Section II - Chapter 2
Drugs used in Cardiovascular Disorders

2.1 Anti-anginal agents

2.1.1 Nitrates

Glyceryl trinatre
Isosorbide dinitrate
Isosobide mononitrate

2.1.2 Beta-blocker

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Bisoprolol
Carvedilol
Metoprolol
Propranolol

2.1.3 Calcium channel blockers

Diltiazem
Verapamil

2.2 Antiarrhythmic agents

Adenosine
Amiodarone
Atenolol
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Disopyramide
Isoprenaline
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Procainamide
Propranolol
Verapamil

2.3 Antihypertensive agents

2.3.1 Angiotensin converting enzyme inhibitor (ACEI)

Captopril
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Ramipril

2.3.2 Angiotensin receptor blockers

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Telmisartan
Valsartan

2.3.3 Beta blockers

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Bisoprolol
Metoprolol
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Nebivolol

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2.3.4 Calcium channel blockers

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Felodipine
Nifedipine

2.3.5 Centrally acting antihypertensive

Clonidine

2.3.6 Diuretics

Chlorthalidone
Furosemide:
Hydrochlorothiazide
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2.3.7 Others

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Methyldopa
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Terazosin

2.4 Drugs used in cardiovascular shock

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Dobutamine
Epinephrine/Adrenaline
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Phenylephrine
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2.5 Drug used in heart failure

Bisoprolol
Carvedilol
Dobutamine
Digoxin
Dopamine
Epinephrine /adrenaline
Furosemide
Losartan
Metoprolol
Milrinone
Norepinephrine/noradrenaline
Ramipril
Spironolactone
Valsartan

2.6 Drugs used in pulmonary hypertension

Bosentan
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Cholestyramine
Clofibrates
Ezetimide
Fenofibrate
Gemfibrozil
Nicotinic acid
Simvastatin
Rosuvastatin

2.1 Anti-angina agents

2.1.1 Nitrates

GLYCERYL TRINATRE (Nitroglycerine)

Dosage form and strength: *Solution (infusion):* 25 mg/250 ml, 50 mg/250 ml, 100 mg/250 ml; *Solution (injection):* 5 mg/ ml

Indications: Prophylaxis and acute attack of angina pectoris, Hypertensive emergencies, acute decompensated heart failure

Contraindications/Precautions: Avoid in hypersensitivity to nitrates, hypotension, hypovolemia, hypertrophic obstructive cardiomyopathy, aortic stenosis, cardiac tamponade, constrictive pericarditis, mitral stenosis, marked anemia, head trauma, cerebral hemorrhage, angle-closure glaucoma. Use caution in severe hepatic impairment, hypothyroidism, malnutrition, hypothermia, recent history of myocardial infarction. Renal impairment: 10-50 ml/min: never administer. Uninterrupted infusion > 24 hours produces tolerance.

Dosage schedule:

- *Angina (acute attack):* Intravenous infusion, adult: initially 5–10 mcg/min. The rate of the infusion may be increased by 10 mcg/min every 3–5 min until symptoms are relieved, systolic arterial pressure falls to <100 mm Hg, or the dose reaches 200 mcg/min
- *Hypertensive emergencies:* Intravenous infusion, adult: 5-10 mcg/min initial dose and up to 200 mcg/min as long as hemodynamic stability is maintained) for the first 24–48 h after the onset of infarction.
- *Acute decompensated heart failure:* Intravenous infusion, adult: 10–20 mcg/min, increase up to 200 mcg/min. *Intravenous infusion, Children:* Initially 0.25- 0.5 mcg/kg/min to titrate to 0.5-1.0 mcg/kg/min. Maximum dose 20 mcg/kg/min
- Start with the lowest dose. Subsequent doses and intervals of administration should be adjusted according to the blood pressure response and duration of action.

Adverse effects: Throbbing headache (most frequent in early therapy), flushing, dizziness, postural hypotension, Tachycardia, syncope, paradoxical bradycardia

Drug and food interaction: Increases the effect of beta-blockers, ACE inhibitors, angiotensin receptor blockers, calcium channel blockers. Avoid in concomitant/recent use of erectile dysfunction products (sildenafil, tadalafil, vardenafil) - may cause severe hypotension and death. Avoid alcohol intake.

ISOSORBIDE DINITRATE

Dosage form and strength: *Tablet (sublingual):* 5 mg, 10 mg

Indications: Prophylaxis and treatment of angina, left ventricular failure.

Contraindications/Precautions: See under glyceryl trinitrate

Patients taking isosorbide dinitrate for the long-term management of angina may often develop tolerance to the antianginal effect; avoid by giving the second of 2 daily doses of longer-acting oral preparations after an 8-hour rather than a 12-hour interval, thus ensuring a nitrate-free interval each day.

Dosage schedule:

- *Angina (acute attack):* Sublingual, adult: 5–10 mg repeated as required.
- *Angina (prophylaxis):* Oral, adult: 30-120 mg daily in divided doses. Intravenous infusion: 2-10 mg daily, maximum dose 20 mg/hour.
- *Left ventricular failure:* Oral, adult 40-160 mg daily in divided doses, maximum dose 240 mg daily in divided doses. Intravenous infusion: 2-10 mg daily, maximum dose 20 mg/hour.

Adverse effects: See under glyceryl trinitrate, tolerance (in long term, uninterrupted use)

ISOSOBIDE MONONITRATES

Dosage form and strength: *Tablet:* 10 mg, 20 mg, 40 mg; *Sustained release tablets:* 30 mg.

Indications: Prophylaxis of angina pectoris, adjunct in congestive heart failure.

Contraindications/Precautions: See under glyceryl trinitrate

Dosage schedule: *Prophylaxis for angina:* Oral(immediate release), adult: initially 20 mg 2-3 times daily or 40 mg twice daily or 10 mg twice daily (in those who have not previously received nitrates) maximum dose 120 mg in 2-3 divided doses daily.

Adverse effects: See under glyceryl trinitrate

2.1.2 Beta blocker

ATENOLOL

Dosage form and strength: *Tablet:* 25 mg, 50 mg, 100 mg; *Solution:* 500 mcg/ml in 10ml vial.

Indications: Chronic stable angina, secondary prevention after myocardial infarction, supra ventricular arrhythmia, mild CHF, hypertension, migraine prophylaxis.

Contraindications/Precautions: Avoid in history of asthma or bronchospasm (if no alternative, then use with extreme caution and under specialist supervision), uncontrolled heart failure, prinzemetal angina, bradycardia (heart rate <50 bpm), hypotension, sick sinus syndrome, second and third degree atrioventricular block, cardiogenic shock, metabolic acidosis, severe peripheral arterial disease, pheochromocytoma (unless used with an alpha blocker). Use caution in patients with first –degree atrioventricular block, portal hypertension, renal impairment (reduce dose), diabetes mellitus (small decrease in glucose tolerance, which can mask symptoms of hypoglycemia), history of hypersensitivity and myasthenia gravis, obstructive airway disease, portal hypertension, psoriasis. Pregnancy- avoid (IUGR, neonatal hypoglycemia and bradycardia). Breast feeding: avoid. Monitor lung function in inadequate cardiac function and bronchospasm disease. Symptoms of hypoglycemia and thyrotoxicosis may get masked. Assess weight daily, watch for CHF (rales/crackles, jugular vein distension, weight gain, and edema). Abrupt withdrawal of drug may exacerbate angina symptoms or precipitate myocardial infarction in patients with coronary artery disease.

Dosage schedule:

- *Hypertension:* Oral, adult: 25 – 50 mg daily. Oral, child: 0.5-1.0 mg/kg/dose in 1-2 divided doses daily. Maximum dose- 2mg/kg/day or 100 mg/day
- *Angina:* Oral, adult: 100 mg, maximum dose 200 mg daily 1 or 2 doses.
- *Arrhythmias:* Oral, adult: 50-100 mg daily. Intravenous, adult: 2.5 mg at rate of 1 mg/min repeated at 5 min interval to a maximum of 10 mg/dose. Intravenous infusion, adult: 150 mcg/kg every 12 hourly over 20 minutes, repeated every 12 hours if required.
- *Early intervention Myocardial infarction (within 12 hour):* slow intravenous infusion, adult: 5 mg by then oral 50 mg after 15 minutes then oral 50 mg after 12 hours then 100 mg daily.
- *Migraine prophylaxis:* Oral, adult: 50–200 mg daily in divided doses

Adverse effects: Bradycardia, gastrointestinal disturbances including nausea, vomiting, diarrhea, constipation, abdominal cramp, fatigue, cold hands and feet, hypertriglyceridemia.

Drug and food interaction: Avoid with verapamil. Hypotensive effect increases with diuretics, ACE inhibitors, Angiotensin II receptor antagonist, calcium channel blocker. Atenolol may enhance bradycardia produced by cardiac glycosides.

BISOPROLOL

Dosage form and strength: *Tablet:* 2.5 mg, 5 mg, 10 mg

Indications: Hypertension, angina, adjunct in heart failure

Contraindications/Precautions: See under atenolol

Dosage schedule:

- *Hypertension and angina:* Oral, adult: 5-10 mg once daily, 20 mg daily (maximum).
- *Adjunct in heart failure:* Oral, adult: initially 1.25 mg once daily (in the morning) for 1 week then, if well tolerated, increased to 2.5 mg once daily for 1 week, then 3.75 mg once daily for 1 week, then 5 mg once daily for 4 weeks, then 7.5 mg once daily for 4 weeks, then 10 mg once daily, maximum 10 mg daily.

Adverse effects: See under atenolol

Drug and food interaction: See under atenolol

CARVEDILOL

Dosage form and strength: *Tablet:* 3.125 mg, 6.25 mg, 12.5 mg, 25 mg

Indications: Angina, hypertension, adjunct to diuretics/digoxin/ACE inhibitors in heart failure

Contraindications/Precautions: See under atenolol. Avoid in acute decompensated heart failure requiring intravenous inotropes. Check for edema in feet, legs daily. Rise slowly from sitting or lying position to minimize orthostatic hypotension

Dosage schedule:

- *Hypertension:* Oral, adult: Initially 12.5 mg once daily for 2 days, then increased to 25 mg once daily; increased if necessary up to 50 mg daily, dose to be increased at intervals of at least 2 weeks and can be given as a single dose or in divided doses daily.

- *Angina:* Oral, adult: initially 12.5 mg once daily, increased after 2 days to 25 mg twice daily.
- *Adjunct in heart failure:* Oral, adult: initially 3.125 mg twice daily to 6.25 mg twice daily, then to 12.5 mg twice daily then to 25 mg twice daily. Dose increased at intervals of at least 2 weeks

Adverse effects: Allergic skin reactions, angina, AV block, changes in liver enzymes, depressed mood, disturbances of micturition, influenza-like symptoms, leucopenia, nasal stuffiness, postural hypotension, thrombocytopenia, wheezing, headache, dizziness, bradycardia and impotence

Drug and food interaction: Conduction disturbances increases with calcium channel blocker. Carvedilol increases the effect of antidiabetic drugs.

METOPROLOL

Dosage form and strength: *Tablets:* 50 mg, 100 mg; *Injection:* 1 mg/ml

Indications: Angina, hypertension, arrhythmias, migraine prophylaxis, hyperthyroidism adjunct, early intervention in myocardial infarction.

Contraindications/Precautions: See under atenolol. Abrupt withdrawal may cause MI, ventricular arrhythmias, myocardial ischemia; taper dose over 7-14 days.

Dosage schedule:

- *Angina:* Oral, adult: 50- 100 mg, 2-3 times daily.
- *Hypertension:* Oral, adult: initially 100 mg daily, maximum dose 400 mg daily in 1-2 doses.
- *Arrhythmias:* Oral, adult: 50-100 mg, 2-3 times daily, maximum dose 300 mg daily in divided doses. Intravenous, adult: up to 5 mg at rate 1-2 mg/minute repeated after 5 minutes if necessary, total dose 10-15 mg.
- *Migraine prophylaxis:* Oral, adult: 100 -200 mg daily in divided doses.
- *Early intervention in myocardial infarction (within 12 hours):* Intravenous, adult: 5 mg every 2 minutes to a maximum dose of 15 mg, followed after 15 minutes by oral 50 mg every 6 hours for 48 hours; maintenance oral 200 mg daily in divided doses.
- *Hyperthyroidism (adjunct):* Oral, adult: 50 mg 4 times a day
- *In surgery:* intravenous 2-4 mg by slow injection to control arrhythmias developing during anesthesia; 2 mg doses may be repeated, maximum dose 10 mg.
- *Oral, child:* 1-2 mg/kg/day in 2 divided doses daily. Maximum dose 6 mg/kg/day up to 200 mg/day

Assess ECG directly when giving IV during initial treatment.

Adverse effects: See under atenolol

Drug and food interaction: See under atenolol

PROPRANOLOL

Dosage form and strength: *Tablet:* 10 mg, 20 mg, 40 mg, 80 mg. *Injection:* 1 mg/ml

Indications: Chronic stable angina, hypertension, secondary prevention after acute myocardial infraction, anxiety, thyrotoxicosis, migraine prophylaxis, pheochromocytoma (only with alpha blocker), prophylaxis of variceal

bleeding in portal hypertension, hypertrophic obstructive cardiomyopathy, mitral valve prolapse, essential tremor, child with cyanotic spells or hypertension or infantile hemangioma

Contraindications/Precautions: See under atenolol. Use caution in inadequate cardiac function and bronchospastic disease. Reduce oral dose in renal and hepatic impairment. Pregnancy (C) breast feeding: safety not established. Do not discontinue abruptly; as dysrhythmia, angina, myocardial ischemia may occur so taper over at least a few weeks. Symptoms of hypoglycemia may get masked- monitor blood glucose.

Dosage schedule:

- *Hypertension:* Oral, adult: initially 80 mg twice daily, increased at weekly intervals as required; maintenance dose 160-320 mg daily. Oral, c*hild:* 1-4 mg/kg/day in 3-4 divided doses.
- *Prophylaxis of variceal bleeding in portal hypertension:* Oral, adult: initially 40 mg twice daily increased to 80 mg twice daily according to heart rate; maximum dose 160 mg twice daily.
- *Pheochromocytoma (only with an alpha blocker):* Oral, adult: 60 mg daily for 3 days before surgery. 30 mg daily for patients not fit for surgery
- *Angina:* Oral, adult: initially 40 mg 2-3 time daily; maintenance 120-240 mg daily.
- *Arrhythmias, hypertrophic obstructive cardiomyopathy, anxiety, tachycardia and thyrotoxicosis (adjunct):* Oral, adult: 10-40 mg in 3-4 divided doses daily
- Anxiety (with symptoms such as palpitation, sweating, tremor): Oral, adult: 40 mg once daily; may increase to 40 mg 3 times daily, if necessary.
- *Prophylaxis after infraction:* Oral, adult: 40 mg 4 times daily for 2-3 days, then 80 mg twice daily, beginning 5-21 days after infraction.
- *Essential tremor:* Oral, adult: initially 40 mg 2-3 times daily; maintenance 80-160 mg daily.
- *Migraine prophylaxis:* Oral, adult: 80-240 daily divided doses.
- *Arrhythmias and thyrotoxic crisis:* Intravenous injection; 1 mg over 1 minute.
- *Cyanotic spells: Child, intravenous:* 0.15-0.25 mg/kg/day in 4 divided dose, not to exceed 1 mg for infants and 3 mg for children. Oral, child: 2-4 mg/kg/day in 4 divided doses
- *Infantile hemangioma:* Oral, c*hild:* 1-2 mg/kg/day in 3 divided doses

Adverse effects: See under atenolol. Hallucination, nightmare, sexual dysfunction.

Drug and food interaction: See under atenolol. Hypersensitivity to catecholamine during withdrawal

2.1.3 Calcium channel blockers

DILTIAZEM

Dosage form and strength: *Tablet:* 30 mg, 60 mg

Indications: Angina pectoris

Contraindications/Precautions: Avoid in acute porphyria, left ventricular failure with pulmonary congestion, second- or third-degree AV block (unless pacemaker fitted), severe bradycardia, sick sinus syndrome. Use caution

bradycardia (avoid if severe), first degree AV block, heart failure, prolonged PR interval, significantly impaired left ventricular function. Pregnancy: avoid. Hepatic impairment reduce dose. Renal impairment, start with smaller dose.

Dosage schedule:

- *Angina:* Oral, adult: Initially 60 mg 3 times a day, adjusted according to response; maximum 360 mg/day. Elderly: Initially 60 mg twice daily, adjusted according to response; maximum 360 mg per day
- *Oral, child:* 1.5-2 mg/kg/day in 3-4 divided doses (maximum dose: < 6mg/kg/day up to 360 mg/day

Adverse effects: Asthenia, AV block, bradycardia, dizziness, gastro-intestinal disturbances, headache, hot flushes, hypotension, malaise, edema (notably of ankles), palpitation, Sino-atrial block

VERAPAMIL

Dosage form and strength: *Verapamil Hydrochloride: Tablet (immediate release):* 40 mg, 80 mg, 240 mg. *Solution:* 2.5 mg/ml

Verapamil injection should be protected from light.

Indications: Angina pectoris, supra ventricular arrhythmias, hypertension, migraine prophylaxis, supraventricular tachycardia in children

Contraindications/Precautions: Hypotension, bradycardia, second- and third-degree heart block, sick sinus syndrome; cardiogenic shock, history of heart failure , atrial flutter or fibrillation complicating Wolff-Parkinson-White syndrome, acute porphyria. First-degree atrioventricular block, acute phase of myocardial infarction (avoid if bradycardia, hypotension, or left ventricular failure present), hepatic impairment; children (specialist advice only); Pregnancy and breastfeeding: Avoid use in neonate and young infants. Not to discontinue abruptly, chest pain may occur.

Dosage schedule:

- *Angina, supraventricular arrhythmia:* Oral, adult: 40-120 mg 3 times daily
- *Hypertension:* Oral, adult: 240-480 mg daily in 2- 3 divided doses. By slow intravenous injection over 2 minutes (3 minutes in elderly), 5 - 10 mg (preferably with ECG monitoring)
- *Paroxysmal tachyarrhythmia:* slow intravenous injection, adult: initially 5-10 mg further 5 mg after 5-10 minutes if required over 2 minutes (over 3 minutes in elderly) under ECG monitoring.
- *Supraventricular tachycardia: Child, intravenous:* 0.1-0.3 mg/kg/dose may be repeated in 30 min. Maximum first dose 5 mg, and second dose 10 mg
- *Supraventricular arrhythmias:* slow intravenous injection, adult: 5-10 mg, over 2 minutes (over 3 minutes in elderly) under ECG monitoring

Adverse effects: Constipation; less commonly nausea, vomiting, flushing, headache, dizziness, fatigue, and ankle edema; rarely allergic reactions including pruritus, urticaria, angioedema, and erythema multiforme (Stevens-Johnson syndrome); myalgia, arthralgia, paresthesia, erythromelalgia; increased prolactin concentration; gynecomastia and gingival hyperplasia on long-term treatment; hypotension, heart failure, bradycardia, heart block, and asystole (due to negative inotropic effect) with high doses.

2.2 Antiarrhythmic agents

ADENOSINE

Dosage form and strength: *Injection:* 6 mg/2 ml vial

Indications: Paroxysmal supraventricular tachycardia (including Wolff-Parkinson-White syndrome)

Contraindications/Precautions: Pre-existing second or third degree AV block, asthma and sick sinus syndrome. Use cautiously in arterial fibrillation or flutter and heart transplant.

Dosage schedule:

- *Rapid intravenous injection into central or large peripheral vein:* 3 mg over 2 seconds with cardiac monitoring; if necessary followed by 6 mg after 1-2 minutes and then by 12 mg after a further 1-2 minutes.
- *Neonate, intravenous:* 0.05 mg/kg over 1-2 sec may increase dose by 0.05 mg/kg every 2 mins. Maximum dose 0.25 mg/kg
- *Child, intravenous:* 0.1-0.2 mg/kg (initial maximum dose 6 mg) over 1-2 sec. May increase dose by 0.05mg/kg every 2 mins to maximum of 0.25 mg/kg

Follow each dose with normal saline flush. Assess the cardiopulmonary and respiratory status.

Adverse drug reactions: Chest pain, transient facial flush, bronchospasm, nausea and severe bradycardia, difficult or labored breathing, chest tightness

Drug and food interactions: Increased risk for higher degree of heart block: carbamazepine. Increased risk of ventricular fibrillation with digoxin, verapamil. Increased effects with dipyridamole. Methylxanthines decrease the activity of adenosine

Patient's information: Patient should report facial flushing, dizziness, sweating, palpitations, and chest pain (usually transient).

AMIODARONE

Dosage form and strength: *Tablet:* 100 mg, 200 mg; *Solution:* 25 mg/ml, 30 mg/ml, 50 mg/ml

Indications: Paroxysmal supraventricular, nodal and ventricular tachycardia, atrial fibrillation or flutter, ventricular arrhythmia (unresponsive to others) and ventricular fibrillation, all atrial and ventricular tachycardia

Contraindications/Precautions: Avoid in sinus bradycardia, SA heart block, Iodine sensitivity, cardiogenic shock, second or third degree AV block, thyroid dysfunctions, severe hepatic, pneumonitis, pulmonary fibrosis, hypokalemia, CHF (with inadequate compensation). Pregnancy: risk of neonatal goiter. Breast feeding: avoid. Clinical monitoring (baseline and every 3 to 6 months) of serum potassium; chest X-ray, pulmonary function tests (with diffusion capacity), liver function test and thyroid function tests is recommended. Toxicity is reversible when managed early.

Dosage schedule:

- Arrhythmias: Oral, adult: 200 mg 3 times daily for 1 week reduced to 200 mg twice daily
- *Ventricular fibrillation: intravenous infusion, adult:* 300 mg over at least 3 minutes.
- *Drug resistant refractory cardiac arrhythmia: Oral, child:* < 1 year: 600-

800 mg/1.73m^2/day in 1-2 divided dose for 1-14 days. > 1 years: 10-15 mg/kg/day in 1-2 divided doses for -14 days and/or until adequate control is achieved, then reduce to 5 mg/kg/day. *Child, intravenous:* 5 mg/kg over 30 min followed by continuous infusion at the rate of 5 mcg/kg/min. Maximum dose: 15 mcg/kg/min or 20 mg/kg/day

- Infusion should be diluted in glucose 5%, concentration should not exceed 2 mg/ml.

Marked hypotension on IV administration.

Adverse effects: Nausea, vomiting, raised serum transaminases, bradycardia, ventricular arrhythmia, ventricular fibrillation. Neurologic dysfunction (dizziness, paresthesia, tremor and involuntary movements, lack of co-ordination, abnormal gait and ataxia), thyroid dysfunction, pulmonary toxicity (pneumonitis and fibrosis) on long term use.

Drug and food interactions: Inhibits CYP450 enzymes and may increase concentrations of Digoxin, Methotrexate, Theophylline, Procainamide. Increase risk of myopathy with simvastatin. Increased risk of bradycardia with beta-blockers, calcium channel blockers. Increased risk of QT prolongation with azoles, fluoroquinolones, macrolides

Patient's information: Do not discontinue abruptly. Use sunscreen or stay out of sun to prevent burns, use dark glasses to prevent photophobia. Skin discoloration is usually reversible

ATENOLOL: See under section 2.1 Antianginal agents

DIGOXIN

Dosage and strength: *Injection:* 250 mcg/ml in 2-ml ampoule; *Oral liquid:* 50 mcg/ml; *Tablet:* 62.5 mcg, 250 mcg

Indications: Supraventricular arrhythmias, particularly atrial fibrillation; heart failure

(considered for selected patients who remain symptomatic despite treatment with an ACE inhibitor, a diuretic, and a suitable beta-blocker)

Contraindications/Precautions: Avoid in hypertrophic obstructive cardiomyopathy (unless also atrial fibrillation and heart failure); Wolff-Parkinson-White syndrome or other accessory pathway, particularly if accompanied by atrial fibrillation; ventricular tachycardia or fibrillation; intermittent complete heart block; second-degree atrioventricular block. Use caution in recent myocardial infarction; sick sinus syndrome; severe Pulmonary disease; thyroid disease; the elderly (reduce dose); renal impairment; avoid hypokalemia; avoid rapid intravenous administration (nausea and increased risk of arrhythmias); Pregnancy (C) Breastfeeding: use with caution. Obtain ECG after 6 hours to assess toxicity. Monitor apical pulse for 1 full minute before administration .Withhold dose if pulse rate is <60 bpm in an adult, <70 bpm is a child or <90 bpm in an infant. Monitor blood pressure periodically, monitor ECG throughout IV administration and 6 hrs. after each dose. Therapeutic drug monitoring is advised in patient receiving digoxin. Take missed doses within 12 hrs. of scheduled dose. Do not double the dose.

Digoxin has been associated with an increased risk of falls in the elderly, so

patient and family should be advised for monitoring.

Dosage schedule:

- *Atrial fibrillation:* Oral, adult: initially 1–1.5 mg in divided doses over 24 hours for rapid digitalization (or 250 mcg once or twice daily if digitalization less urgent) followed by: 62.5–500 mcg daily (higher dose may be divided), according to renal function and heart rate response; usual maintenance dose: 125–250 mcg daily (lower dose more appropriate in the elderly).
- *Emergency control of atrial fibrillation:* intravenous infusion over at least 2 hours, adult: 0.75–1 mg.

NOTE. Infusion dose may need to be reduced if digoxin or other cardiac glycoside has been given in previous 2 weeks.

Child: doses unit is mcg/kg/day

	Total daily dose (mcg)		Daily maintenance (mcg)	
	PO	IV/IM	PO	IV/IM
Premature neonate	20	15	5	3-4
Full Term Neonate	30	20	8-10	6-8
1 month-2 years	40-50	30-40	10-12	7.5-9
2-10 years	30-40	20-30	8-10	6-8
> 10 years	10-15	8-12	2.5-5	2-3

Initially, half of the total daily dose, then other half total daily dose every 8 hours in 2 divided doses

Adverse effects: Usually only with high doses; gastrointestinal disturbances including anorexia, nausea, vomiting, diarrhea, and abdominal pain; visual disturbances, headache, fatigue, drowsiness, confusion, dizziness, delirium, hallucinations, depression; all arrhythmias except for rapidly conducted atrial arrhythmias (atrial fibrillation and atrial flutter) and except Mobitz type II second degree heart block; rarely rash, and intestinal ischemia; gynecomastia on long-term use; thrombocytopenia reported.

Drug and food interactions: When digoxin is administered with beta blockers and verapamil, there is increased risk of AV block and bradycardia.

DISOPYRAMIDE

Dosage form and strength: *Capsules:* 100 mg, 150 mg; *Injection:* 10 mg in 5 ml ampoule.

Indication: Atrial and ventricular arrhythmias including those resistant to lignocaine.

Contraindications/Precautions: Avoid in preexisting second or third degree AV block, cardiogenic shock, heart failure (can produce severe hypotension due to negative inotropic properties). Renal or hepatic insufficiency, third trimester of pregnancy, glaucoma, myasthenia gravis or urinary retention. Use caution in the elderly and children because they may be more sensitive to its effects.

Dosage schedule: Oral (immediate release), adult: 300-800 mg daily in divided doses. Slow intravenous injection, adult: 2 mg/kg over at least 5 minutes to a maximum of 150 mg with ECG monitoring.

Take disopyramide on a regular schedule around the clock, unless otherwise

directed by your doctor. If you miss a dose of disopyramide, take it if you remember within 4 hours. If it has been more than 4 hours since your missed dose, skip the missed dose and go back to your regular doses schedule. Do not take 2 doses at once.
Adverse effects: Angle-closure glaucoma, antimuscarinic effects, AV block, blurred vision, cholestatic jaundice, dry mouth, gastro-intestinal irritation, hypoglycemia, hypotension, myocardial depression, psychosis, urinary retention, ventricular tachycardia, ventricular fibrillation or torsade de pointes (usually associated with prolongation of QRS complex or QT interval).
Drug and food interactions: The effects of disopyramide can increase with metoprolol and alcohol (minor).
Patient's information: Do not drive, operate machinery. Do not stop the drug suddenly.

ISOPRENALINE

Dosage form and strength: *Injection:* 0.2 mg/ml. *Tablet:* 20 mg
Indications: Torsade de pointes, bradycardia in patients with heart block, control attacks of Stokes Adam syndrome.
Contraindications/Precautions: Preexisting cardiac arrhythmia (especially tachycardia).
Dosage schedule:
- *Intravenous injection, adult:* 0.5-10 mcg/minute
- *Oral, adult:* initially 30 mg every 6hours, range, 90-840 mg daily (but oral route is rarely used).

Adverse effect: Tachycardia, hypotension, arrhythmia, tremor, sweating

LIDOCAINE/ LIGNOCAINE

Dose form and strength: *Injection:* 20 mg/ml in 5 ml ampoule
Indication: Ventricular arrhythmias (especially after myocardial infarction), local anesthesia
Contraindications/Precautions: Avoid in Sino atrial nodal disorder, any grade of atrioventricular block or any other type of conduction disturbances, severe myocardial depression, acute porphyria or hypovolemia, Wolff-Parkinson-White syndrome, Stokes Adams syndrome. Lower dosage in congestive heart failure and following cardiac surgery, bradycardia, hepatic impairment, severe respiratory depression, the elderly, pregnancy and breastfeeding, hypothermia, electrolyte imbalance (potassium and magnesium imbalance). Monitor for ECG
Dosage schedule:
- *Ventricular arrhythmias:* intravenous injection, adult: loading dose of 50-100 mg (or 1-1.5 mg/kg) at a rate of 25-50 mg/minute, followed immediately by intravenous infusion of 1-4 mg/minute, with ECG monitoring of all patients (reduce infusion dose if required for longer than 24 hours).
- Intravenous, child: 1 mg/kg/dose slow IV, may repeat 10-15 min. Maximum total dose: 3-5 mg/kg within first hour.

Lidocaine has a short duration of action (15-20 minutes), if the intravenous infusion cannot be given immediately, the initial intravenous injection of 50-100 mg can be repeated once or twice at intervals of not less than 10 minutes.

Adverse effects: Flushing or redness, dizziness, paresthesia, itching, drowsiness, confusion, apnea, respiratory depression, coma, seizure and convulsions, hypotension, arrhythmia, heart block, cardiovascular collapse, bradycardia (may lead to cardiac arrest), nystagmus (often an early sign of lidocaine overdose).

Drug and food interactions: Increased cardiac depression and toxicity with amiodarone, phenytoin, procainamide, propranolol. Increased neuromuscular blockade with neuromuscular blockers. Increased hypotensive effects with MAO inhibitors, antihypertensive. Increased effects of lorazepam (additive CNS depressants) and alprazolam effects (increase CNS side effects)

METOPROLOL: See under section 2.1 Antianginal agents

PROCAINAMIDE

Dosage form and strength: *Solution:* 100 mg /ml in 10 ml ampoule; *tablet:* 250 mg

Indications: Severe ventricular arrhythmias (especially those resistant to lidocaine or those appearing after myocardial infarction); atrial tachycardia, atrial fibrillation; maintenance of sinus rhythm after cardioversion of atrial fibrillation.

Contraindications/Precautions: Avoid in Torsade's de pointes, SLE, 2nd and 3rd degree heart block, heart failure, hypotension, elderly, renal impairment, hepatic impairment, asthma, myasthenia gravis, pregnancy, breastfeeding, electrolyte imbalance (hyperkalemia, hypokalemia, magnesium disorders). Discontinue treatment in case of drop in leukocyte and platelet count. Perform complete blood count twice a week for 3 months.

Dosage schedule:

- *Oral, adult:*, up to 50 mg/kg daily in divided doses every 3-6 hours, preferably controlled by monitoring plasma-procainamide concentration (therapeutic concentration usually within 3-10 mcg/ml); in atrial arrhythmia, higher doses may be required.
- *Slow intravenous injection, adult:* rate not exceeding 50 mg/minute, 100 mg repeated at 5 minute intervals until arrhythmia controlled; maximum 1g.
- Intravenous infusion, *adult:* 500-600 mg over 25-30 minutes, followed by maintenance at rate of 2-6 mg/minute, then if necessary oral anti-arrhythmic treatment as above, starting 3-4 hours after infusion.

When using IV, monitor continuously by ECG.

Adverse effects: Nausea, vomiting, diarrhea, anorexia, rash, pruritus, urticarial, flushing, fever, myocardial depression, heart failure, angioedema, depression, dizziness, psychosis; blood disorders including leukopenia, hemolytic anemia and agranulocytosis after prolonged treatment, SLE like syndrome, high plasma procainamide concentration may impair cardiac conduction.

Patient's information: A wax matrix may appear in stools. Do not discontinue without prescriber's approval. Notify prescriber if lupus-like symptoms appear, leucopenia (sore mouth, gums, and throat) or thrombocytopenia, bleeding, bruising). Avoid driving until product effect is known

PROPRANOLOL: See under section 2.1 Antianginal agents

VERAPAMIL: See under section 2.1 Antianginal agents

2.3 Antihypertensive agents

2.3.1 Angiotensin converting enzyme inhibitor (ACEI)

CAPTOPRIL

Dosage form and strength: *Tablet:* 25 mg, 50 mg
Indications: Mild to moderate essential hypertension, adjunctive treatment in congestive heart failure, severe hypertension resistant to other treatment, following myocardial infraction, diabetic nephropathy in insulin dependent diabetes.
Contraindications/ precautions: Avoid in bilateral renal artery stenosis, pregnancy, hyperkalemia, pre-existing cough. Use caution in severe or symptomatic aortic stenosis. Monitor renal function before and during treatment.
Dosage schedule: *Hypertension:* Oral, adult: initially 5 mg once daily, lower initial dose if used in addition to diuretic or in renal impairment; usual maintenance dose 20 mg once daily; maximum 40 mg once daily. Take 1-2 hours after meals.
Adverse effect: alopecia, rash, profound hypotension (usually with first dose, especially in patients taking high dose of diuretics on low sodium diet, dehydration, taste impairment, leucopenia, proteinuria, persistent dry cough, sleep disorder, dyspnea, pallor, neutropenia, Raynaud's syndrome.
Drug and food interaction: With potassium sparing diuretics hyperkalemia may result especially in existing renal impairment. With alcohol, alpha blocker, general anesthetic, angiotensin 2 receptor antagonist, beta blocker, calcium channel blocker, hypotensive effect is increased.
Patient's information: Avoid activities that require concentration, the person may feel dizziness, fainting, and light headedness. Not to discontinue product abruptly, if dose is missed, take as soon as remembered but do not double the doses. Rise slowly to sitting or standing position to minimize orthostatic hypotension.

ENALAPRIL

Dosage form and strength: *Tablets:* 2.5 mg, 5 mg, 10 mg
Indications: Hypertension, heart failure
Contraindications/Precautions: See under captopril. Avoid in renal impairment when GFR < 30 ml/1.73m^2/min. use cautious in impaired liver function and neonates. Monitor renal function.
Dosage schedule:

- *Hypertension:* Oral, adult: 5 mg once daily, if used in addition to diuretic or in renal impairment or in elderly patient, 2.5 mg daily initially, maintenance dose 20 mg once daily: maximum 40 mg once daily. *Oral, child:* 0.1- 0.6 mg/kg/day in 1-2 divided doses. Maximum dose 40 mg/day

Adverse drug reaction: Dizziness, headache, nausea, diarrhea, dry cough,

fatigue, asthenia, angioedema, urticaria, rashes, hyperkalemia, impaired perspiration

Drug and food interaction: See captopril

Patient's information: Avoid activities requiring coordination, the drug may cause skin rash, or angioedema. Discontinue if angioedema occurs.

LISINOPRIL

Dosage form and strength: *Tablets:* 2.5 mg, 5 mg, 10 mg, 20 mg

Indications: Essential and renovascular hypertension, adjunctive treatment in congestive heart failure, following myocardial infarction in hemodynamically stable patients, diabetic nephropathy in normotensive insulin-dependent and hypertensive non-insulin dependent diabetes mellitus.

Contraindications/ precautions: Avoid in pregnancy, hereditary angioedema, breast-feeding. Also see under captopril

Dosage schedule:

- *Hypertension:* initially 10 mg daily, if used in addition to diuretic or in patient with renal impairment, initially 2.5-5 mg daily; usual maintenance dose 20 mg once daily(maximum 80 mg daily).
- *Heart failure (adjunct): Oral, adult:* initially 2.5 mg daily; usual maintenance dose 5-20 mg daily.
- *Diabetic nephropathy: Oral, adult:* initially 2.5 mg daily adjusted to achieve diastolic blood pressure below 75 mm Hg in normotensive insulin dependent diabetes and below 90 mm Hg in hypertensive non-insulin dependent diabetes; usual dose range 10-20 mg daily.
- *Prophylaxis after myocardial infarction: Oral, adult:* 5 mg within 24 hours if systolic blood pressure over 120 mm Hg, followed by further 5 mg 24 hours later, then 10 mg after a further 24 hours, and continuing with 10 mg once daily for 6 weeks; if systolic blood pressure 100-120 mm Hg, initially 2.5 mg, increasing to maintenance dose of 5 mg once daily.

Adverse effects: Profound hypotension, hyperkalemia, rash, tachycardia, myocardial infarction, sweating, impotence, dizziness, upper respiratory tract infection, fatigue, diarrhea.

Patient's information: Drink plenty of water each day while taking the medication. Avoid potassium rich diet.

RAMIPRIL

Dosage form and strength: *Tablets/Capsules:* 1.25 mg, 2.5 mg, 5 mg, 10 mg

Indication: Hypertension, congestive heart failure, prophylaxis after myocardial infarction, prophylaxis of cardiovascular events or stroke.

Contraindications/Precautions: Also See under Lisinopril, Enalapril

Dosage schedule:

- *Hypertension: Oral, adult:* initially 1.25 mg once daily, increased at intervals of 1-2 weeks; usual range 2.5-5 mg once daily; maximum 10 mg once daily.
- *Congestive heart failure (adjunct): Oral, adult:* initially 1.25 mg once daily under close medical supervision, increased if necessary at intervals of 1-2 weeks; maximum 10 mg daily.
- *Prophylaxis after myocardial infarction: Oral, adult:* initially 2.5 mg twice daily, increased after 2 days to 5 mg twice daily; maintenance 2.5-5 mg

twice daily.
- *Prophylaxis of cardiovascular events or stroke:* initially 2.5 mg once daily, increased after 1 week to 5 mg once daily, then increased after a further 3 weeks to 10 mg once daily.

Adverse effects: See under Enalapril

2.3.2 Angiotensin receptor blockers (ARBs)

IRBESARTAN

Dosage form and strength: *Tablet:* 75 mg, 150 mg

Indications: Hypertension, hypertension in patients receiving hemodialysis, renal disease in hypertensive with type 2 diabetes mellitus

Contraindication/ Precautions: Avoid in renal artery stenosis, moderate to severe renal impairment or liver impairment, aortic or mitral valve stenosis.

Dosage schedule:
- *Hypertension: Oral, adult (18–74 years):* Initially 150 mg once daily, increased if necessary to 300 mg once daily.
- *Hypertension: Oral, adult (>75 years):* Initially 75–150 mg once daily, increased if necessary to 300 mg once daily.
- *Hypertension in patients receiving hemodialysis:* Oral, adult: Initially 75–150 mg once daily, increased if necessary to 300 mg once daily.
- *Renal disease in hypertensive type 2 diabetes mellitus:* Oral, adult (18–74 years): Initially 150 mg once daily, increased if tolerated to 300 mg once daily.
- *Renal disease in hypertensive type 2 diabetes mellitus:* Oral, adult (>75 years): Initially 75–150 mg once daily, increased if tolerated to 300 mg once daily

Adverse effects: Fatigue, musculoskeletal pain, nausea, vomiting

LOSARTAN

Dosage form and strength: *Tablet:* 25 mg, 50 mg

Indications: Hypertension, congestive heart failure, diabetic nephropathy in type 2 diabetes mellitus

Contraindications/Precautions: Avoid in pregnancy and breast feeding, children of 6 years or younger, CHF, renal impairment (GFR < 30 ml/min/1.73m^2, renal artery stenosis. Use caution in moderate to severe renal impairment or liver impairment, aortic or mitral valve stenosis.

Dosage schedule:
- *Hypertension:* Oral, adult: 50 mg (in intravascular volume depletion initially/ elderly >75 years: initially 25 mg) once daily for several weeks, then increase up to 150 mg in weekly interval if necessary and tolerated. Oral, Child: 0.75 mg/kg/dose once daily up to 50 mg/day. Maximum dose: 1.4 mg/kg/day or 100 mg/day
- *Diabetic nephropathy in DM type II:* Oral, adult: initially 50 mg (elderly >75 years: 25 mg) once daily for several weeks then increase up to 100 mg in weekly interval if necessary and tolerated.
- *CHF with ACE inhibitors unsuitable or contraindicated:* Oral, adult: Initially 12.5 mg once daily, increase if tolerated to up to 150 mg once daily, to be

increased daily.

Adverse effects: Hypotension, dizziness, diarrhea, pruritus, rash, taste disturbance, thrombocytopenia, photosensitivity

Drug and food interactions: With lithium, increases lithium toxicity. With hypertensive agents, increases antihypertensive effect. Avoid use in Aliskiren.

Patient's information: Rise slowly to sitting or standing position to minimize orthostatic hypotension. Avoid sunlight, salt substitutes, alcohol, over the counter products unless approved by prescriber.

TELMISARTAN

Dosage form and strength: *Tablet:* 20 mg, 40 mg, 80 mg

Indications: Hypertension, prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease or type 2 diabetes mellitus with target-organ damage.

Contraindication: Avoid in bilateral renal artery stenosis, pregnancy and breast feeding, in severe impairment or biliary obstruction.

Dosage schedule:

- *Hypertension: Oral, adult:* Initially 20–40 mg once daily for at least 4 weeks, increased if necessary up to 80 mg once daily
- *Prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease or type 2 diabetes mellitus with target-organ damage:* Oral, adult: 80 mg once daily
- *Severe renal impairment:* Oral, adult: Initial dose of 20 mg once daily.

Adverse effects: Arthralgia, back pain, chest pain, eczema, gastro-intestinal disturbances, influenza like symptoms, leg cramps, myalgia, pharyngitis, sinusitis, urinary-tract infection, abnormal vision, anxiety, dry mouth, increased sweating, tendonitis- like symptoms, vertigo

Drug and food interactions: Avoid use with ACE inhibitor, aspirin, acebutolol, aceclofenac, amiloride, atenolol, chlorthiazide, digoxin, enoxaparin, furosemide, ibuprofen, insulin, irbesartan, ketorolac, piroxicam, potassium chloride, spironolactone, sulfasalazine, torsemide, trimethoprim.

VALSARTAN

Dosage and strength: *Tablet:* 40 mg, 80 mg, 160 mg

Indications: Hypertension, myocardial infarction with left ventricular failure or left ventricular systolic dysfunction.

Contraindications/Precautions: See under Losartan. Avoid in biliary cirrhosis, cholestasis, severe hepatic impairment, renal impairment when eGFR <10 ml/min/ 1.73m^2. Use caution in mild to moderate renal and hepatic impairment.

Dosage schedule:

- *Hypertension:* Oral, adult: 80 mg once daily (initially 40 mg once daily in intravascular volume depletion); if necessary increased after at least 4 weeks to 160 mg daily.
- *Myocardial infarction:* Oral, adult: initially 20 mg twice daily increased over several weeks to 160 mg twice daily if tolerated.
- *Mild to moderate hepatic impairment:* maximum dose of 80 mg daily.

Take medicine before meal.

Adverse effects: See under losartan.
Drug and food interactions: Food interferes with absorption.

2.3.3 Beta blockers

ATENOLOL: See under section 2.1 Antianginal agents

BISOPROLOL: See under section 2.1 Antianginal agents

LABETALOL

Dosage form and strength: *Tablet:* 100 mg, 200 mg; *Solution:* 100 mg/20ml
Indications: Hypertension, Hypertensive emergencies, hypertension following myocardial infarction, hypertension of pregnancy
Contraindication/ Precautions: See under contraindication in Atenolol under Antianginal of this chapter. Avoid in severe liver damage. Hepatic impairment: avoid as reported. Renal impairment: Dose reduction may be required. Pregnancy: possibly harmful in the first trimester. If labetalol used close to delivery, monitor infants for signs of alpha-blockade (as well as beta blockade). Breast feeding: monitor infants for possible toxicity due to alpha-blockade (in addition to beta-blockade. Laboratory testing needed at first symptom of liver dysfunction and if laboratory evidence of damage (or if jaundice) labetalol should be stopped and not restarted.
Dosage schedule:

- *Hypertension:* Oral, adult: Initially 100 mg (50 mg for elderly) twice daily, dose to be increased at intervals of 14 days; usual dose 200 mg twice daily, increased if necessary up to 800 mg daily in 2 divided doses, higher doses to be given in 3–4 divided doses; maximum 2.4 g per day. To be taken with food
- *Hypertension/ hypertensive emergencies: Intravenous injection:* adult: 50 mg, administer over at least 1 minute, then 50 mg after 5 minutes if required; maximum 200 mg per course.
- *Hypertension/ hypertensive emergencies: Intravenous infusion:* adult: Initially 2 mg/minute until a satisfactory response is achieved, then discontinue; usual dose 50–200 mg
- *Hypertension following myocardial infarction:* Intravenous Infusion, adult: 15 mg/hour, maximum dose 120 mg/hour, dose to be increased gradually.
- *Hypertension of pregnancy:* Intravenous infusion, adult: Initially 20 mg/hour, then increased if necessary to 40 mg/hour after 30 minutes, then increased if necessary to 80 mg/hour after 30 minutes, then increased if necessary to 160 mg/hour after 30 minutes, adjusted according to response. Maximum 160 mg/hour.
- *Hypertension: Oral, child:* 4 mg/kg/day in 2 divided doses. Maximum dose up to 40 mg/kg/day.
- *Hypertensive emergencies: Child, intravenous:* 0.2-1.0 mg/kg/dose every 10 min as required. Maximum dose: 20 mg/dose
- *Hypertensive emergencies: Child, infusion:* 0.4-1.0 mg/kg/hr. Maximum dose 3mg/kg/hr.

Adverse effects: Difficulty in micturition, epigastric pain, liver damage,

nausea, postural hypotension, vomiting, weakness, severe hepatocellular injury (with short or long term use)

Drug and food interaction: Interferes with laboratory tests for catecholamine. Concurrent use of digitalis increases the risk of bradycardia

Patient's information: For oral formulation, take medicine after food. Patient should remain supine up to 3 hrs. after intravenous administration.

METOPROLOL: See under section 2.1 Antianginal agents

NEBIVOLOL

Dosage form and strength: *Tablets:* 2.5 mg, 5 mg

Indications: Essential hypertension, hypertension in patient with renal impairment, adjunct in stable mild to moderate heart failure

Contraindication: See under contraindication Atenolol in Antianginal agents. Avoid in acute or decompensated heart failure requiring intravenous inotropes, decompensated heart failure, severe hepatic impairment (Child-Pugh class C). Pregnancy (C). Breast feeding: avoid. Renal impairment: avoid in heart failure if serum creatinine greater than 250 micromole/liter

Dosage schedule:

- *Essential hypertension:* Oral, adult: 5 mg daily; elderly: Initially 2.5 mg daily, then increased if necessary to 5 mg daily
- *Hypertension in patient with renal impairment:* Oral, adult: Initially 2.5 mg once daily, then increased if necessary to 5 mg once daily.
- *Adjunct in stable mild to moderate heart failure:* Oral, elderly (≥ 70 years): Initially 1.25 mg once daily for 1–2 weeks, then increased if tolerated to 2.5 mg once daily for 1–2 weeks, then increased if tolerated to 5 mg once daily for 1–2 weeks, then increased if tolerated to 10 mg once daily.

Adverse effects: See under adverse effect Atenolol in Antianginal agents. Depression, edema.

METOPROLOL: See under section 2.1 Antianginal agents

PROPRANOLOL: See under section 2.1 Antianginal agents

2.3.4 Calcium channel blockers

AMLODIPINE

Dosage form and strength: *Tablet:* 2.5 mg, 5 mg, 10 mg

Indications: Hypertension, angina pectoris

Contraindication/ Precautions: Cardiogenic shock, unstable angina, significant aortic stenosis. In hepatic impairment: dose reduction. Try to avoid large amount of alcohol. Pregnancy and breastfeeding: avoid.

Dosage schedule:

- *Hypertension or angina:* Oral, adult: initially 5 mg once daily; maximum dose 10 mg once daily.
- *Oral, child:* 0.1-0.6 mg/kg/day in 1-2 divided doses. Maximum dose: 20 mg/day

Adverse effects: Abdominal pain, nausea, flushing, edema (ankle edema),

headache, dizziness, sleep disturbances, fatigue, alopecia, arthralgia, asthenia, back pain, dry mouth, dyspnea, impotence, gynecomastia, myalgia, muscle cramp, skin discoloration.
Drug and food interaction: See under verapamil

FELODIPINE
Dosage form and strength: *Tablet:* 2.5 mg, 10 mg
Indications: Angina, hypertension
Contraindication/Precautions: Avoid in Cardiac outflow obstruction, aortic stenosis uncontrolled heart failure, unstable angina, within 1 month of myocardial infarction. Predisposition to tachycardia, severe left ventricular dysfunction, withdraw if cardiogenic shock develops, if ischemic pain occurs shortly after initiating treatment. Pregnancy- avoid. Breast feeding- safe. In hepatic impairment, reduce dose.
Dosage schedule:
- *Angina:* Oral, adult: 5 mg/day, maximum dose 10 mg/day. Oral, elderly: 2.5 mg/day, maximum dose 10 mg/day.
- *Hypertension:* initially 5 mg (elderly 2.5 mg) daily in the morning; usual maintenance dose 5-10 mg once daily.

Adverse effects: flushing, headache, peripheral edema.
Drug and food interaction: See under verapamil

NIFEDIPINE
Dosage form and strength: *Capsule:* 5 mg, 10 mg; *Tablet:* 30 mg
Indications: prophylaxis of angina, hypertension, Raynaud's phenomenon, pulmonary hypertension.
Contraindication/ Precautions: Avoid in congestive heart failure or aortic stenosis, especially in those receiving concomitant beta blocking agents. In patients with angina, the drug may cause increased angina. Pregnancy (D)
Dosage schedule:
- *Hypertension and angina prophylaxis:* Oral, adult: 20 mg twice daily. Usual maintenance 10-40 mg twice daily.
- *Raynaud's phenomenon:* Oral, adult: initially 5 mg 3 times daily with or after food; usual maintenance 5-20 mg 3 times daily.
- *Pulmonary hypertension:* Oral, adult: 120 to 240 mg once daily dose.
- *Hypertension: Child, sublingual:* 0.25-0.5 mg/kg/dose may be repeated 6 hourly. Maximum dose 10 mg/dose.
- *Hypertension: Child, sustained release tablet:* 0.25-3 mg/kg/day in 1-2 divided dose. Maximum dose 120 mg/day

To be taken with or after food.
Adverse effects: dizziness, giddiness, flushing, light headedness, peripheral edema and palpitation.
Drug and food interaction: *See* under verapamil

2.3.5 Centrally acting antihypertensives

CLONIDINE
Dosage form and strength: *Tablet:* 25 mcg, 100 mcg.

Indications: Hypertension, prevention of recurrent migraine, prevention of vascular headache, treatment for acute withdrawal in opioid dependent patients.

Contraindication/Precautions: Avoid in severe bradyarrhythmia secondary to second- or third-degree AV block or sick sinus syndrome. Use caution in cerebrovascular disease, constipation, heart failure, history of depression, mild to moderate bradyarrhythmia, polyneuropathy, Raynaud's syndrome or other occlusive peripheral vascular disease. In hypertension, must be withdrawn gradually to avoid severe rebound hypertension. Pregnancy: use caution, may lower fetal heart rate. Breast feeding: avoid. Renal impairment: Use with caution in severe impairment, reduce initial dose and increase gradually.

Dosage schedule:

- *Hypertension: Oral, adult:* Initially 50–100 mcg 3 times a day, increase initial dose every second or third day, usual maximum dose 1.2 mg daily
- *Prevention of recurrent migraine/Prevention of vascular headache:* Oral, adult: Initially 50 micrograms twice daily for 2 weeks, then increased if necessary to 75 micrograms twice daily
- *Treatment for acute withdrawal in opioid dependent patients: Oral, adult:* 0.1-0.3 mg every 4-6 hours; increase by 0.1 mg/day; 0.15-0.75 mg/day if required; do not exceed 2.4 mg/day

Adverse effects: Constipation, depression, dizziness, drowsiness, dry mouth, headache, malaise, nausea, postural hypotension, salivary gland pain, sexual dysfunction, sleep disturbances, vomiting. Uncommon: bradycardia, delusion, hallucination, paresthesia, pruritus, rash, Raynaud's syndrome, urticarial

Drug and food interaction: concomitant use of alcohol may enhance effects of alcohol

Patient's information: Drowsiness may affect performance of skilled tasks (e.g. driving)

2.3.6 Diuretics

CHLORTHALIDONE
FUROSEMIDE
HYDROCHLOROTHIAZIDE
METOLAZONE
SPIRONOLACTONE
TORSEMIDE

See under section 5.1 Diuretics in drugs used in Renal Disorders, Chapter 5

2.3.7 Others

HYDRALAZINE HYDROCHLORIDE

Dosage form and strength: *Powder for injection:* 20 mg in ampoule; *Tablet:* 25 mg, 50 mg

Indication: Moderate and severe hypertension (adjunct), hypertensive emergencies in pregnant (not a first line agent), hypertension with renal

complication and children
Contraindications/Precautions: Avoid in severe tachycardia, high output heart failure, myocardial insufficiency due to mechanical obstruction, corpulmonale, dissecting aortic aneurysm, porphyria, idiopathic systemic lupus erythematosus. Use caution in hepatic impairment, renal impairment, coronary artery disease (may provoke angina, avoid after myocardial infraction), pregnancy, elderly, cerebrovascular disease. Complete blood count, LE cell preparation, antinuclear antibody should be performed before and periodically during prolonged hydralazine therapy. Intravenous hydralazine is not advisable in older patients, hypertensive patient with coronary artery disease or cardiovascular risk factors. Monitor blood glucose regularly in diabetics.
Dosage schedule:
- *Mild or moderate hypertension (as adjunct): Oral, adult:* 25 mg twice daily, increased to a maximum of 50 mg twice daily.
- *Hypertensive emergencies (including pregnancy/ hypertension with renal complications): intravenous infusion, adult:* initially 200-300 mcg/minute, maintenance usually 50-150 mcg/minute. Slow *intravenous injection, adult: 5-10 mg, to be diluted with 10 ml of 0.9% saline, dose may be repeated after 20-30 min.*
- *Hypertension: Oral, child:* 0.75-1.0 mg/kg/day in 2-4 divided doses. Maximum dose: 25 mg/dose. May increase to infants: 5mg/kg/day-, Children: 7.5 mg/kg/day or 200mg/day
- *Hypertension: Child, intravenous or intramuscular: Hypertensive crisis:* 0.1-0.2 mg/kg/dose every 4-6 hours. Maximum dose: 20 mg/dose. Usual IV/IM dose: 1.7-3.5 mg/kg/day

Adverse effect: Tachycardia, palpitation, hypotension, nausea, vomiting, systemic lupus erythematosus like syndrome, weight gain and headache, muscle weakness, cramps, dizziness. Patients who are slow acetylator of hydralazine may have high risk of developing SLE.
Drug and food interaction: With diuretic or other antihypertensives, the hypotensive effect increases.
Patient's information: Take drug early in day to avoid nocturia. Rise slowly from sitting or lying position.

METHYLDOPA

Dosage form and strength: *Tablet:* 250 mg
Indication: Hypertension, hypertension in pregnancy
Contraindications/Precautions: Avoid in acute porphyria, depression, pheochromocytoma. Use cautiously in patients with history of liver disease and renal impairment, Sino atrial dysfunction; May precipitate severe bradycardia and sinus arrest. Screening for hepatotoxicity (e.g. with determination of gamma-glutamyl transpeptidase or alanine aminotransferase) at 3 weeks then at 3 months following initiation of treatment. Coomb's test may be positive in up to 30% of patients, but discontinue only if hemolysis develops. Pregnancy and breast feeding: safe.
Dosage schedule: *Hypertension, Hypertension in pregnancy:* Oral, adult: 250 mg, 2-3 times a day. Single dose administration at bedtime minimizes

sedative effect but it is not sufficient for some patients, dose can be gradually increased up to 3 g daily (maximum).
Protect the medication from light. Oral, elderly: initially 125 mg twice daily, increase gradually up to maximum dose of 2 gm daily.
Adverse effects: Sedation, dryness of mouth, decreased libido, parkinsonian signs, hyperprolactinemia, gynecomastia, hepatitis and hepatotoxicity, hemolytic anemia, leucopenia, lupus like syndrome, myocarditis, retroperitoneal fibrosis, pancreatitis, malabsorbtion, diarrhea, amenorrhea, Bell's palsy, bone marrow depression, depression, eosinophilia, drug fever, nasal congestion, nightmares, sialadenitis, toxic epidermal necrolysis.

PRAZOSIN

Dosage form and strength: *Tablet:* 1 mg, 2.5 mg, 5 mg
Indications: Hypertension, benign prostatic hyperplasia.
Contraindications/Precautions: Avoid in history of micturition syncope and postural hypotension, congestive heart failure due to mechanical obstruction (e.g. aortic stenosis). Use caution cataract surgery (risk of intra-operative floppy iris syndrome), elderly, renal or hepatic impairment. Pregnancy (C), Breast feeding: use caution.
Dosage schedule:

- *Hypertension:* Oral, adult: 500 mcg 2-3 times daily for 3-7 days, the initial dose on retiring to bed at night; increased to 1 mg 2-3 times daily for further 3-7 days then increased if necessary. Maximum dose 20 mg daily in divided doses
- *Benign prostatic hyperplasia:* Oral, adult: Initially 500 mcg twice daily for 3–7 days, subsequent doses should be adjusted according to response, maintenance 2 mg twice daily, initiate with lowest possible dose in elderly patients.

Adverse effects: Postural hypotension, dizziness, headache, palpitation, nervousness, drowsiness, priapism, blurred vision, depression, dry mouth, dyspnea, gastrointestinal disturbances, nasal congestion, edema, palpitations, syncope, urinary frequency, vertigo, weakness.
Drug and food interactions: Concomitant use with diuretics or other antihypertensive drug may cause an additive hypertensive effect.
Patient's information: First dose may cause collapse due to hypotension, take first dose at bedtime; do not to drive/operate machine for 4 hr. after first dose.

SODIUM NITROPRUSSIDE

Dosage form and strength: Intravenous solution: 10 mg/ml
Indication: Hypertensive crisis, controlled hypotension in anesthesia, acute or chronic heart failure.
Contraindications/Precautions: Severe hepatic impairment, compensatory hypertension, severe vitamin B12 deficiency, Leber optic atrophy. Elderly, hyponatremia, hypothermia, hypothyroidism, impaired cerebral circulation, ischemic heart disease. Impaired pulmonary function; hypothyroidism; renal impairment, ischemic heart disease, impaired cerebral circulation; hyponatremia; raised intracranial pressure; Monitor blood pressure and

blood cyanide concentration; monitor blood. Thiocyanate concentration if given for more than 3 days; avoid sudden withdrawal (reduce infusion over 15–30 minutes to avoid rebound effects); Pregnancy: Avoid prolonged use, potential for accumulation of cyanide in fetus. Breast feeding: safety information not available. Caution advised due to thiocyanate metabolite.

Dosage schedule:

- *Hypertensive crisis:* Intravenous infusion, adult: initially 0.5–1.5 mcg/kg/minute, increased gradually to 0.5–6 mcg/kg/minute; (lower doses in patients already being treated with antihypertensives); maximum, 8 mcg/kg/minute. Stop infusion, if response is unsatisfactory after 10 minutes at the maximum dose.
- *Heart failure:* 10- 15 mcg /minute, increased every 5-10 minutes as necessary, usual range10-200 mcg/minute.

Adverse effects: severe hypotension; associated with over-rapid. Reduction in blood pressure include headache, dizziness; retrosternal discomfort, nausea, retching, abdominal pain; perspiration; palpitations, anxiety, perspiration; rarely reduced platelet count, and acute transient phlebitis.

TAMSULOSIN

Dosage form and strength: *Capsule:* 400 mg.

Indications: Benign prostatic hyperplasia

Contraindications/Precautions: Avoid in micturition syncope, postural hypotension, severe liver impairment. Use caution if eGFR <10 ml/min/1.73m^2.

Dosage schedule: *Oral, adult:* 400 mcg daily as once daily.

Adverse effects: Postural hypotension, dizziness, headache, palpitation, drowsiness, priapism, pruritus, angioedema, asthenia, blurred vision, rash, rhinitis, tachycardia, depression, intraoperative floppy iris syndrome, gastrointestinal disturbances.

Patient's information: Do not drive, use machinery, or do any activity that requires alertness until you are sure you can perform such activities safely. Not to crush, break, chew on oral intake.

TERAZOSIN

Dosage form and strength: *Tablet:* 1 mg, 2 mg, 5 mg.

Indication: Benign prostatic hyperplasia (BPH), mild to moderate hypertension

Contraindication /Precaution: See under Prazosin

Dosage schedule:

- *Hypertension (mild to moderate): Oral, adult:* Initially 1 mg once daily at bedtime, dose doubled after 7 days if necessary, usual maintenance dose 2-10 mg according to response.
- *BPH: Oral, adult:* Initially 1 mg orally once daily at a bedtime. If necessary dose may be doubled at intervals of 1-2 weeks according to response, maintenance 5–10 mg daily; maximum 10 mg per day.

Adverse effects: Postural hypotension and syncope (especially on the start of therapy), dizziness, drowsiness, dry mouth, chest pain, pedal edema, palpitation, headache, priapism, thrombocytopenia, decreased libido, erectile disorders, weight gain, dyspnea, Angioedema, pain in extremities,

blurred vision

Drug and food interactions: With Metoprolol causes additive hypotensive effect

2.4 Drugs used in cardiovascular shock

DOPAMINE HYDROCHLORIDE
DOBUTAMINE
EPINEPHRINE /ADRENALINE
NOREPINEPHRINE/ NORADRENALINE

See under section 2.5 in Drugs used in heart failure

PHENYLEPHRINE

Dosage form and strength: *Solution:* 10 mg/ml

Indications: Acute hypotension, Priapism

Contraindication: Avoid in hypertension, severe hyperthyroidism. Hypertensive response of Phenylephrine has a longer duration of action than noradrenaline (norepinephrine) and an excessive vasopressor response may cause a prolonged rise in blood pressure. Pregnancy: avoid

Dosage schedule:

- *Acute hypotension:* subcutaneous injection/ intramuscular injection, adult: Initially 2–5 mg, followed by 1–10 mg, after at least 15 minutes, if required. Slow intravenous injection, adult: 100–500 mcg, repeated as necessary after at least 15 minutes; 1 mg/ ml solution to be used. Intravenous infusion, adult: Initially up to 180 mcg /minute, reduced to 30–60 mcg/min, adjusted according to response. Intravenous infusion give intermittently in Glucose 5% or Sodium chloride 0.9%. Dilute 10 mg in 500 mL infusion fluid.
- *Priapism:* Intracavernosal injection, adult: 100–200 mcg every 5–10 minutes; maximum 1 mg per course. For intracavernosal injection, if suitable strength of phenylephrine injection is not available, it may be specially prepared by diluting 0.1 mL of the phenylephrine 1% (10 mg/mL) injection to 5 mL with sodium chloride 0.9%.

Adverse effects: Arrhythmias, hypertension, palpitation, tachycardia, angle-closure glaucoma, anorexia, anxiety, bradycardia (also reflex bradycardia), confusion, dyspnea, headache, hypoxia, insomnia, nausea, peripheral ischemia, psychosis, tremor, urinary retention, vomiting, weakness

VASOPRESSIN: See under section 5.2 Antidiuretics Hormones in Drugs used in Renal Disorders, Chapter 5

2.5 Drugs used in heart failure

BISOPROLOL: See under section 2.1 Antianginal agents

CARVEDILOL: See under section 2.1 Antianginal agents

DIGOXIN: See under section 2.2 Antiarrhythmic agents

DOBUTAMINE

Dosage form and strength: *Injection solution:* 12.5 mg/ml in 20 ml vial.
Indications: Inotropic support in infarction, cardiac surgery, septic shock, cardiogenic shock and during positive end expiratory pressure ventilation.
Contraindications/Precautions: Avoid in hypersensitivity, pheochromocytoma. Use caution in severe hypotension, complicating cardiogenic shock, heart failure.
Dosage schedule: *Intravenous infusion, adult:* 2.5-10 mcg/kg/minute, adjusted according to response, alternatively 0.5-40 mcg/kg/min
Adverse effect: Tachycardia, increase in systolic blood pressure, phlebitis. Extravasation of the drug causes tissue necrosis
Drug and food interactions: Additive (synergistic) effective with Nitroprusside. Atenolol may negate the effect of dopamine. Do not mix with sodium bicarbonate, furosemide and other alkaline solutions.

DOPAMINE

Dosage form and strength: *Injection:* 40 mg/ml in 5ml, 10ml vial.
Indications: Cardiogenic shock including in myocardial infarction and cardiac surgery.
Contraindications/Precautions: Avoid in tachyarrhythmia, ventricular fibrillation, ischemic heart disease; pheochromocytoma, hyperthyroidism. Correct hypovolemia before, and maintain blood volume during the treatment; correct hypoxia, hypercapnia, and metabolic acidosis before or at same time as starting treatment; use low dose in cardiogenic shock due to myocardial infarction; history of peripheral vascular disease (increased risk of ischemia of extremities. Pregnancy: use only if potential benefit outweighs risk. Breast Feeding: May suppress lactation.
Dosage schedule: *Cardiogenic shock:* intravenous infusion, adult: initially 2–5 mcg/kg/minute into a large vein (preferably via central venous catheter), gradually increased by 5-10 mcg/kg/minute according to blood pressure, cardiac output, and urine output (seriously ill patients, up to 20–50 mcg/kg/minute)
Prepared immediately before use in accordance with the manufacture's instruction. Protect medication from light.
Adverse effects: Nausea, vomiting, peripheral vasoconstriction; hypotension with dizziness, fainting, flushing; tachycardia, ectopic beats, palpitations, anginal pain; headache, dyspnea; hypertension particularly in over dosage. Extravasation of the drug causes tissue necrosis.
Drug and food interaction: Propranolol and Metoprolol antagonize the cardiac effects of dopamine. Ventricular arrhythmias and hypertension may occur with halothane or cyclopropane anesthesia.

EPINEPHRINE /ADRENALINE

Dosage form and strength: *Injection:* 1 mg in 1000 ml
Indications: Cardiac arrest, adjunct with local anesthetics, acute anaphylaxis
Contraindications/Precautions: Shock (other than anaphylactic shock), second stage labor. Do not use the drug if the color of the injection is cloudy or brownish. While using this drug monitor blood pressure, heart rate.

Dosage schedule: *Acute anaphylaxis:* intramuscular injection, adult: 0.5-1 ml, to be repeated every 10 minutes according to blood pressure and pulse, until improvement occurs. Intramuscular injection, child (2-5 years): 0.2-0.4 ml; (6-12 years): 0.5 ml. Dosage to be repeated as in adult**.**
Acute hypotension: continuous intravenous infusion, neonate and child: 100 nanogram/kg/min (up to 1.5 mcg/kg/min) adjusted according to response.
Cardiopulmonary resuscitation: Intravenous injection, adult: 1 mg every 3-5 min as required, 1 in 10000(100 mcg/ml) solution is recommended.
Adverse effect: Tachycardia, hypertension, tremor, chest pain, irregular heartbeats, headache, nausea, vomiting, nervousness, restlessness, and weakness.
Drug and food interactions: It should be avoided in patients who are on tricyclic antidepressants as it may be cause arrhythmias, hypertension or tachycardia.
Patient's information: Notify doctor if side effects (anaphylaxis) are seen.

FUROSEMIDE: See under section 5.2 Antidiuretics Hormones in Drugs used in Renal Disorders, Chapter 5

LOSARTAN: See under section 2.3 Antihypertensive agents
TELMISARTAN: See under section 2.3 Antihypertensive agents
METOPROLOL: See under section 2.1 Antianginal agents

MILRINONE
Dosage form and strength: Injection: 1 mg/ml, 10mg/10ml solution in ampoules.
Indications: Short-term treatment of severe congestive heart failure unresponsive to conventional maintenance therapy (not immediately after myocardial infarction), acute heart failure, including low output states following heart surgery
Contraindication/ Precautions: Avoid in severe hypovolemia. Use caution in hypokalemia, renal impairment, heart failure associated with hypertrophic cardiomyopathy, stenotic or obstructive valvular disease or other outlet obstruction. Pregnancy: use with caution- use only if potential benefit outweighs risk. Breast feeding: avoid.
Dosage schedule: *Short-term treatment of severe congestive heart failure unresponsive to conventional maintenance therapy (not immediately after myocardial infarction)/ acute heart failure, including low output states following heart surgery:* intravenous injection, adult: Initially 50 mcg/kg, given over 10 minutes, followed by intravenous infusion 375–750 nanogram/kg/minute usually given following surgery for up to 12 hours or in congestive heart failure for 48-72 hours; maximum dose: 1.13 mg/kg per day. Renal impairment: Reduce dose and monitor response if eGFR < 50 mL/min/1.73 m^2
Adverse effects: Ectopic beats, headache, hypotension, supraventricular arrhythmias (more likely in patients with pre-existing arrhythmias), ventricular tachycardia. Less commonly seen: Chest pain, hypokalemia, thrombocytopenia, tremor, ventricular fibrillation.

NOREPINEPHRINE/NORADRENALINE

Dosage form and strength: Injection: 1 mg/ml. Noradrenaline (base) 4 mg/4 ml concentrate for solution for infusion ampoules.
Indications: Acute hypotension
Contraindication/ Precautions: Hypertension. Use caution in coronary vascular thrombosis, diabetes mellitus, elderly, following myocardial infarction, hypercapnia, hyperthyroidism, hypoxia, mesenteric vascular thrombosis, peripheral vascular thrombosis, variant angina, uncorrected hypovolemia. Pregnancy: Avoid, may reduce placental perfusion.
Dosage schedule: *Acute hypotension:* intravenous, adult: Initially 0.16–0.33 mL/minute, solution containing noradrenaline 40 mcg (base)/ml, adjusted according to response into large vein (preferably via central venous catheter). 1 mg of noradrenaline base is equivalent to 2 mg of noradrenaline acid tartrate. Doses expressed as the base. For treatment of acute hypotension in adults, use a solution containing noradrenaline 40 mcg (base)/ml. For intravenous infusion, give continuously in Glucose 5% or 0.9% saline and glucose via a controlled infusion device. For administration via syringe pump, dilute 2 mg (2 mL of solution) noradrenaline base with 48 mL infusion fluid. For administration via drip counter dilute 20 mg (20 mL of solution) noradrenaline base with 480 mL infusion fluid; preferably through a central venous catheter; incompatible with alkalis.
Adverse effects: Angle-closure glaucoma, anorexia, anxiety, arrhythmias, bradycardia, confusion, dyspnea, headache, hypertension, hypoxia, insomnia, nausea, palpitation, peripheral ischemia, psychosis, tachycardia, tremor, urinary retention, vomiting, weakness. Avoid extravasation, may cause pain and subcutaneous tissue ischemia at the site.
Drug and food interactions: incompatible with alkalis.

RAMIPRIL: See under section 2.3 Antihypertensive agents

SPIRONOLACTONE: See under section 5.2 Antidiuretics Hormones in Drugs used in Renal Disorders, Chapter 5

VALSARTAN: See under section 2.3 Antihypertensive agents

2.6 Drugs used in pulmonary hypertension

BOSENTAN

Dosage form and strength: *Tablet:* 62.5 mg, 125 mg
Indications: Pulmonary arterial hypertension, systemic sclerosis with ongoing digital ulcer disease (to reduce number of new digital ulcers)
Contraindication/ Precautions: Avoid in acute porphyria, systemic systolic blood pressure is <85 mmHg. Pregnancy (X) Breast feeding: avoid. Hepatic impairment: avoid in moderate to severe impairment. Effective contraception required during administration (hormonal contraception not considered effective). Monthly pregnancy tests advised. Monitor: Hemoglobin before and during treatment (monthly for first 4 months then 3-monthly); Liver function before treatment, at monthly intervals during treatment and 2

weeks after dose increase (reduce dose or suspend treatment if liver enzymes raised significantly)—discontinue if symptoms of liver impairment.

Dosage schedule:

- *Pulmonary arterial hypertension:* Oral, adult: Initially 62.5 mg twice daily for 4 weeks, then increased to 125 mg twice daily; maximum 500 mg per day in 2 divided doses.
- *Systemic sclerosis with ongoing digital ulcer disease (to reduce number of new digital ulcers):* Oral, adult: Initially 62.5 mg twice daily for 4 weeks, then increased to 125 mg twice daily

Avoid abrupt withdrawal.

Adverse effects: Anemia, diarrhea, flushing, gastro-esophageal reflux, headache, hypotension, edema, palpitation, syncope, liver cirrhosis, liver failure, leucopenia, neutropenia, thrombocytopenia.

SILDENAFIL

Dosage form and strength: *Tablet:* 25 mg, 50 mg, 100 mg

Indications: Pulmonary arterial hypertension (PAH), erectile dysfunction

Contraindication/ Precautions: Avoid in hypotension, myocardial infarction, unstable angina, not for use in children with PAH. Use caution in patients with anatomic deformation of penis, retinitis pigmentosa, ischemic heart disease.

Dosage schedule:

Erectile dysfunction: Oral, adult: 50 mg 1 hr. before sexual activity, maximum dose 100 mg or minimum dose 25 mg and maximum of 1 dose per day.

PAH: Oral, adult: 25 mg three times daily.

Adverse effects: headache, flushing, epistaxis, dyspepsia, insomnia, erythema, diarrhea, migraine, myalgia, nasal congestion, visual disturbance, back pain.

Drug and food interactions: Avoid concomitant use with nitrates. With alcohol may cause dizziness, fainting or blurred vision. With sildenafil, patient with heart problem, are at increased risk of heart related side effect.

2.7 Hypolipidemic / lipid lowering drugs

ATORVASTATIN

Dosage form and strength: *Tablet:* 10 mg

Indications: Primary hypercholesterolemia, homozygous or heterozygous familial hypercholesterolemia or mixed hyperlipidemia in patients who have not responded adequately to diet and other appropriate measures.

Contraindications/Precautions: Avoid in pregnancy, breastfeeding, active liver disease (or in patients with persistently abnormal lover function tests). Use caution in patients with liver disease, elderly or with a high alcohol intake. Non serious and reversible cognitive side effects may occur. Liver function tests should be carried out before and within 1-3 months of starting treatment and thereafter at intervals of 6 months for 1 year, unless indicated sooner by signs or symptoms suggestive of hepatotoxicity.

Dosage schedule:

- *Primary hyperlipidemia and combined hyperlipidemia:* Oral, adult: 10 mg

once daily; if necessary may be increased at intervals of at least 4 weeks to maximum 80 mg once daily. Oral, child (10-13 years usually): 10 mg once daily.

- *Familial hypercholesterolemia:* Oral, adult: initially 10 mg daily, increased at intervals of at least 4 weeks to 40 mg once daily; if necessary, further increased to maximum 80 mg once daily. Oral, child (10-13 years): up to 20 mg once daily.

Adverse effects: reversible myositis, headache, angina, chest pain, arthralgia, anorexia, weight gain, epistaxis, back pain, nasopharyngitis, hyperglycemia.

Drug and food interactions: With clarithromycin increases plasma concentration of atorvastatin. Reduced dose required (max. 10 mg daily) with concomitant cyclosporine/ tipranavir combined with ritonavir. Maximum dose of 40 mg once daily when combined with anion-exchange resin for heterozygous familial hypercholesterolemia. Use with caution in patient with high alcohol intake.

CHOLESTYRAMINE RESINS

Dosage form and strength: *Powder (sachet):* 4 gm

Indications: Adjunct to dietary therapy to decrease elevated serum cholesterol and LDL concentrations, cholestasis induced pruritus.

Contraindications/Precautions: Avoid in severe hypertriglyceridemia.

Dosage schedule:

- *Lipid reduction (after initial introduction over 3-4 week):* Oral, adult: 12-24 g daily in water in single or up to 4 divided doses, up to 36 g daily if necessary
- *Cholestasis induced pruritus:* Oral, adult: 4-8 g daily in water.

Adverse effects: Bloating, dyspepsia, constipation, abdominal pain and distention, anorexia, biliary colic, and skin rash.

Drug and food interactions: Long term high-dose cholestyramine therapy may impair the absorption of fat-soluble vitamins. Concomitant use causes reduced absorption of thyroid hormones, warfarin.

Patient's information: Adverse effects can be substantially reduced if the drug is completely suspended in liquid several hours before ingestion (e.g. evening doses can be mixed in morning and refrigerated similarly morning in previous evening)

EZETIMIBE

Dosage form and strength: *Tablet:* 10 mg.

Indications: Adjunct to dietary measures and statin treatment in primary hypercholesterolemia, adjunct to dietary measures and statin in homozygous familial hypercholesterolemia, Primary hypercholesterolemia (if statin inappropriate or not tolerated), Adjunct to dietary measures in homozygous sitosterolemia

Contraindication/Precautions: Avoid in moderate to severe hepatic impairment, myopathy, elevated hepatic transaminases, renal impairment (CrCl less than or equal to 30 ml/min/1.73 m^2). Pregnancy (C) Breast feeding: avoid.

Dosage schedule: Oral, adult: 10 mg daily

Adverse effects: Fatigue, gastro-intestinal disturbances, headache, myalgia.

Rare: anaphylaxis, angioedema, arthralgia, hepatitis, hypersensitivity reactions, rash. Very rare: cholecystitis, cholelithiasis, myopathy, pancreatitis, raised creatine kinase, rhabdomyolysis, and thrombocytopenia

Drug and food interaction: An increased risk of rhabdomyolysis if Ezetimibe is used in combination with a statin. Avoid use with cyclosporine.

FENOFIBRATE

Dosage form and strength: *Capsule:* 160 mg

Indications: Severe hypertriglyceridemia.

Contraindications/Precautions: Avoid in gall bladder disease, hypoalbuminemia, nephrotic syndrome, during pregnancy, breast feeding, severe hepatic impairment. Use caution in mild to moderate renal and hepatic impairment. Monitor serum liver transaminases enzymes every 3 month for a year then periodically during therapy

Dosage schedule: Initially 160 mg once daily dose.

Adverse effects: Gastrointestinal disturbances, rash, urticaria, fatigue, headache, impotence.

Drug and food interactions: Avoid use with ketoprofen, other fibrates, photosensitivity seen.

Patient's information: Restrict fat diet during the therapy.

GEMFIBROZIL

Dosage form and strength: *Capsule:* 300 mg

Indications: Adjunct to dietary therapy in hyperlipidemias of types II a, II b, III, IV and V.

Contraindications/Precautions: Avoid in preexisting gallbladder disease, hepatic dysfunction, history of hypersensitivity to the drug. Risk for myopathy/ rhabdomyolysis increases with renal impairment. Assess the liver function test, CBC and electrolytes every 3-6 months and then yearly during therapy. Safety and efficacy in children younger than 18 years of age have not been established. Pregnancy (C). Breast feeding: Avoid

Dosage schedule: Oral, adult: 1.2 g daily usually in 2 divided doses; range 0.9-1.2 g daily.

Adverse effects: abdominal and epigastric pain, diarrhea, nausea, anorexia, headache, sexual dysfunction, myopathy, myositis, urticaria and pruritus.

Drug and food interactions: May potentiate the anticoagulant effects of oral anticoagulants, may increase the effects of sulfonylurea and oral hypoglycemia agents.

NICOTINIC ACID (NIACIN)

Dosage form and strength: *Tablet:* 50 mg, 250 mg

Indications: Adjunct to statin in hypertriglyceridemia and or used alone if statin not tolerated.

Contraindications/Precautions: Avoid in arterial hemorrhage, active peptic ulcer, and breast feeding. Use caution in liver disease, gout, diabetes mellitus, gallbladder disease, renal impairment. Pregnancy (A, C- for doses exceeding RDA). Breast feeding: use caution.

Dosage schedule: Oral, adult: Initially 100-200 mg 3 times daily, gradually

increased over 2-4 weeks to l-2 g 3 times daily.
Adverse effects: diarrhea, nausea, vomiting, flushing, palpitations, dizziness, pruritus and rash.
Drug and food interactions: May potentiate the anticoagulant effects of oral anticoagulants. Increased risk of rhabdomyolysis and other toxicitites with HMC co-A reductase inhibitors.

SIMVASTATIN

Dosage form and strength: *Tablet:* 5 mg, 10 mg, 20 mg, 40 mg
Indication: Primary and secondary prevention of atherosclerotic cardiovascular disease, in high risk individuals (e.g. with diabetes mellitus, post Myocardial infarction)
Contraindications/Precautions: Avoid in pregnancy(X), breast-feeding, active liver disease (or in patients with persistently abnormal liver function tests). Use caution in elderly (>65 years), hepatic or renal dysfunction, and uncontrolled hypothyroidism and perioperative periods and other factors inhibiting statin catabolism due to increased risk of myopathy. Dose should be reduced if the aforementioned drugs should be used concomitantly. As soon as myopathy is suspected, blood analysis should be done to document significant elevation of creatinine phosphokinase (CPK) levels (>3 times the upper limit of normal) then statin use should be discontinued.
Dosage schedule: *For prevention of cardiovascular events:* Oral, adult: initially 20-40 mg once daily at night (maximum 80 mg once daily at night- only for those with severe hypercholesterolemia and at high risk of cardiovascular complications).
Adverse effects: Upper respiratory tract infection, myalgia, myopathy (dose dependent), myositis, rhabdomyolysis, eosinophilia, eczema, vertigo, abdominal pain, dyspepsia, raised serum transaminases, hepatitis, jaundice, peripheral neuropathy, paresthesia, anemia, alopecia, and rashes, hypersensitivity reactions (angioedema and anaphylaxis), cognitive side effects (non serious and reversible), hyperglycemia (HbA1c and fasting glucose level increase), immune mediated necrotizing myopathy (rare)
Drug and food interactions: With gemfibrozil, cyclosporine, digoxin, warfarin, verapamil, diltiazem, macrolide antibiotics (erythromycin, clarithromycin), azole antifungals, niacin, HIV protease inhibitors, and amiodarone. These drug reduce the catabolism of statins and cause myopathy and rhabdomyolysis

ROSUVASTATIN

Dosage form and strength: *Tablet:* 5 mg
Indications: Primary hypercholesterolemia (type IIa including heterozygous familial hypercholesterolemia), mixed dyslipidemia (type IIb), or homozygous familial hypercholesterolemia in patients who have not responded adequately to diet and other appropriate measures with or without high cardiovascular risk, Prevention of cardiovascular events in patients at high risk of a first cardiovascular event and with risk factors for myopathy or rhabdomyolysis
Contraindication/Precautions: Avoid in pregnancy, breast feeding, severe renal impairment (eGFR less than 30 ml/ minute/1.73 m^2), hepatic

impairment. Use caution in mild to moderate renal impairment. In patients with high cardiovascular risk. Breast feeding: avoid.

Dosage schedule:

- *Primary hypercholesterolemia* (type IIa including heterozygous familial hypercholesterolemia), mixed dyslipidemia (type IIb), or homozygous familial hypercholesterolemia in patients who have not responded adequately to diet and other appropriate measures / Prevention of cardiovascular events in patients at high risk of a first cardiovascular event and with risk factors for myopathy or rhabdomyolysis: Oral, adult: Initially 5 mg once daily, then increased if necessary up to 20 mg once daily, dose to be increased at intervals of at least 4 weeks.
- *Severe primary hypercholesterolemia* in patients with high cardiovascular risk (under expert supervision): Oral, adult: Initially 5–10 mg once daily, increased if necessary to 20 mg once daily, then increased if necessary to 40 mg once daily, dose to be increased at intervals of at least 4 weeks
- *Dose adjustments with concomitant fibrate:* Initially 5 mg once daily increased if necessary to max. 20 mg daily.
- Renal impairment (eGFR 30–60 ml/minute/1.73 m^2): Initially 5 mg once daily (do not exceed 20 mg daily)

Adverse effects: Flulike symptoms, constipation, urinary tract infection, proteinuria. Gynecomastia, hematuria, peripheral neuropathy, arthralgia.