETICS

Tetrabenazine

l Antidepressants: risk of CNS toxicity when tetrabenazine given with l MAOIS (avoid tetrabenazine for 2 weeks after MAOIs)

▶ Antipsychotics: increased risk of extrapyramidal side-effects when tetrabenazine given with ANTIPSYCHOTICS

▶ Dopaminergics: increased risk of extrapyramidal side-effects when tetrabenazine given with AMANTADINE

▶ Metoclopramide: increased risk of extrapyramidal side-effects when tetrabenazine given with METOCLOPRAMIDE

Tetracosactide *see* Corticosteroids Tetracycline *see* Tetracyclines Tetracyclines

▶ ACE Inhibitors: absorption of tetracyclines reduced by

QUINAPRIL tablets (quinapril tablets contain magnesium carbonate)

▶ Adsorbents: absorption of tetracyclines possibly reduced by

KAOLIN

▶ Antacids: absorption of tetracyclines reduced by ANTACIDS

▶ Antibacterials: plasma concentration of doxycycline reduced by RIFAMPICIN—consider increasing dose of doxycycline; tetracyclines possibly antagonise effects of PENICILLINS

l Anticoagulants: tetracyclines possibly enhance anticoagulant effect of l COUMARINS and l PHENINDIONE

▶ Antidiabetics: tetracyclines possibly enhance hypoglycaemic effect of SULFONYLUREAS

▶ Antiepileptics: metabolism of doxycycline accelerated by CARBAMAZEPINE (reduced effect); metabolism of doxycycline accelerated by FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE (reduced plasma concentration)

▶ Atovaquone: tetracycline reduces plasma concentration of

ATOVAQUONE

▶ Calcium Salts: absorption of tetracycline reduced by CALCIUM SALTS

▶ Cytotoxics: doxycycline or tetracycline increase risk of

METHOTREXATE toxicity

▶ Dairy Products: absorption of tetracyclines (except doxycycline and minocycline) reduced by DAIRY PRODUCTS

▶ Diuretics: manufacturer of lymecycline advises avoid concomitant use with DIURETICS

▶ Ergot Alkaloids: increased risk of ergotism when tetracyclines given with ERGOTAMINE

▶ Iron Salts: absorption of tetracyclines reduced by *oral* IRON SALTS, also absorption of *oral* iron salts reduced by tetracyclines

▶ Lipid-regulating Drugs: absorption of tetracycline possibly reduced by COLESTIPOL and COLESTYRAMINE

l Retinoids: possible increased risk of benign intracranial hypertension when tetracyclines given with l RETINOIDS (avoid concomitant use)

Tetracyclines (continued)

▶ Strontium Ranelate: absorption of tetracyclines reduced by STRONTIUM RANELATE (manufacturer of strontium ranelate advises avoid concomitant use)

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▶ Ulcer-healing Drugs: absorption of tetracyclines reduced by

SUCRALFATE and TRIPOTASSIUM DICITRATOBISMUTHATE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

▶ Zinc: absorption of tetracyclines reduced by ZINC, also absorption of zinc reduced by tetracyclines

Theophylline

▶ Allopurinol: plasma concentration of theophylline possibly increased by ALLOPURINOL

▶ Anaesthetics, General: increased risk of convulsions when theophylline given with KETAMINE

▶ Anti-arrhythmics: theophylline antagonises anti-arrhythmic effect of ADENOSINE—manufacturer of adenosine advises avoid theophylline for 24 hours before adenosine; plasma concentration of theophylline increased by PROPAFENONE

l Antibacterials: plasma concentration of theophylline possibly increased by CLARITHROMYCIN and ISONIAZID; plasma concentration of theophylline increased by l ERYTHROMYCIN (also theophylline may reduce absorption of *oral* erythromycin); plasma concentration of theophylline increased by l CIPROFLOXACIN and l NORFLOXACIN; metabolism of theophylline accelerated by RIFAMPICIN (reduced plasma concentration); possible increased risk of convulsions when theophylline given with l QUINOLONES

l Antidepressants: plasma concentration of theophylline increased by l FLUVOXAMINE (concomitant use should usually be avoided, but where not possible halve theophylline dose and monitor plasma-theophylline concentration); plasma concentration of theophylline possibly reduced by ST JOHN’S WORT

l Antiepileptics: metabolism of theophylline accelerated by

CARBAMAZEPINE, l PHENOBARBITAL and l PRIMIDONE (reduced

effect); plasma concentration of both drugs reduced when theophylline given with l FOSPHENYTOIN and l PHENYTOIN

l Antifungals: plasma concentration of theophylline possibly increased by l FLUCONAZOLE and l KETOCONAZOLE

l Antivirals: plasma concentration of theophylline possibly increased by ACICLOVIR and VALACICLOVIR; metabolism of theophylline accelerated by l RITONAVIR (reduced plasma concentration)

▶ Anxiolytics and Hypnotics: theophylline possibly reduces effects of BENZODIAZEPINES

▶ Caffeine citrate: avoidance of theophylline advised by manufacturer of CAFFEINE CITRATE

l Calcium-channel Blockers: plasma concentration of theophylline possibly increased by l CALCIUM-CHANNEL BLOCKERS (enhanced effect); plasma concentration of theophylline increased by DILTIAZEM; plasma concentration of theophylline increased by l VERAPAMIL (enhanced effect)

▶ Corticosteroids: increased risk of hypokalaemia when theophylline given with CORTICOSTEROIDS

▶ Cytotoxics: plasma concentration of theophylline possibly increased by METHOTREXATE

l Deferasirox: plasma concentration of theophylline increased by l DEFERASIROX (consider reducing dose of theophylline)

▶ Disulfiram: metabolism of theophylline inhibited by

DISULFIRAM (increased risk of toxicity)

▶ Diuretics: increased risk of hypokalaemia when theophylline given with ACETAZOLAMIDE, LOOP DIURETICS or THIAZIDES AND RELATED DIURETICS

▶ Doxapram: increased CNS stimulation when theophylline given with DOXAPRAM

l Interferons: metabolism of theophylline inhibited by

l INTERFERON ALFA and l PEGINTERFERON ALFA (consider

reducing dose of theophylline)

▶ Leukotriene Receptor Antagonists: plasma concentration of theophylline possibly increased by ZAFIRLUKAST, also plasma concentration of zafirlukast reduced

▶ Lithium: theophylline increases excretion of LITHIUM (reduced plasma concentration)

▶ Oestrogens: plasma concentration of theophylline increased by OESTROGENS (consider reducing dose of theophylline)

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Theophylline (continued)

▶ Pentoxifylline: plasma concentration of theophylline increased by PENTOXIFYLLINE

▶ Roflumilast: avoidance of theophylline advised by manufacturer of ROFLUMILAST

▶ Sulfinpyrazone: plasma concentration of theophylline reduced by SULFINPYRAZONE

▶ Sympathomimetics: manufacturer of theophylline advises avoid concomitant use with EPHEDRINE in children

▶ Sympathomimetics, Beta2: increased risk of hypokalaemia when theophylline given with high doses of BETA2 SYMPATHOMIMETICS

l Ulcer-healing Drugs: metabolism of theophylline inhibited by l CIMETIDINE (increased plasma concentration); absorption of theophylline possibly reduced by SUCRALFATE (give at least 2 hours apart)

▶ Vaccines: plasma concentration of theophylline possibly increased by INFLUENZA VACCINE

Thiazolidinediones *see* Antidiabetics Thiopental *see* Anaesthetics, General Thiotepa

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Muscle Relaxants: thiotepa enhances effects of SUXAMETHONIUM

Thioxanthenes *see* Antipsychotics

Thyroid Hormones

▶ Antacids: absorption of levothyroxine possibly reduced by

ANTACIDS

▶ Anti-arrhythmics: serum concentrations of thyroid hormones can be affected by AMIODARONE—monitor thyroid function closely

▶ Antibacterials: metabolism of levothyroxine accelerated by RIFAMPICIN (may increase requirements for levothyroxine in hypothyroidism)

l Anticoagulants: thyroid hormones enhance anticoagulant effect of l COUMARINS and l PHENINDIONE

▶ Antidepressants: thyroid hormones enhance effects of AMITRIPTYLINE and IMIPRAMINE; thyroid hormones possibly enhance effects of TRICYCLICS

▶ Antiepileptics: metabolism of thyroid hormones accelerated by

CARBAMAZEPINE, PHENOBARBITAL and PRIMIDONE (may increase

requirements for thyroid hormones in hypothyroidism); metabolism of thyroid hormones accelerated by FOSPHENYTOIN and PHENYTOIN (may increase requirements in hypothyroidism), also plasma concentration of fosphenytoin and phenytoin possibly increased

▶ Beta-blockers: levothyroxine accelerates metabolism of

PROPRANOLOL

▶ Calcium Salts: absorption of levothyroxine reduced by CALCIUM SALTS

▶ Colestilan: manufacturer of colestilan advises give

levothyroxine at least 1 hour before or 3 hours after

COLESTILAN

▶ Cytotoxics: plasma concentration of levothyroxine possibly reduced by IMATINIB

▶ Iron Salts: absorption of levothyroxine reduced by *oral* IRON SALTS (give at least 2 hours apart)

▶ Lanthanum: absorption of levothyroxine reduced by

LANTHANUM (give at least 2 hours apart)

▶ Lipid-regulating Drugs: absorption of levothyroxine reduced by COLESEVELAM; absorption of thyroid hormones reduced by COLESTIPOL and COLESTYRAMINE

▶ Oestrogens: requirements for thyroid hormones in hypothyroidism may be increased by OESTROGENS

▶ Orlistat: possible increased risk of hypothyroidism when levothyroxine given with ORLISTAT

▶ Polystyrene Sulfonate Resins: absorption of levothyroxine reduced by POLYSTYRENE SULFONATE RESINS

▶ Sevelamer: absorption of levothyroxine possibly reduced by

SEVELAMER

▶ Ulcer-healing Drugs: absorption of levothyroxine reduced by

CIMETIDINE and SUCRALFATE

Tiagabine

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED

Tiagabine

l Antidepressants (continued)

ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antiepileptics: plasma concentration of tiagabine reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Tiaprofenic Acid *see* NSAIDs

Tibolone

▶ Antibacterials: metabolism of tibolone accelerated by

RIFAMPICIN (reduced plasma concentration)

▶ Antiepileptics: metabolism of tibolone accelerated by CARBAMAZEPINE (reduced plasma concentration); metabolism of tibolone accelerated by FOSPHENYTOIN and PHENYTOIN

Ticagrelor

l Antibacterials: plasma concentration of ticagrelor possibly increased by l CLARITHROMYCIN—manufacturer of ticagrelor advises avoid concomitant use; plasma concentration of ticagrelor possibly increased by ERYTHROMYCIN; plasma concentration of ticagrelor reduced by l RIFAMPICIN

l Anticoagulants: ticagrelor increases plasma concentration of

l DABIGATRAN

▶ Antidepressants: possible increased risk of bleeding when ticagrelor given with CITALOPRAM, PAROXETINE or SERTRALINE

▶ Antiepileptics: plasma concentration of ticagrelor possibly reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL,

PHENYTOIN and PRIMIDONE

l Antifungals: plasma concentration of ticagrelor increased by l KETOCONAZOLE—manufacturer of ticagrelor advises avoid concomitant use

l Antivirals: plasma concentration of ticagrelor possibly increased by l ATAZANAVIR and l RITONAVIR—manufacturer of ticagrelor advises avoid concomitant use

▶ Calcium-channel Blockers: plasma concentration of ticagrelor increased by DILTIAZEM

l Cardiac Glycosides: ticagrelor increases plasma concentration of l DIGOXIN

▶ Ciclosporin: plasma concentration of ticagrelor increased by

CICLOSPORIN

l Ergot Alkaloids: ticagrelor possibly increases plasma concentration of l ERGOT ALKALOIDS

l Lipid-regulating Drugs: ticagrelor increases plasma concentration of l SIMVASTATIN (increased risk of toxicity); separating administration from ticagrelor by 12 hours advised by manufacturer of LOMITAPIDE

Ticarcillin *see* Penicillins

Tick-borne Encephalitis Vaccine *see* Vaccines

Tigecycline

▶ Anticoagulants: tigecycline possibly enhances anticoagulant effect of COUMARINS

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Timolol *see* Beta-blockers

Tinidazole

▶ Alcohol: possibility of disulfiram-like reaction when tinidazole given with ALCOHOL

▶ Antibacterials: plasma concentration of tinidazole possibly reduced by RIFAMPICIN

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Tinzaparin *see* Heparins

Tioguanine

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cytotoxics: increased risk of hepatotoxicity when tioguanine given with BUSULFAN

Tiotropium *see* Antimuscarinics

Tipranavir

▶ Analgesics: plasma concentration of tipranavir possibly reduced by BUPRENORPHINE

▶ Antacids: absorption of tipranavir reduced by ANTACIDS (give at least 2 hours apart)

l Antibacterials: tipranavir increases plasma concentration of l CLARITHROMYCIN (reduce dose of clarithromycin in renal impairment), also plasma concentration of tipranavir increased by clarithromycin; tipranavir increases plasma concentration of l RIFABUTIN (reduce dose of rifabutin); plasma concentration of tipranavir possibly reduced by

l RIFAMPICIN—avoid concomitant use; avoidance of concomitant tipranavir in severe renal and hepatic impairment advised by manufacturer of l TELITHROMYCIN

▶ Anticoagulants: avoidance of tipranavir advised by manufacturer of APIXABAN and RIVAROXABAN

l Antidepressants: plasma concentration of tipranavir possibly reduced by l ST JOHN’S WORT—avoid concomitant use

▶ Antiepileptics: plasma concentration of tipranavir possibly reduced by CARBAMAZEPINE

▶ Antifungals: plasma concentration of tipranavir increased by

FLUCONAZOLE

l Antimalarials: caution with tipranavir advised by manufacturer of ARTEMETHER WITH LUMEFANTRINE; tipranavir possibly increases plasma concentration of l QUININE (increased risk of toxicity)

▶ Antimuscarinics: avoidance of tipranavir advised by manufacturer of DARIFENACIN

l Antipsychotics: tipranavir possibly increases plasma concentration of l ARIPIPRAZOLE (reduce dose of aripiprazole—consult aripiprazole product literature); tipranavir possibly increases plasma concentration of

l QUETIAPINE—manufacturer of quetiapine advises avoid concomitant use

l Antivirals: tipranavir reduces plasma concentration of

l ABACAVIR, l FOSAMPRENAVIR, l LOPINAVIR, l SAQUINAVIR and

l ZIDOVUDINE; plasma concentration of tipranavir increased by ATAZANAVIR (also plasma concentration of atazanavir reduced); manufacturer of tipranavir advises avoid concomitant use with BOCEPREVIR and TELAPREVIR; tipranavir reduces plasma concentration of DIDANOSINE—manufacturer of tipranavir advises tipranavir and didanosine *capsules* should be taken at least 2 hours apart; tipranavir reduces the plasma concentration of l DOLUTEGRAVIR (see under Dolutegravir, p. 557); tipranavir reduces plasma concentration of l ETRAVIRINE, also plasma concentration of tipranavir increased (avoid concomitant use)

l Beta-blockers: manufacturer of tipranavir advises avoid concomitant use with l METOPROLOL for heart failure

▶ Bosentan: manufacturer of tipranavir advises avoid concomitant use with BOSENTAN

l Cobicistat: plasma concentration of both drugs reduced when tipranavir given with l COBICISTAT (avoid concomitant use)

l Lipid-regulating Drugs: increased risk of myopathy when tipranavir given with l ATORVASTATIN (see under Atorvastatin,

p. 179); tipranavir increases plasma concentration of

l ROSUVASTATIN—adjust dose of rosuvastatin (consult product literature); tipranavir possibly increases plasma concentration of l SIMVASTATIN—avoid concomitant use; avoidance of tipranavir advised by manufacturer of

l LOMITAPIDE (plasma concentration of lomitapide possibly increased)

l Orlistat: absorption of tipranavir possibly reduced by

l ORLISTAT

l Ranolazine: tipranavir possibly increases plasma concentration of l RANOLAZINE—manufacturer of ranolazine advises avoid concomitant use

▶ Sildenafil: manufacturer of tipranavir advises avoid concomitant use of SILDENAFIL for pulmonary arterial hypertension

▶ Sympathomimetics, Beta2: manufacturer of tipranavir advises avoid concomitant use with SALMETEROL

l Ulcer-healing Drugs: tipranavir reduces plasma concentration of l ESOMEPRAZOLE and l OMEPRAZOLE

▶ Vardenafil: manufacturer of tipranavir advises caution with

VARDENAFIL

Tipranavir (continued)

▶ Vitamins: increased risk of bleeding when tipranavir given with high doses of VITAMIN E

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Tirofiban

▶ Iloprost: increased risk of bleeding when tirofiban given with

ILOPROST

Tizanidine *see* Muscle Relaxants Tobramycin *see* Aminoglycosides Tocilizumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Tolazoline *see* Alpha-blockers Tolbutamide *see* Antidiabetics Tolcapone

▶ Antidepressants: avoid concomitant use of tolcapone with

MAOIS

▶ Memantine: effects of dopaminergics possibly enhanced by

MEMANTINE

▶ Methyldopa: antiparkinsonian effect of dopaminergics antagonised by METHYLDOPA

Tolfenamic Acid *see* NSAIDs Tolterodine *see* Antimuscarinics Tolvaptan

▶ Antibacterials: plasma concentration of tolvaptan reduced by

RIFAMPICIN

▶ Antifungals: plasma concentration of tolvaptan increased by KETOCONAZOLE—manufacturer of ketoconazole advises avoid concomitant use

▶ Cardiac Glycosides: tolvaptan increases plasma concentration of DIGOXIN (increased risk of toxicity)

l Grapefruit Juice: plasma concentration of tolvaptan increased by l GRAPEFRUIT JUICE—avoid concomitant use

▶ Lipid-regulating Drugs: separating administration from tolvaptan by 12 hours advised by manufacturer of LOMITAPIDE

Topiramate

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antidiabetics: topiramate possibly increases plasma concentration of METFORMIN; topiramate possibly reduces plasma concentration of GLIBENCLAMIDE

l Antiepileptics: plasma concentration of topiramate often reduced by CARBAMAZEPINE; topiramate increases plasma concentration of l FOSPHENYTOIN and l PHENYTOIN (also plasma concentration of topiramate reduced); topiramate reduces plasma concentration of PERAMPANEL; plasma concentration of topiramate possibly reduced by PHENOBARBITAL and PRIMIDONE; hyperammonaemia and CNS toxicity reported when topiramate given with SODIUM VALPROATE and VALPROIC ACID

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

▶ Diuretics: plasma concentration of topiramate possibly increased by HYDROCHLOROTHIAZIDE

▶ Lithium: topiramate possibly affects plasma concentration of

LITHIUM

l Oestrogens: topiramate accelerates metabolism of

l OESTROGENS (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings—see Contraceptive Interactions in BNF)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

l Progestogens: topiramate accelerates metabolism of

l PROGESTOGENS (reduced contraceptive effect with combined oral contraceptives, progestogen-only oral contraceptives, contraceptive patches, vaginal rings, etonogestrel-releasing implant, and emergency hormonal contraception—see Contraceptive Interactions in BNF)

Interactions | Appendix 1

Torasemide *see* Diuretics

Toremifene

l Anticoagulants: toremifene possibly enhances anticoagulant effect of l COUMARINS

▶ Antiepileptics: metabolism of toremifene possibly accelerated by CARBAMAZEPINE (reduced plasma concentration); metabolism of toremifene possibly accelerated by FOSPHENYTOIN and PHENYTOIN; metabolism of toremifene accelerated by PHENOBARBITAL and PRIMIDONE (reduced plasma concentration)

l Cytotoxics: possible increased risk of ventricular arrhythmias when toremifene given with l VANDETANIB—avoid concomitant use

▶ Diuretics: increased risk of hypercalcaemia when toremifene given with THIAZIDES AND RELATED DIURETICS

Trabectedin

l Alcohol: manufacturer of trabectedin advises avoid concomitant use with l ALCOHOL

l Antibacterials: plasma concentration of trabectedin reduced by

l RIFAMPICIN

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when trabectedin given with live l VACCINES—avoid concomitant use

Tramadol *see* Opioid Analgesics Trandolapril *see* ACE Inhibitors Tranylcypromine *see* MAOIs Trastuzumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Trazodone *see* Antidepressants, Tricyclic (related)

Tretinoin *see* Retinoids Triamcinolone *see* Corticosteroids Triamterene *see* Diuretics Trientine

▶ Iron Salts: trientine reduces absorption of *oral* IRON SALTS

▶ Zinc: trientine reduces absorption of ZINC, also absorption of trientine reduced by zinc

Trifluoperazine *see* Antipsychotics Trihexyphenidyl *see* Antimuscarinics Trimethoprim

▶ ACE Inhibitors: possible increased risk of hyperkalaemia when

trimethoprim given with ACE INHIBITORS

▶ Angiotensin-II Receptor Antagonists: possible increased risk of hyperkalaemia when trimethoprim given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Anti-arrhythmics: possible increased risk of ventricular arrhythmias when trimethoprim (as co-trimoxazole) given with AMIODARONE—manufacturer of amiodarone advises avoid concomitant use of co-trimoxazole

▶ Antibacterials: plasma concentration of trimethoprim possibly reduced by RIFAMPICIN; plasma concentration of both drugs may increase when trimethoprim given with DAPSONE

▶ Anticoagulants: trimethoprim possibly enhances anticoagulant effect of COUMARINS

▶ Antidiabetics: trimethoprim possibly enhances hypoglycaemic effect of REPAGLINIDE—manufacturer advises avoid concomitant use; trimethoprim rarely enhances the effects of SULFONYLUREAS

l Antiepileptics: trimethoprim increases plasma concentration of l FOSPHENYTOIN and l PHENYTOIN (also increased antifolate effect)

l Antimalarials: increased antifolate effect when trimethoprim given with l PYRIMETHAMINE

▶ Antivirals: trimethoprim (as co-trimoxazole) increases plasma concentration of LAMIVUDINE—avoid concomitant use of high-dose co-trimoxazole

l Azathioprine: increased risk of haematological toxicity when trimethoprim (also with co-trimoxazole) given with

l AZATHIOPRINE

▶ Cardiac Glycosides: trimethoprim possibly increases plasma concentration of DIGOXIN

Trimethoprim (continued)

l Ciclosporin: increased risk of nephrotoxicity when trimethoprim given with l CICLOSPORIN, also plasma concentration of ciclosporin reduced by *intravenous* trimethoprim

l Cytotoxics: increased risk of haematological toxicity when trimethoprim (also with co-trimoxazole) given with

l MERCAPTOPURINE or l METHOTREXATE

▶ Diuretics: increased risk of hyperkalaemia when trimethoprim given with EPLERENONE; possible increased risk of hyperkalaemia when trimethoprim given with SPIRONOLACTONE

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Trimipramine *see* Antidepressants, Tricyclic

Tripotassium Dicitratobismuthate

▶ Antibacterials: tripotassium dicitratobismuthate reduces absorption of TETRACYCLINES

Tropicamide *see* Antimuscarinics Trospium *see* Antimuscarinics Typhoid Vaccine (oral) *see* Vaccines

Typhoid Vaccine (parenteral) *see* Vaccines

Ubidecarenone

▶ Anticoagulants: ubidecarenone may enhance or reduce anticoagulant effect of WARFARIN

Ulcer-healing Drugs *see* Histamine H2-antagonists, Proton Pump Inhibitors, Sucralfate, and Tripotassium Dicitratobismuthate

Ulipristal

l Antibacterials: manufacturer of *low-dose* ulipristal advises avoid concomitant use with CLARITHROMYCIN and TELITHROMYCIN; plasma concentration of *low-dose* ulipristal increased by ERYTHROMYCIN—manufacturer of *low-dose* ulipristal advises avoid concomitant use; manufacturer of ulipristal advises avoid concomitant use with l RIFAMPICIN (contraceptive effect of ulipristal possibly reduced)

▶ Anticoagulants: manufacturer of ulipristal advises give

DABIGATRAN at least 1.5 hours before or after ulipristal

l Antidepressants: manufacturer of ulipristal advises avoid concomitant use with l ST JOHN’S WORT (contraceptive effect of ulipristal possibly reduced)

l Antiepileptics: manufacturer of ulipristal advises avoid concomitant use with l CARBAMAZEPINE, l FOSPHENYTOIN, l PHENOBARBITAL, l PHENYTOIN and l PRIMIDONE

(contraceptive effect of ulipristal possibly reduced)

▶ Antifungals: plasma concentration of *low-dose* ulipristal increased by KETOCONAZOLE—manufacturer of *low-dose* ulipristal advises avoid concomitant use; manufacturer of ulipristal advises avoid concomitant use with ITRACONAZOLE

▶ Antihistamines: manufacturer of ulipristal advises give

FEXOFENADINE at least 1.5 hours before or after ulipristal

l Antivirals: manufacturer of ulipristal advises avoid concomitant use with l RITONAVIR (contraceptive effect of ulipristal possibly reduced)

▶ Calcium-channel Blockers: manufacturer of *low-dose* ulipristal advises avoid concomitant use with VERAPAMIL

▶ Cardiac Glycosides: manufacturer of ulipristal advises give

DIGOXIN at least 1.5 hours before or after ulipristal

▶ Grapefruit Juice: manufacturer of *low-dose* ulipristal advises avoid concomitant use with GRAPEFRUIT JUICE

l Progestogens: ulipristal possibly reduces contraceptive effect of l PROGESTOGENS

Umeclidinium *see* Antimuscarinics Ursodeoxycholic Acid *see* Bile Acids Ustekinumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Vaccines

l Abatacept: risk of generalised infections when live vaccines given with l ABATACEPT—avoid concomitant use

▶ Aminophylline: influenza vaccine possibly increases plasma concentration of AMINOPHYLLINE

Vaccines (continued)

l Anakinra: risk of generalised infections when live vaccines given with l ANAKINRA—avoid concomitant use

▶ Antibacterials: oral typhoid vaccine inactivated by

ANTIBACTERIALS—see under Typhoid Vaccine in BNF

▶ Anticoagulants: influenza vaccine possibly enhances anticoagulant effect of WARFARIN

▶ Antiepileptics: influenza vaccine enhances effects of

FOSPHENYTOIN and PHENYTOIN

▶ Antimalarials: oral typhoid vaccine inactivated by

ANTIMALARIALS—see under Typhoid Vaccine in BNF

l Corticosteroids: immune response to vaccines impaired by high doses of l CORTICOSTEROIDS—avoid concomitant use with live vaccines

l Cytotoxics: risk of generalised infections when live vaccines given with l DOXORUBICIN, l MONOCLONAL ANTIBODIES,

l PIXANTRONE or l TRABECTEDIN—avoid concomitant use

l Dexrazoxane: risk of generalised infections when live vaccines given with l DEXRAZOXANE—avoid concomitant use

l Etanercept: risk of generalised infections when live vaccines given with l ETANERCEPT—avoid concomitant use

l Immunoglobulins: impaired immune response to *oral* poliomyelitis vaccine might occur with l ANTI-D IMMUNOGLOBULINS and l NORMAL IMMUNOGLOBULIN—give *oral*

poliomyelitis vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; impaired immune response to BCG vaccine, MMR vaccine, oral typhoid vaccine, rotavirus vaccine, smallpox vaccine, varicella-zoster vaccine and yellow fever vaccine might occur with l ANTI-D IMMUNOGLOBULINS—give BCG vaccine, MMR vaccine, oral typhoid vaccine, rotavirus vaccine, smallpox vaccine, varicella-zoster vaccine and yellow fever vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins; impaired immune response to live influenza vaccine might occur with l ANTI-D IMMUNOGLOBULINS and l NORMAL IMMUNOGLOBULIN—give live

influenza vaccine at least 3 weeks before or 3 months after anti-d immunoglobulins and normal immunoglobulin; impaired immune response to BCG vaccine, MMR vaccine, oral typhoid vaccine, rotavirus vaccine, smallpox vaccine, varicella-zoster vaccine and yellow fever vaccine might occur with l NORMAL IMMUNOGLOBULIN—give BCG vaccine, MMR vaccine, oral typhoid vaccine, rotavirus vaccine, smallpox vaccine, varicella-zoster vaccine and yellow fever vaccine at least 3 weeks before or 3 months after normal immunoglobulin

▶ Interferons: avoidance of vaccines advised by manufacturer of

INTERFERON GAMMA

l Leflunomide: risk of generalised infections when live vaccines given with l LEFLUNOMIDE—avoid concomitant use

l Teriflunomide: risk of generalised infections when live vaccines given with l TERIFLUNOMIDE—avoid concomitant use

▶ Theophylline: influenza vaccine possibly increases plasma concentration of THEOPHYLLINE

Valaciclovir

▶ Aminophylline: valaciclovir possibly increases plasma concentration of AMINOPHYLLINE

▶ Ciclosporin: increased risk of nephrotoxicity when valaciclovir given with CICLOSPORIN

▶ Mycophenolate: plasma concentration of valaciclovir increased by MYCOPHENOLATE, also plasma concentration of inactive metabolite of mycophenolate increased

▶ Tacrolimus: possible increased risk of nephrotoxicity when valaciclovir given with TACROLIMUS

▶ Theophylline: valaciclovir possibly increases plasma concentration of THEOPHYLLINE

Valganciclovir

l Antibacterials: increased risk of convulsions when valganciclovir given with l IMIPENEM WITH CILASTATIN

l Antivirals: valganciclovir possibly increases plasma concentration of DIDANOSINE; profound myelosuppression when valganciclovir given with l ZIDOVUDINE (if possible avoid concomitant administration, particularly during initial valganciclovir therapy)

▶ Mycophenolate: plasma concentration of valganciclovir possibly increased by MYCOPHENOLATE, also plasma

Valganciclovir

Mycophenolate (continued)

Interactions | Appendix 1

concentration of inactive metabolite of mycophenolate possibly increased

▶ Tacrolimus: possible increased risk of nephrotoxicity when valganciclovir given with TACROLIMUS

Valproic Acid

▶ Analgesics: effects of valproic acid enhanced by ASPIRIN

l Antibacterials: metabolism of valproic acid possibly inhibited by ERYTHROMYCIN (increased plasma concentration); avoidance of valproic acid advised by manufacturer of

l PIVMECILLINAM; plasma concentration of valproic acid reduced by l CARBAPENEMS—avoid concomitant use

▶ Anticoagulants: valproic acid possibly enhances anticoagulant effect of COUMARINS

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

l Antiepileptics: plasma concentration of valproic acid reduced by CARBAMAZEPINE, also plasma concentration of active metabolite of carbamazepine increased; valproic acid possibly increases plasma concentration of ETHOSUXIMIDE; valproic acid increases or possibly decreases plasma concentration of FOSPHENYTOIN and PHENYTOIN, also plasma concentration of valproic acid reduced; valproic acid increases plasma concentration of l LAMOTRIGINE (increased risk of toxicity—reduce lamotrigine dose); valproic acid sometimes reduces plasma concentration of an active metabolite of OXCARBAZEPINE; valproic acid increases plasma concentration of PHENOBARBITAL and PRIMIDONE (also plasma concentration of valproic acid reduced); valproic acid possibly increases plasma concentration of RUFINAMIDE (reduce dose of rufinamide); hyperammonaemia and CNS toxicity reported when valproic acid given with TOPIRAMATE

l Antimalarials: anticonvulsant effect of antiepileptics

antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered); valproic acid possibly increases or decreases plasma concentration of CLOZAPINE; increased risk of side- effects including neutropenia when valproic acid given with l OLANZAPINE

▶ Antivirals: plasma concentration of valproic acid possibly reduced by RITONAVIR; valproic acid possibly increases plasma concentration of ZIDOVUDINE (increased risk of toxicity)

▶ Anxiolytics and Hypnotics: plasma concentration of valproic acid possibly increased by CLOBAZAM; increased risk of side- effects when valproic acid given with CLONAZEPAM; valproic acid possibly increases plasma concentration of DIAZEPAM and LORAZEPAM

▶ Bupropion: valproic acid inhibits the metabolism of BUPROPION

▶ Cytotoxics: valproic acid increases plasma concentration of

TEMOZOLOMIDE

▶ Lipid-regulating Drugs: absorption of valproic acid possibly reduced by COLESTYRAMINE

▶ Oestrogens: plasma concentration of valproic acid possibly reduced by ETHINYLESTRADIOL

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

▶ Sodium Benzoate: valproic acid possibly reduces effects of

SODIUM BENZOATE

l Sodium Oxybate: valproic acid increases the plasma concentration of l SODIUM OXYBATE (see under Sodium Oxybate, p. 425)

▶ Sodium Phenylbutyrate: valproic acid possibly reduces effects of SODIUM PHENYLBUTYRATE

l Ulcer-healing Drugs: metabolism of valproic acid inhibited by

l CIMETIDINE (increased plasma concentration) Valsartan *see* Angiotensin-II Receptor Antagonists Vancomycin

▶ Anaesthetics, General: hypersensitivity-like reactions can occur

when *intravenous* vancomycin given with GENERAL ANAESTHETICS

Interactions | Appendix 1

Vancomycin (continued)

l Antibacterials: increased risk of nephrotoxicity and ototoxicity when vancomycin given with l AMINOGLYCOSIDES, CAPREOMYCIN or COLISTIMETHATE SODIUM; increased risk of nephrotoxicity when vancomycin given with POLYMYXINS

▶ Antifungals: possible increased risk of nephrotoxicity when vancomycin given with AMPHOTERICIN

l Ciclosporin: increased risk of nephrotoxicity when vancomycin given with l CICLOSPORIN

▶ Cytotoxics: increased risk of nephrotoxicity and possibly of ototoxicity when vancomycin given with CISPLATIN

l Diuretics: increased risk of otoxicity when vancomycin given with l LOOP DIURETICS

▶ Lipid-regulating Drugs: effects of *oral* vancomycin antagonised by COLESTYRAMINE

l Muscle Relaxants: vancomycin enhances effects of

l SUXAMETHONIUM

▶ Tacrolimus: possible increased risk of nephrotoxicity when vancomycin given with TACROLIMUS

▶ Vaccines: antibacterials inactivate ORAL TYPHOID VACCINE—see under Typhoid Vaccine in BNF

Vandetanib

l Analgesics: possible increased risk of ventricular arrhythmias when vandetanib given with l METHADONE—avoid concomitant use

l Anti-arrhythmics: possible increased risk of ventricular arrhythmias when vandetanib given with l AMIODARONE or l DISOPYRAMIDE—avoid concomitant use

l Antibacterials: possible increased risk of ventricular arrhythmias when vandetanib given with *parenteral*

l ERYTHROMYCIN—avoid concomitant use; possible increased risk of ventricular arrhythmias when vandetanib given with l MOXIFLOXACIN—avoid concomitant use; plasma concentration of vandetanib reduced by l RIFAMPICIN— manufacturer of vandetanib advises avoid concomitant use

▶ Antidepressants: manufacturer of vandetanib advises avoid concomitant use with ST JOHN’S WORT (plasma concentration of vandetanib possibly reduced)

▶ Antidiabetics: vandetanib possibly increases plasma concentration of METFORMIN (consider reducing dose of metformin)

▶ Antiepileptics: manufacturer of vandetanib advises avoid concomitant use with CARBAMAZEPINE, PHENOBARBITAL and PRIMIDONE (plasma concentration of vandetanib possibly reduced)

l Antihistamines: possible increased risk of ventricular arrhythmias when vandetanib given with l MIZOLASTINE— avoid concomitant use

l Antimalarials: possible increased risk of ventricular arrhythmias when vandetanib given with l ARTEMETHER WITH LUMEFANTRINE—avoid concomitant use

l Antipsychotics: possible increased risk of ventricular arrhythmias when vandetanib given with l AMISULPRIDE,

l CHLORPROMAZINE, l HALOPERIDOL, l PIMOZIDE, l SULPIRIDE or

l ZUCLOPENTHIXOL—avoid concomitant use; avoid concomitant use of cytotoxics with l CLOZAPINE (increased risk of agranulocytosis)

l Beta-blockers: possible increased risk of ventricular arrhythmias when vandetanib given with l SOTALOL—avoid concomitant use

▶ Cardiac Glycosides: vandetanib increases plasma concentration of DIGOXIN—possible increased risk of bradycardia

l Cytotoxics: possible increased risk of ventricular arrhythmias when vandetanib given with l ARSENIC TRIOXIDE—avoid concomitant use

l Hormone Antagonists: possible increased risk of ventricular arrhythmias when vandetanib given with l TOREMIFENE— avoid concomitant use

l 5HT3-receptor Antagonists: increased risk of ventricular arrhythmias when vandetanib given with l ONDANSETRON— avoid concomitant use

l Pentamidine Isetionate: possible increased risk of ventricular arrhythmias when vandetanib given with l PENTAMIDINE ISETIONATE—avoid concomitant use

Vardenafil

l Alpha-blockers: enhanced hypotensive effect when vardenafil given with l ALPHA-BLOCKERS—when patient is stable on the alpha blocker initiate vardenafil at the lowest possible dose— separate doses by 6 hours (except with tamsulosin)

▶ Anti-arrhythmics: avoidance of vardenafil advised by manufacturer of DISOPYRAMIDE (risk of ventricular arrhythmias)

▶ Antibacterials: plasma concentration of vardenafil possibly increased by CLARITHROMYCIN (consider reducing initial dose of vardenafil); plasma concentration of vardenafil increased by ERYTHROMYCIN (reduce dose of vardenafil)

l Antifungals: plasma concentration of vardenafil increased by l KETOCONAZOLE—avoid concomitant use; plasma concentration of vardenafil possibly increased by

l ITRACONAZOLE—avoid concomitant use

l Antivirals: plasma concentration of vardenafil possibly increased by FOSAMPRENAVIR; plasma concentration of vardenafil increased by l INDINAVIR and l RITONAVIR—avoid concomitant use; increased risk of ventricular arrhythmias when vardenafil given with l SAQUINAVIR—avoid concomitant use; avoidance of vardenafil advised by manufacturer of

l TELAPREVIR; caution with vardenafil advised by manufacturer of TIPRANAVIR

▶ Calcium-channel Blockers: enhanced hypotensive effect when vardenafil given with NIFEDIPINE

l Cobicistat: plasma concentration of vardenafil possibly increased by l COBICISTAT—manufacturer of cobicistat advises reduce dose of vardenafil (consult cobicistat product literature)

▶ Dapoxetine: avoidance of vardenafil advised by manufacturer of DAPOXETINE

l Grapefruit Juice: plasma concentration of vardenafil possibly increased by l GRAPEFRUIT JUICE—avoid concomitant use

l Nicorandil: possible increased hypotensive effect when vardenafil given with l NICORANDIL—avoid concomitant use

l Nitrates: possible increased hypotensive effect when vardenafil given with l NITRATES—avoid concomitant use

l Riociguat: possible enhanced hypotensive effect when vardenafil given with l RIOCIGUAT—avoid concomitant use

Varicella-zoster Vaccine *see* Vaccines

Vasodilator Antihypertensives

▶ ACE Inhibitors: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ACE INHIBITORS

▶ Adrenergic Neurone Blockers: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ADRENERGIC NEURONE BLOCKERS

▶ Alcohol: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ALCOHOL

▶ Aldesleukin: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ALDESLEUKIN

▶ Alpha-blockers: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ALPHA-BLOCKERS

▶ Anaesthetics, General: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with GENERAL ANAESTHETICS

▶ Analgesics: hypotensive effect of hydralazine, minoxidil and sodium nitroprusside antagonised by NSAIDS

▶ Angiotensin-II Receptor Antagonists: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ANGIOTENSIN-II RECEPTOR ANTAGONISTS

▶ Antidepressants: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with MAOIS; enhanced hypotensive effect when hydralazine or sodium nitroprusside given with TRICYCLIC-RELATED ANTIDEPRESSANTS

▶ Antipsychotics: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with PHENOTHIAZINES

▶ Anxiolytics and Hypnotics: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ANXIOLYTICS AND HYPNOTICS

▶ Beta-blockers: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with BETA-BLOCKERS

Vasodilator Antihypertensives (continued)

▶ Calcium-channel Blockers: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with CALCIUM-CHANNEL BLOCKERS

▶ Clonidine: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with CLONIDINE

▶ Corticosteroids: hypotensive effect of hydralazine, minoxidil and sodium nitroprusside antagonised by CORTICOSTEROIDS

▶ Diazoxide: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with DIAZOXIDE

▶ Diuretics: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with DIURETICS

▶ Dopaminergics: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with CO-BENELDOPA; enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with CO-CARELDOPA; enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with LEVODOPA

▶ Methyldopa: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with METHYLDOPA

▶ Moxisylyte: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with MOXISYLYTE

▶ Moxonidine: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with MOXONIDINE

▶ Muscle Relaxants: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with BACLOFEN; enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with TIZANIDINE

▶ Nicorandil: possible enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with NICORANDIL

▶ Nitrates: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with NITRATES

▶ Oestrogens: hypotensive effect of hydralazine, minoxidil and sodium nitroprusside antagonised by OESTROGENS

▶ Prostaglandins: enhanced hypotensive effect when hydralazine, minoxidil or sodium nitroprusside given with ALPROSTADIL

▶ Vasodilator Antihypertensives: enhanced hypotensive effect when hydralazine given with MINOXIDIL or SODIUM NITROPRUSSIDE; enhanced hypotensive effect when minoxidil given with SODIUM NITROPRUSSIDE

Vecuronium *see* Muscle Relaxants

Vedolizumab

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Vaccines: risk of generalised infections when monoclonal antibodies given with live l VACCINES—avoid concomitant use

Vemurafenib

▶ Antibacterials: manufacturer of vemurafenib advises avoid concomitant use with RIFABUTIN and RIFAMPICIN

l Anticoagulants: vemurafenib possibly enhances anticoagulant effect of l WARFARIN

▶ Antidepressants: manufacturer of vemurafenib advises avoid concomitant use with ST JOHN’S WORT

▶ Antiepileptics: manufacturer of vemurafenib advises avoid concomitant use with CARBAMAZEPINE, FOSPHENYTOIN and PHENYTOIN

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Cytotoxics: avoidance of vemurafenib advised by manufacturer of IPILIMUMAB

l Oestrogens: manufacturer of vemurafenib advises contraceptive effect of l OESTROGENS possibly reduced

l Progestogens: manufacturer of vemurafenib advises contraceptive effect of l PROGESTOGENS possibly reduced

Venlafaxine

l Analgesics: increased risk of bleeding when venlafaxine given with l NSAIDS or l ASPIRIN; possible increased serotonergic effects when SSRI-related antidepressants given with FENTANYL; possible increased serotonergic effects when venlafaxine given with TRAMADOL

l Anticoagulants: venlafaxine possibly enhances anticoagulant effect of l WARFARIN; possible increased risk of bleeding when SSRI-related antidepressants given with l DABIGATRAN

Venlafaxine (continued)

l Antidepressants: possible increased serotonergic effects when venlafaxine given with ST JOHN’S WORT, DULOXETINE or MIRTAZAPINE; enhanced CNS effects and toxicity when venlafaxine given with l MAOIS (venlafaxine should not be started until 2 weeks after stopping MAOIs, avoid MAOIs for 1 week after stopping venlafaxine); after stopping SSRI- related antidepressants do not start l MOCLOBEMIDE for at least 1 week

Interactions | Appendix 1

l Antimalarials: avoidance of antidepressants advised by manufacturer of l ARTEMETHER WITH LUMEFANTRINE and l ARTENIMOL WITH PIPERAQUINE

▶ Antipsychotics: venlafaxine increases plasma concentration of

HALOPERIDOL

▶ Atomoxetine: possible increased risk of convulsions when antidepressants given with ATOMOXETINE

l Dapoxetine: possible increased risk of serotonergic effects when venlafaxine given with l DAPOXETINE (manufacturer of dapoxetine advises venlafaxine should not be started until 1 week after stopping dapoxetine, avoid dapoxetine for 2 weeks after stopping venlafaxine)

l Dopaminergics: caution with venlafaxine advised by manufacturer of ENTACAPONE; increased risk of hypertension and CNS excitation when venlafaxine given with l SELEGILINE (selegiline should not be started until 1 week after stopping venlafaxine, avoid venlafaxine for 2 weeks after stopping selegiline)

▶ 5HT1-receptor Agonists: possible increased serotonergic effects when venlafaxine given with 5HT1 AGONISTS

▶ 5HT3-receptor Antagonists: possible increased serotonergic

effects when SSRI-related antidepressants given with 5HT3 ANTAGONISTS

▶ Lithium: possible increased serotonergic effects when venlafaxine given with LITHIUM

l Methylthioninium: risk of CNS toxicity when SSRI-related antidepressants given with l METHYLTHIONINIUM—avoid concomitant use (if avoidance not possible, use lowest possible dose of methylthioninium and observe patient for up to 4 hours after administration)

Verapamil *see* Calcium-channel Blockers

Vigabatrin

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antiepileptics: vigabatrin reduces plasma concentration of

FOSPHENYTOIN and PHENYTOIN

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Vilanterol *see* Sympathomimetics, Beta2 Vildagliptin *see* Antidiabetics Vinblastine

l Aldesleukin: avoidance of vinblastine advised by manufacturer

of l ALDESLEUKIN

l Antibacterials: toxicity of vinblastine increased by

l ERYTHROMYCIN—avoid concomitant use; possible increased risk of ventricular arrhythmias when vinblastine given with l DELAMANID

l Antifungals: possible increased risk of vinblastine toxicity when given with l ITRACONAZOLE; metabolism of vinblastine possibly inhibited by l POSACONAZOLE (increased risk of neurotoxicity)

l Antimalarials: avoidance of vinblastine advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Antivirals: plasma concentration of vinblastine possibly increased by RITONAVIR

Interactions | Appendix 1

Vincristine

l Antibacterials: possible increased risk of ventricular arrhythmias when vincristine given with l DELAMANID

l Antifungals: increased risk of vincristine toxicity when given with l ITRACONAZOLE; metabolism of vincristine possibly inhibited by l POSACONAZOLE (increased risk of neurotoxicity)

l Antimalarials: avoidance of vincristine advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

▶ Calcium-channel Blockers: metabolism of vincristine possibly inhibited by NIFEDIPINE

▶ Cardiac Glycosides: vincristine possibly reduces absorption of

DIGOXIN *tablets*

Vindesine

l Antibacterials: possible increased risk of ventricular arrhythmias when vindesine given with l DELAMANID

l Antifungals: possible increased risk of vindesine toxicity when given with l ITRACONAZOLE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Vinflunine

l Antibacterials: plasma concentration of vinflunine possibly reduced by l RIFAMPICIN—manufacturer of vinflunine advises avoid concomitant use; increased risk of ventricular arrhythmias when vinflunine given with l DELAMANID

l Antidepressants: plasma concentration of vinflunine possibly reduced by l ST JOHN’S WORT—manufacturer of vinflunine advises avoid concomitant use

l Antifungals: plasma concentration of vinflunine increased by l KETOCONAZOLE—manufacturer of vinflunine advises avoid concomitant use; possible increased risk of vinflunine toxicity when given with l ITRACONAZOLE

l Antimalarials: avoidance of vinflunine advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

l Antivirals: plasma concentration of vinflunine possibly increased by l RITONAVIR—manufacturer of vinflunine advises avoid concomitant use

▶ Grapefruit Juice: plasma concentration of vinflunine possibly increased by GRAPEFRUIT JUICE—manufacturer of vinflunine advises avoid concomitant use

Vinorelbine

l Antibacterials: possible increased risk of neutropenia when vinorelbine given with l CLARITHROMYCIN; possible increased risk of ventricular arrhythmias when vinorelbine given with l DELAMANID

l Antifungals: possible increased risk of vinorelbine toxicity when given with l ITRACONAZOLE

l Antimalarials: avoidance of vinorelbine advised by manufacturer of l ARTENIMOL WITH PIPERAQUINE

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Vismodegib

l Antibacterials: manufacturer of vismodegib advises avoid concomitant use with l RIFAMPICIN (plasma concentration of vismodegib possibly reduced)

l Antidepressants: manufacturer of vismodegib advises avoid concomitant use with l ST JOHN’S WORT (plasma concentration of vismodegib possibly reduced)

l Antiepileptics: manufacturer of vismodegib advises avoid concomitant use with l CARBAMAZEPINE, l FOSPHENYTOIN and l PHENYTOIN (plasma concentration of vismodegib possibly reduced)

l Antipsychotics: avoid concomitant use of cytotoxics with

l CLOZAPINE (increased risk of agranulocytosis)

Vitamin A *see* Vitamins Vitamin D *see* Vitamins Vitamin E *see* Vitamins

Vitamin K (Phytomenadione) *see* Vitamins

Vitamins

▶ Antibacterials: absorption of vitamin A possibly reduced by

NEOMYCIN

Vitamins (continued)

l Anticoagulants: vitamin E possibly enhances anticoagulant effect of l COUMARINS; vitamin K antagonises anticoagulant effect of l COUMARINS and l PHENINDIONE

▶ Antiepileptics: alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol or vitamin D requirements possibly increased when given with CARBAMAZEPINE; alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol or vitamin D requirements possibly increased when given with FOSPHENYTOIN; alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol or vitamin D requirements possibly increased when given with PHENOBARBITAL; alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol or vitamin D requirements possibly increased when given with PHENYTOIN; alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol or vitamin D requirements possibly increased when given with PRIMIDONE

▶ Antifungals: plasma concentration of paricalcitol possibly increased by KETOCONAZOLE; effects of alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol and vitamin D possibly reduced by MICONAZOLE

▶ Antivirals: increased risk of bleeding when high doses of vitamin E given with TIPRANAVIR

▶ Ciclosporin: vitamin E possibly affects plasma concentration of

CICLOSPORIN

▶ Cytotoxics: effects of alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol and vitamin D possibly reduced by DACTINOMYCIN; avoidance of vitamin E advised by manufacturer of IBRUTINIB

▶ Diuretics: increased risk of hypercalcaemia when alfacalcidol, calcitriol, colecalciferol, dihydrotachysterol, ergocalciferol, paricalcitol or vitamin D given with THIAZIDES AND RELATED DIURETICS

▶ Dopaminergics: pyridoxine reduces effects of LEVODOPA when given without dopa-decarboxylase inhibitor

▶ Lipid-regulating Drugs: absorption of calcitriol possibly reduced by COLESTYRAMINE (give at least 1 hour before or 4 to 6 hours after colestyramine)

l Retinoids: risk of hypervitaminosis A when vitamin A given with l RETINOIDS—avoid concomitant use

▶ Selenium: ascorbic acid possibly reduces absorption of

SELENIUM (give at least 4 hours apart)

▶ Sevelamer: absorption of calcitriol reduced by SEVELAMER

(give at least 1 hour before or 3 hours after sevelamer)

Voriconazole *see* Antifungals, Triazole

Warfarin *see* Coumarins

Wasp Venom Extracts

l ACE Inhibitors: possible severe anaphylactoid reaction when wasp venom extracts given with l ACE INHIBITORS

Xipamide *see* Diuretics

Xylometazoline *see* Sympathomimetics

Yellow Fever Vaccine *see* Vaccines

Zafirlukast *see* Leukotriene Receptor Antagonists Zaleplon *see* Anxiolytics and Hypnotics Zidovudine

NOTE Increased risk of toxicity with nephrotoxic and myelosuppressive drugs—for further details consult product literature

▶ Analgesics: increased risk of haematological toxicity when zidovudine given with NSAIDS; plasma concentration of zidovudine possibly increased by METHADONE

▶ Antibacterials: absorption of zidovudine reduced by CLARITHROMYCIN tablets (give at least 2 hours apart); manufacturer of zidovudine advises avoid concomitant use with RIFAMPICIN

▶ Antiepileptics: zidovudine increases or decreases plasma concentration of FOSPHENYTOIN and PHENYTOIN; plasma concentration of zidovudine possibly increased by SODIUM VALPROATE and VALPROIC ACID (increased risk of toxicity)

l Antifungals: plasma concentration of zidovudine increased by

l FLUCONAZOLE (increased risk of toxicity)

▶ Antimalarials: increased antifolate effect when zidovudine given with PYRIMETHAMINE

Zidovudine (continued)

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l Antivirals: profound myelosuppression when zidovudine given with l GANCICLOVIR or l VALGANCICLOVIR (if possible avoid concomitant administration, particularly during initial ganciclovir or valganciclovir therapy); increased risk of granulocytopenia when zidovudine given with l NEVIRAPINE; increased risk of anaemia when zidovudine given with

l RIBAVIRIN—avoid concomitant use; zidovudine possibly inhibits effects of l STAVUDINE (manufacturers advise avoid concomitant use); plasma concentration of zidovudine reduced by l TIPRANAVIR

▶ Atovaquone: plasma concentration of zidovudine increased by

ATOVAQUONE (increased risk of toxicity)

l Orlistat: absorption of zidovudine possibly reduced by

l ORLISTAT

Zinc

▶ Antibacterials: zinc reduces absorption of CIPROFLOXACIN, LEVOFLOXACIN, MOXIFLOXACIN and OFLOXACIN; zinc reduces

absorption of NORFLOXACIN (give at least 2 hours apart); zinc reduces absorption of TETRACYCLINES, also absorption of zinc reduced by tetracyclines

▶ Calcium Salts: absorption of zinc reduced by CALCIUM SALTS

▶ Eltrombopag: zinc possibly reduces absorption of

ELTROMBOPAG (give at least 4 hours apart)

▶ Iron Salts: absorption of zinc reduced by *oral* IRON SALTS, also absorption of *oral* iron salts reduced by zinc

▶ Penicillamine: absorption of zinc reduced by PENICILLAMINE, also absorption of penicillamine reduced by zinc

▶ Trientine: absorption of zinc reduced by TRIENTINE, also absorption of trientine reduced by zinc

Zoledronic Acid *see* Bisphosphonates

Zolmitriptan *see* 5HT1-receptor Agonists (under HT)

Zolpidem *see* Anxiolytics and Hypnotics

Zonisamide

l Antidepressants: anticonvulsant effect of antiepileptics possibly antagonised by MAOIS and l TRICYCLIC-RELATED ANTIDEPRESSANTS (convulsive threshold lowered); anticonvulsant effect of antiepileptics antagonised by l SSRIS and l TRICYCLICS (convulsive threshold lowered)

▶ Antiepileptics: plasma concentration of zonisamide reduced by CARBAMAZEPINE, FOSPHENYTOIN, PHENOBARBITAL, PHENYTOIN and PRIMIDONE

l Antimalarials: anticonvulsant effect of antiepileptics antagonised by l MEFLOQUINE

l Antipsychotics: anticonvulsant effect of antiepileptics antagonised by l ANTIPSYCHOTICS (convulsive threshold lowered)

▶ Diuretics: manufacturer of zonisamide advises avoid concomitant use with CARBONIC ANHYDRASE INHIBITORS in children

l Orlistat: possible increased risk of convulsions when antiepileptics given with l ORLISTAT

Zopiclone *see* Anxiolytics and Hypnotics

Zuclopenthixol *see* Antipsychotics