Chapter 3
CARDIOVASCULAR DRUGS

3.1 BETA-ADRENOCEPTOR BLOCKING DRUGS

Beta-adrenoceptor blocking drugs (beta-blockers) are effective as antihypertensive, antiarrhythmic and antianginal (with exception of prinzmetal's angina) agents by blocking the beta-adrenoreceptors in the heart. Beta-blockers decrease mortality in acute phase of myocardial infarction and in post infarction period. Beta-blockers also block beta-adrenoreceptors in liver, bronchi, pancreas and peripheral vasculature.

Some beta-blockers having intrinsic sympathomimetic activity (ISA, partial agonist activity) have the capacity to stimulate as well as to block adreneregic repceptors. **Acebutolol, pindolol** and **celiprolol** have intrinsic sympathomimetic activity and they tend to cause less bradycardia than the other beta-blockers and may also cause less coldness of the extremities.

Some beta-blockers are lipid soluble and some are water soluble. **Atenolol, celiprolol, nadolol** and **sotalol** are the most water-soluble; they are less likely to cross the blood-brain barrier and may therefore cause less insomnia and night mares. The water-soluble beta-blockers are excreted by the renal route. So these drugs should be used with caution in renal impairment where reduction of dose is often necessary.

Bata-blockers having short duration of action are to be given two or three times daily. Many of these are now available as modified release preparations so that single daily dose is adequate for hypertension. Twice-daily administration may be needed for angina even with a slow-release formulation. Some beta-blockers can be given only once daily; e.g. **atenolol, betaxolol** and **nadolol**.

All beta-blockers slow the heart by depressing myocardium. They are therefore contraindicated in patients with second or third degree heart block. Beta-blockers may precipitate or aggravate heart failure. However, **bisoprolol, carvedilol** and **metoprolol** are known to reduce mortality in patients having stable chronic heart diseases.

Labetalol, celiprolol, carvedilol, and **nebivolol** are beta-blockers that have, in addition, an arteriolar vasodilating action, by diverse mechanisms, and thus lower peripheral resistance. There is no evidence that these drugs have important advantages over other beta-blockers in the treatment of hypertension.

Beta-blockers may precipitate or worsen bronchial asthma and this effect can be life threatening. A cardioselective beta-blocker may be prescribed with extreme caution under specialist supervision in patients who have been suffering from bronchial ashma or chronic obstructive airways disease. **Atenolol, bisoprolol metoprolol and nebivolol** are relatively cardioselective, but they are not cardiospecific. They have a lesser blocking effect on $beta_2$ receptors of brochial smooth muscle but are not free of this side-effect.

Beta-blockers can affect carbohydrate metabolism, causing hypoglycaemia or hyperglycaemia in patients with or without diabetes; they can also interfere with metabolic and autonomic responses to hypoglycaemia, thereby masking symptoms such as tachycardia. However, beta-blockers are not contra-indicated in diabetes, although the cardioselective beta-blockers (see above) may be preferred. Beta-blockers should be avoided altogether in those with frequent episodes of hypoglycaemia. Beta-blockers, especially when combined with a thiazide diuretic, should be avoided for the routine treatment of uncomplicated hypertension in patients with diabetes or in those at high risk of developing diabetes.

HYPERTENSION. Beta-blockers reduce cardiac output, change baroceptor's reflex sensitivity and block peripheral adrenoceptors. Some beta-blockers decrease plasma renin secretion. Some central effect may also contribute to their antihypertensive effect. A beta-blocker alone or with a thiazide can adequately control blood pressure. Combination

preparations of thiazide and beta-blockers preparations should only be used in selected cases. **Betaxolol**, **carteolol**, **levobunolol**, **metoprolol** and **timolol, labetalol** can be prescribed in hypertension in pregnancy, hypertension with angina, and hypertension following acute myocardial infarction; hypertensive crisis and controlled hypotension in anaesthesia. **Labetalol** can cause excessive bradycardia which can be managed with intravenous injection of atropine sulphate 0.6-2.4 mg in divided doses of 600 micrograms. Phenoxybenzamine should always be used together with the beta-blocker in phaeochrmocytoma to avoid hypertensive emergency.

ANGINA. Beta-blockers improve exercise tolerance by reducing cardiac work and relieve symptoms in patients with angina. Beta-blockers and verapamil should not be prescribed together in ischaemic heart disease.

MYOCARDIAL INFARCTION. Atenolol and **metoprolol** may reduce early mortality after intravenous and subsequent oral administration in the acute phase. **Acebutolol**, **metoprolol**, **propranolol** and **timolol** have protective value when started early in the convalescent phase. Sudden cessation of treat-ment with beta-blockers may cause a sudden rebound worsening of myocardial ischaemia.

ARRHYTHMIA. Beta-blockers act as anti-arrhythmic drugs by blocking sympathetic effects on the heart. They may be used in addition with digoxin to control the ventricular response in atrial fibrillation. Beta-blockers are also useful in the management of supraventricular tachycardias. **Esmolol** with a very short duration of action is a relatively cardioselective beta-blocker, used intravenously for the short term treatment of supraventricular arrhythmias, sinus tachycardia or hypertension, particularly in the preoperative period. **Sotalol,** a noncardioselcetive beta-blocker with additional antiarrhythmic activity is used for prophylaxis in paroxysmal supraventri-cular arrhythmias. It also suppresses ventricular ectopic beats and non-sustained ventricular tachycardia. It has been shown to be more effective than lingocaine in the termination of spontaneous sustained ventricular tachycardia due to coronary disease or cardiomyopathy. However, it may induce torsades de pointes in susceptible patients. Esmolol and sotalol are used for the management of arrhythmia only.

HEART FAILURE. Beta-blockers may produce benefit in heart failure by blocking sympathetic activity. **Bisoprolol** and **carvedilol** reduce mortality in any grade of stable heart failure; nebivolol is licensed for stable mild to moderate heart failure in patients over 70 year.

Thyrotoxicosis. Beta-blockers are also used before operation for the preparation for thyroidectomy. The thyroid gland becomes less vascular which makes surgery easier.

Other Uses. Beta-blockers have been used to relieve symptoms of anxiety in patients with palpitations, tremor and tachycardia. Beta-blockers are also used in the prophylaxis of migraine.

ATENOLOL[ED]

Indications : *see under dose*
Cautions: *see under propranolol hydrochloride;* reduce dose in renal impairment
Contraindications: *see under propranolol hydrochloride*
Interactions: *see Appendix-2*
Side-effects: *see under propranolol hydrochloride*
Dose: *by mouth,* Hypertension, 50-100 mg daily (higher doses rarely necessary)
Angina, 50-100 mg daily in 1 or 2 doses.
By intravenous injection, 2.5 mg at a rate of 1mg/minute, repeated at 5 minute interval of a max. of 10 mg
Note. excessive bradycardia can be managed with intravenous injection of atropine sulphate 0.6-2.4 mg in divided doses of 600 micrograms. Arrhythmias, by intravenous infusion 150 mg/kg over 20 minutes repeated every 12 hours if required.

Proprietary Preparations
Apicard *(APC),* Tab., 50 mg, Tk.0.75/Tab.

Atebit *(Asiatic),* Tab., 50 mg, Tk. 0.77/Tab.; 100 mg, Tk. 1.38/Tab.
Ateloc *(Popular),* Tab., 50 mg, Tk. 0.77/Tab.
Atenolol *(Albion),* Tab., 50 mg, Tk. 0.77/Tab.; 100 mg, Tk.1.38/Tab.;
Atenolol *(Amico),* Tab., 25 mg, Tk. 0.45/Tab.; 50 mg, Tk. 0.77/Tab.
Atin *(Jayson),* Tab., 50 mg, Tk. 0.76/Tab.
Betanol (*Sanofi),* Tab., 25 mg, Tk. 0.45/Tab.; 50 mg, Tk. 0.77/Tab.; 100 mg, Tk. 1.37/Tab.
Betasec *(Opsonin),* Tab., 50 mg, Tk. 0.58/Tab.
Cardilock *(Alco),* Tab., 50 mg, Tk. 0.77/Tab.
Cardipro *(Square),* Tab., 50 mg, Tk.0.77/Tab.; 100mg, Tk. 1.36/Tab.
Carsec *(Medimet),* Tab., 100mg, Tk.1.35/Tab.; 50mg, Tk.0.75/Tab.
Etnol *(Biopharma),* Tab., 50 mg, Tk.0.77/Tab.; 100 mg, Tk. 1.38/Tab.
Lonet *(Beximco),* Tab., 50 mg, Tk. 0.77/Tab.
Lopres *(Orion),* Tab., 50 mg, Tk.0.70/Tab.
Normaten *(Navana),* Tab., 50 mg, Tk.0.76/Tab.
Norpress *(Kemiko),* Tab., 50 mg, Tk.0.75/Tab.
Tenocard *(Aristo),* Tab., 50 mg, Tk. 0.75/Tab.
Tenol *(Sonear),* Tab., 50 mg, Tk. 0.76/Tab.
Tenoloc *(Acme),* Tab., 50 mg, Tk. 0.77/Tab.; 100 mg, Tk. 1.37/Tab.
Tenomin *(Pacific),* Tab., 50 mg, Tk. 0.58/Tab.
Tenoren *(ACI),* Tab., 25 mg, Tk. 0.45/Tab.; 50mg,
Atenolol 50 mg + Chlorthalidone25 mg.
Cardipro 50 Plus *(Square),* Tk. 2.76/Tab.
Tenoren Plus *(ACI),* Tab., + Tk. 3.01/Tab.

BISOPROLOL FUMARATE

Indications: hypertension, angina, myocardial infarction, arrhythmias, heart failure
Cautions: *see under Propranolol Hydrochloride*; ensure heart failure not worsening before increasing dose max. 10 mg daily in severe hepatic impairment; reduce dose if GFR less than
20 mL/minute/1.73m2 (max. 10 mg daily)
Contra-indications: *see under Propranolol Hydrochloride*; also acute or decompensated heart failure requiring intravenous inotropes; sino-atrial block
Interactions: *see Appeddix -2*
Side-effects: *see under Propranolol Hydrochloride,* also less commonly depression, muscle weakness, and cramp, rarely hypertriglyceridaemia, syncope, and hearing impairment

Dose: hypertension and angina, usually 10 mg once daily (5 mg may be adequate in some patients); max. 20 mg daily. Adjunct in heart failure, 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; max. 10 mg daily

Proprietary Preparations

Ancor (*Aristo),* Tab. 2.5 mg, Tk.6.00/Tab.; 5mg, Tk.10.00/Tab.; 10 mg, Tk.16.00/Tab.
Betabis *(Acme),* Tab. 2.5 mg, Tk.6.00/Tab.; 5mg, Tk.10.00/Tab.
Betacor *(Popular),* Tab. 2.5mg, Tk.6.00/Tab.; 5mg, Tk.10.00/Tab.
Bislol *(Opsonin),* Tab. 2.5 mg, Tk.4.53/Tab.; 5mg, Tk.7.55.00/Tab.; 10 mg, Tk.12.08/Tab.
Bisocor *(Square),* Tab. 2.5 mg, Tk.6.02/Tab.; 5 mg, Tk.10.04/Tab.; 10 mg, Tk.16.06/Tab.
Bisoloc *(Orion),* Tab. 2.5mg, Tk.6.00/Tab.; 5 mg, Tk.10.00/Tab.
Bisopress *(Nipro JMI),* Tab. 2.5 mg, Tk.6.00/Tab.; 5 mg,Tk.10.00/Tab.
Bisopro *(Incepta),* Tab. 2.5 mg, Tk.6.00/Tab.; 5 mg, Tk.10.00/Tab.
Bisoren *(Renata),* Tab. 2.5 mg, Tk.6.00/Tab.; 5 mg,Tk.10.00/Tab.
B-Prolol *(Sharif),* Tab. 2.5 mg, Tk.6.00/Tab.; 5mg, Tk.10.00/Tab.
Cardicor *(Unimed),* Tab. 2.5 mg, Tk.6.00/Tab.; 5 mg, Tk.10.00/Tab.
Cardinor *(Labaid),* Tab. 2.5 mg,Tk.6.00/Tab.; 5 mg, Tk.10.00/Tab.
Conbis *(RAK),* Tab. 2.5 mg, Tk.6.00/Tab.; 5mg, Tk.10.00/Tab.
Myocard *(General),* Tab. 2.5 mg, Tk.6.00/Tab.; 5 mg, Tk.10.00/Tab.
Myocor *(Biopharma),* Tab. 2.5mg,Tk.6.00/Tab.
Probis *(ACI),* Tab., 2.5mg, Tk.6.00/Tab.; 5mg, Tk.10.00/Tab.
Tabis *(Navana),* Tab. 2.5 mg, Tk.6.00/Tab.; 5mg, Tk.10.00/Tab.
Tenobis *(Drug Intl),* Tab. 2.5 mg, Tk.6.00/Tab.; 5 mg, Tk.10.00/Tab.
Tibeta *(Doctor TIMS),* Tab. 2.5 mg, Tk.6/Tab.

Bisoprolol Fumarate + Hydrochlorothiazide
Ancor Plus *(Aristo),* Tab. 2.5 mg + 6.25 mg, Tk.6.00/Tab.; 5 mg + 6.25 mg, Tk.10.00/Tab.
Bislol Plus *(Opsonin),* Tab. 1.5 mg + 6.25 mg, Tk.4.51/Tab.; 10 mg + 6.25 mg, Tk.12.03/Tab.
Bisocor Plus *(Square),* Tab. 2.5 mg + 6.25 mg, Tk.6.00/Tab.; 5 mg+6.25 mg, Tk.10/Tab.
Bisopro *(Incepta),* Tab. 2.5 mg + 6.25 mg, 10.00/Tab.; 5 mg + 6.25 mg, Tk.6.00/Tab.

Probis Plus *(ACI),* Tab. 2.5 mg + 6.25 mg, Tk. 6.00/Tab.; 5 mg + 6.25 mg, Tk.10.00/Tab.

CARVEDILOL

Indications: hypertension, angina, adjunct to diuretics, digoxin or ACE inhibitors in symptomatic chronic heart failure

Cautions: *see under propranolol hydrochloride,* in heart failure ensure renal function and heart failure not deteriorating before increasing each dose; severe heart failure; avoid in acute or decompensated heart failure requiring intravenous inotropics

Contraindication: *see under propranolol hydrochloride*; hepatic impairment

Interactions: *see Appendix-2*

Side-effects: postural hypotension, dizziness, headache, fatigue, gastrointestinal disturbances, bradycardia, painful extremities,peripheral edema, dry mouth, dry eyes, impotence, disturbances of micturition, AV block, exacerbation of intermittent claudication ,worsening of psoriasis, depressed mood, sleep disturbances, heart failure, changes in liver enzymes, thromobocytopenia ,lecopenia

Dose: hypertension, initially 12.5 mg once daily, increased after 2 days to usual dose of 25 mg once daily; if necessary may be further increased at intervals of at least 2 weeks to max. 50 mg daily in a single or two divided doses. ELDERLY initial dose of 12.5 mg daily may provide satisfactory control

Angina, initially 12.5 mg twice daily, increased after 2 days to 25 mg daily. Heart failure, initially 3.125 mg twice daily (with food); dose increased at intervals of at least 2 weeks to 6.25 mg twice daily, then to 12.5 mg twice daily, then to max. 25 mg twice daily in patients less than 85 kg body weight and max. 50 mg twice daily in patients over 85 kg

Proprietary Preparations

Arilol *(Pacific),* Tab., 6.25 mg, Tk. 2.26/Tab.; 12.5 mg, Tk. 3.76/Tab.; 25 mg, Tk. 6.02/Tab.
Avidol *(Ad-din),* Tab., 6.25 mg, Tk. 3.00/Tab.
Cardivas *(Sun),* Tab., 6.25 mg, Tk. 4.55/Tab.; 12.50 mg, Tk. 6.55/Tab.
Carved *(Biopharma),* Tab., 6.25 mg, Tk.4.50/Tab.; 12.50 mg, Tk. 6.50/Tab.; 25 mg, Tk. 8.03/Tab.
Carvetab *(Medimet),* Tab., 12.5 mg, Tk.5.00/Tab.; 6.25 mg, Tk.3.00/Tab.
Carvipress, *(Acme),* Tab., 6.25 mg, Tk. 3.00/Tab.; 12.50 mg, Tk. 5.01/Tab.; 25 mg, Tk.8.04/Tab.
Carvista *(Incepta),* Tab., 6.25 mg, Tk.3.00/Tab.; 12.50 mg, Tk. 5.00/Tab.; 25 mg, Tk. 8.00/Tab.
Cavelon *(Drug Intl),* Tab., 6.25 mg, Tk.3.00/Tab.; 12.50 mg, Tk. 6.00/Tab.
Dilapress *(Beximco),* Tab., 6.25 mg, Tk.3.00/Tab.; 12.50 mg, Tk. 5.00/Tab.
Dilatrend *(Radiant),* Tab., 6.25 mg, Tk.11/Tab.
Dilgard *(General),* Tab., 6.25 mg, Tk.3.01/Tab.; 12.50 mg, Tk. 5.02/Tab.; 25 mg, Tk. 8.03/Tab.
Dilocard *(White Horse),* Tab., 6.25 mg, Tk.3.00/Tab.; 12.5 mg, Tk. 5.00/Tab.
Diola *(Novartis),* Tab., 6.25 mg, Tk. 6.25/Tab.; 12.50 mg, Tk. 9.50/Tab.
Durol *(Square),* Tab., 6.25 mg, Tk. 3.01/Tab.; 12.5 mg, Tk. 5.01/Tab.; CR Cap., 10 mg, Tk.9.00/Cap.; CR Cap., 20 mg, Tk. 15.00/Cap.
Exepress *(Opsonin),* Tab., 3.125 mg, Tk.1.14/Tab.; 6.25 mg, Tk. 2.26/Tab.;12.50mg, Tk. 3.77/Tab.; 25 mg, Tk. 6.04/Tab.
Karvedil *(ACI),* Tab., 6.25mg, Tk. 3.01/Tab.; 12.5mg, Tk. 4.02/Tab.; 25mg, Tk. 8.03/Tab.
Revodil *(Ibn Sina),* Tab., 6.25 mg, Tk.3.00/Tab.
Rovedilol *(Healthcare),* Tab., 6.25 mg, Tk.4.00/Tab.; 12.5 MG, Tk. 7.00/Tab.
Ucardol *(Unimed),* Tab., 6.25 mg, Tk.3.00/Tab.; 12.50 mg, Tk. 5.00/Tab.; 25 mg, Tk. 9.00/Tab.
Vesodil *(Rangs),* Tab., 12.5 mg, Tk. 5.00/Tab.; 25mg, Tk.8.00/Tab.; 6.25 mg,Tk. 3.00/Tab.

CELIPROLOL HYDROCHLORIDE

Indications: mild to moderate hypertension

Cautions: *see under propranolol hydrochloride*

Contraindication: see under propranolol hydrochlorid

Interactions: *see Appendix-2*

Side-effects: *see under propranolol hydrochlorid*

Dose: 200 mg once daily in the morning, increased to400mg once daily if necessary

Proprietary Preparations
Celepress *(Easkayef*),Tab.200mg,Tk.10/Tab.

LABETALOL HYDROCHLORIDE

Indications: hypertension (including hypertension in pregnancy, hypertension with angina, and hypertension following acute myocardial infarction); hypertensive crisis, controlled hypotension in anaesthesia
Cautions: *see under Propranolol* Hydrochloride; interferes with laboratory tests for catecholamines; liver damage (see below); Renal impairment- dose reduction may be required; if severe hepatocellular damage labetalol should be stopped and not restarted
Contra-indications: *see under Propranolol Hydrochloride*
Interactions: *see Appendix-2*
Side-effects: postural hypotension (avoid upright position during and for 3 hours after intravenous administration), tiredness, weakness, headache, rashes, scalp tingling, difficulty in micturition, epigastric pain, nausea, vomiting; liver damage *(see above)*
Dose: *by mouth,* initially 100 mg (50 mg in elderly) twice daily with food, increased at intervals of 14 days to usual dose of 200 mg twice daily; up to 800 mg daily in 2 divided doses (3–4 divided doses if higher); max. 2.4 g daily
By intravenous injection, 50 mg over at least 1 minute, repeated after 5 minutes if necessary; max. total dose 200 mg **:** Excessive bradycardia can be countered with intravenous injection of atropine sulphate 0.6–2.4mg in divided doses of 600 micrograms
By intravenous infusion, 2 mg/minute until satisfactory response then discontinue; usual total dose 50–200 mg, (not recommended for phaeochromocytoma) Hypertension of pregnancy, 20 mg/hour, doubled every 30 minutes; usual max. 160 mg/hour
Hypertension following myocardial infarction, 15 mg/hour, gradually increased to max. 120 mg/hour

Proprietary Preparations
Labeta *(Beximco),* Tab., 200 mg, Tk.10.04/Tab.
Labecard *(Popular),* Tab., 100 mg, Tk.6.02/Tab.; 200 mg, Tk. 10.04/Tab.; Inj., 5mg/ml, Tk. 100.38/Vial

METOPROLOL TARTARATE

Indications : *see under Dose*

Caution : *see under propranolol hydro-chloride*

Interactions: *see Appendix-2*

Side-effects: *see under propranolol hydrochloride*

Dose: *by mouth;* hypertension, initially 100 mg daily, main-tenance 100-200 mg daily in 2 divided doses;
Angina, 50-100 mg 2-3 times daily;
Arrhythmias, usually 50mg 2-3 times daily, up to 300 mg daily in divided doses if necessay;
Migraine prophylaxis, 100-200mg daily in divided dose;
Hyperthyroidism (adjunct), 50mg 4 times daily.
By intravenous injection, Arhythmias, up to 5 mg at rate 1-2 mg/minute, repeated after 5 minutes if necessary, total dose 10-15 mg.
Note. excessive bradycardia can be countered with intravenous injection of atropine suplhate 0.6-2.4 mg in divided doses of 600 micrograms

In surgery, 2-4 mg by slow intravenous injection at induction or to control arrhythmias developing during anaesthesia; 2 mg doses may be repeated to a max. of 10 mg.

Early intervention within 12 hours of infarction, 5 mg by intravenous injection every 2 minutes, to a max. of 15 mg, followed after 15 minutes by 50 mg by mouth every 6 hours for 48 hours; maintenance 200 mg daily in divided doses.

Proprietary Preparations
Angilat *(ACI),*Tab.,25 mg,Tk. 1.50/Tab.; 50mg, Tk. 2.00/Tab.
Betacard *(Aristo),* Tab., 50 mg, Tk. 2.00/Tab.
Betaloc *(Drug Int),* XR Tab., 50 mg, Tk.4.00/Tab.; XR Tab., 100 mg, Tk.6.00/Tab.; Tab., 25 mg, Tk. 1.50/Tab.; Tab., 50 mg, Tk.2.00/Tab.
Betaone *(Acme),* Tab., 25 mg, Tk.1.50/Tab.; 50 mg, Tk. 2.00/Tab.
Metocard *(Popular),* Inj., 1 mg/ml, Tk.120.45/Amp.
Metoprol XL *(Beximco),* ET Tab., 100 mg, Tk.5.00/Tab.; ER Tab., 50 mg, Tk. 3.00/Tab.
M-Loc *(Sharif),* Tab., 50 mg, Tk. 2.00/Tab.
Preloc *(Opsonin),* Tab., 50 mg, Tk. 1.50/Tab.
Prolol *(Ad-din),* Tab., 50 mg, Tk. 1.30/Tab.
Presonil *(Incepta),* Tab., 50 mg, Tk. 1.30/Tb.
Selomet *(Unimed),* SR Tab., 50 mg, Tk. 4.00/Tab.;Tab., 25 mg, Tk. 1.50/Tab.;Tab., 50mg, Tk. 2.00/Tab.
Topress *(Eskayef),*Tab, 50 mg, Tk. 2.00/Tab.

NEBIVOLOL

Indications: essential hypertension; adjunct in stable mild to moderate heart failure in patients over 70 years
Cautions: *see under Propranolol Hydrochloride*,renal impairment avoid if serum creatinine greater than 250 micromol/litre
Contra-indications: *see under Propranolol Hydrochloride;* also acute or decompensated heart failure requiring intravenous inotropes
Interactions: *see Appendix-2*
Side-effects: *see under Propranolol Hydrochloride*; also oedema and depression
Dose: Hypertension, 5 mg daily; ELDERLY initially 2.5 mg daily, increased if necessary to 5 mg daily.
Adjunct in heart failure, initially 1.25 mg once daily, then if tolerated increased at intervals of 1–2 weeks to 2.5 mg once daily, then to 5 mg once daily, then to max. 10 mg once daily
Renal impairment for hypertension, initially 2.5 mg once daily, increased to 5 mg once daily if required; for heart failure

Proprietary Preparations
Bipinor *(ACI),* Tab., 2.5 mg, Tk. 5.02/Tab.; 5 mg, Tk. 8.03/Tab.
Nebicard *(Unimed),* Tab., 2.5 mg, Tk. 7.00/Tab.; 5 mg, Tk. 12.00/Tab.
Nebita *(Square),* Tab., 2.5 mg, Tk. 7.00/Tab.
Nebilol *(Opsonin),* Tab., 2.5 mg, Tk. 3.77/Tab.; 5 mg, Tk. 6.04/Tab.

PROPRANOLOL HYDROCHLORIDE[ED]

Indications: *see under dose*

Cautions: pregnancy and breast-feeding, avoid abrupt withdrawal in angina, first-degree AV block,hepatic impairment, renal impairment, diabetes, myasthenia gravis.

Contraindications: asthma or history of obstructive airways disease important: *see bronchospasm below*; uncontrolled heart failure, prinzmetal's angina, marked brady-cardia, hypotension, sick sinus syndrome, second or third degree AV block, cardiogenic shock, metabolic acidosis, severe peripheral arterial disease, phaeochromocytoma.

Bronchospasm. it is advised that beta-blockers including cardioselective ones, should not be given to patients with a history of asthmatic attack or broncho-spasm

Interactions: *see Appendix-2*

Side-effects: bradycardia, heart failure, hypotension, conduction disorders, bron-chospasm, exacerbation of intermittent claudication and Raynaud's phenome-non, gastrointestinal disturbances, sleep disturbances

Dose: *by mouth,* hypertension, initially 80 mg twice daily, increased at weekly intervals as required; maintenance 160-320 mg daily;

Portal hypertension, initially 40 mg twice daily, increased to 80 mg twice daily acccording to heart rate; max. 160 mg twice daily;

Phaeochromocytoma (only with an alpha-blocker), 60 mg daily for 3 days before surgery or 30 mg daily in patients unsuitable for surgery;

Angina, initially 40 mg 2-3 times daily; maintenance 120-240 mg daily;

Arrhythmias, hypertrophic obstructive cardiomyopathy, anxiety tachycardia, and thyrotoxicosis (adjucnt), 10 mg to 40 mg 3-4 times daily;

Anxiety with symptoms such as palpitations, sweating, tremor, 40 mg once daily increased to 40 mg 3 times daily if necessary;

Prophylaxis after myocardial infarction, 40 mg 4 times daily for 2-3 days, then 80 mg twice daily, beginning 5 to 21 days after infarction;

Migraine prophylaxis and essential tremor, initially, 40 mg 2-3 times daily, maintenance 80-160 mg daily.

*By intravenous injection:*Arrrhythmias and thyrotoxic crisis, 1 mg over 1 minute, if necessary repeat at 2 minutes intervals, max. 10mg (5mg in anaesthesia)

Note. excessive bradycardia can be countered with intravenous injection of atropine sulphate 0.6-2.4 mg in divided doses of 600 micrograms *(see also sec. 8.1.3)*

Proprietary Preparations
Adlock *(Sonear),* Tab., 10 mg, Tk. 0.50/Tab.; 40 mg, Tk.1.50/Tab.
Beta *(Sun),* TR Cap., 40 mg, Tk.2.50/Cap.
Indever *(ACI),* Tab., 10 mg, Tk. 0.51/Tab.; 40mg, Tk. 1.50/Tab.
Propanol *(Opsonin),* Tab., 10 mg, Tk.0.38/Tab.; 40 mg, Tk. 1.13/Tab.
Propranolol *(Albion),* Tab., 10 mg, Tk.0.24/Tab.; 40 mg, Tk. 0.34/Tab.

SOTALOL HYDROCHLORIDE

Indications: life threating arrythmias including ventricular tachyarrythmias, symptomic nonsustained ventricular tachyarrhythmias. paroxysmal AV re-entrant tachycardias, paroxysmal supraventricular tachycardia after cardiac surgery, maintenance of sinus rhythm following cardioversion of atrial fibrillation or flutter.
Cautions: *see under propranolol hydrochloride;* when stopping sotalol the dose should be reduced gradually
Contraindications: *see under propranolol hydrochloride;* congenital or acquired long QT syndrom, renal failure angina, hypertension, and thyrotoxicosis or for secondary preventation after myocardial infraction
Interactions: *see Appendix-2*
Side-effects: *see under propranolol hydrochloride*
Dose: *by mouth* with ECG monitoring and mesaurment of corrected QT interval, arrythmias, initially, 80mg daily in divided dose; higher dosesof 480-64mg daily for life threating ventricular arrhythmias under special supervision

Tablets used only in prophylaxis atrial tachycardia or fibrillation

Note. excessive bradycardia can be countered with intravenous injection of atropine suplhate 0.6-2.4 mg in divided doses of 600 micrograms.

Proprietary Preparation
Sotalax *(Unimed),* Tab. 80 mg, Tk. 10.00/Tab.

3.2 DRUGS AFFECTING THE RENIN-ANGIOTENSIN SYSTEM AND SOME OTHER ANTIHYPERTENSIVE DRUGS

Hypertension Lowering raised blood pressure decreases the risk of stroke, coronary events, heart failure, and renal impairment. Advice on antihypertensive therapy in this section takes into account the recommendations of the Joint British Societies (JBS2: British Societies' guidelines on prevention of cardiovascular disease in clinical practice. Heart 2005; 91 (Suppl V): v1–v52) and NICE clinical guidance 127 (August 2011), Hypertension—Clinical management of primary hypertension in adults.

Possible causes of hypertension (e.g. renal disease, endocrine causes), contributory factors, risk factors, and the presence of any complications of hypertension, such as left ventricular hypertrophy, should be established. Patients should be given advice on lifestyle changes to reduce blood pressure or cardiovascular risk; these include smoking cessation, weight reduction, reduction of excessive intake of alcohol and caffeine, reduction of dietary salt, reduction of total and saturated fat, increasing exercise, and increasing fruit and vegetable intake.

Thresholds and targets for treatment Patients presenting with a blood pressure of 140/90mmHg or higher when measured in a clinic setting, should be offered ambulatory blood pressure monitoring (or home blood pressure monitoring if ambulatory blood pressure monitoring is unsuitable) to confirm the diagnosis and stage of hypertension.

Stage 1 hypertension:

- Clinic blood pressure 140/90mmHg or higher, and ambulatory daytime average or home blood pressure average 135/85mmHg or higher
- Treat patients under 80 years who have stage 1 hypertension and target-organ damage (e.g. left ventricular hypertrophy, chronic kidney disease, hypertensive retinopathy), cardiovascular disease, renal disease, diabetes, or a 10 year cardiovascular risk ≥20%; in the absence of these conditions, advise lifestyle changes and review annually. For patients under 40 years with stage 1 hypertension but no overt target-organ damage, cardiovascular disease, renal disease, or diabetes, consider seeking specialist advice for evaluation of secondary causes of hypertension

Stage 2 hypertension:

- Clinic blood pressure 160/100mmHg or higher, and ambulatory daytime average or home blood pressure average 150/95mmHg or higher
- Treat all patients who have stage 2 hypertension, regardless of age

Severe hypertension:

- Clinic systolic blood pressure ≥180mmHg or clinic diastolic blood pressure ≥110 mmHg; treat promptly

A target clinic blood pressure below 140/90mmHg is suggested for patients under 80 years; a target ambulatory or home blood pressure average (during the patient's waking hours) of below 135/ 85mmHg is suggested for patients under 80 years; see also Hypertension in the Elderly, below. A target clinic blood pressure below 130/80mmHg should be considered for those with established atherosclerotic cardiovascular disease, or diabetes in the presence of kidney, eye, or cerebrovascular disease. In some individuals it may not be possible to reduce blood pressure below the suggested targets despite the use of appropriate therapy.

DRUG TREATMENT OF HYPERTENSION A single antihypertensive drug is often inadequate in the management of hypertension, and additional antihypertensive drugs are usually added in a step-wise manner until control is achieved. Unless it is necessary to lower the blood pressure urgently (see Hypertensive Crisis, below), an interval of at least 4 weeks should be allowed to determine response; clinicians should ensure antihypertensive drugs are titrated to the optimum or maximum tolerated dose at each step of treatment. Response to drug treatment may be affected by age and ethnicity.

Patients under 55 years:

Step 1

- ACE inhibitor; if not tolerated, offer an angiotensin-II receptor antagonist.

If both ACE inhibitors and angiotensin-II receptor antagonists are contra-indicated or not tolerated, consider a beta-blocker); beta-blockers, especially when combined with a thiazide diuretic, should be avoided for the routine treatment of uncomplicated hypertension in patients with diabetes or at high risk of developing diabetes

Step 2

- ACE inhibitor or angiotensin-II receptor antagonist in combination with a calcium-channel blocker. If a calcium-channel blocker is not tolerated or if there is evidence of, or a high risk of, heart failure, give a thiazide-related diuretic (e.g. chlortalidone or indapamide). If a beta-blocker was given at Step 1, add a calciumchannel blocker in preference to a thiazide-related diuretic (see Step 1 above)

Step 3

- ACE inhibitor or angiotensin-II receptor antagonist in combination with a calcium-channel blocker and a thiazide-related diuretic

Step 4 (resistant hypertension)

- Consider seeking specialist advice
- Add low-dose spironolactone [unlicensed indication], or use high-dose thiazide related diuretic if plasma-potassium concentration above 4.5 mmol/litre
- Monitor renal function and electrolytes

- If additional diuretic therapy is contra-indicated, ineffective, or not tolerated, consider an alphablocker or a beta-blocker

Patients over 55 years, and patients of any age who are of African or Caribbean family origin:

Step 1

- Calcium-channel blocker; if not tolerated or if there is evidence of, or a high risk of, heart failure, give a
- thiazide-related diuretic (e.g. chlortalidone or indapamide)

Step 2

- Calcium-channel blocker or thiazide-related diuretic in combination with an ACE inhibitor or angiotensin-II receptor antagonist (an angiotensin-II receptor antagonist in combination with a calcium-channel blocker is preferred in patients of African or Caribbean family origin)

Steps 3 and 4

- Treat as for patients under 55 years (see above)

Other measures to reduce cardiovascular risk Aspirin in a dose of 75mg daily reduces the risk of cardiovascular events and myocardial infarction. Unduly high blood pressure must be controlled before aspirin is given. Unless contra-indicated, aspirin is recommended for all patients with established cardiovascular disease. Use of aspirin in primary prevention, in those with or without diabetes, is of unproven benefit.
Lipid-regulating drugs can also be of benefit in cardiovascular disease or in those who are at high risk of developing cardiovascular disease.

Hypertension in the elderly Patients who reach 80 years of age while taking antihypertensive drugs should continue treatment, provided that it continues to be of benefit and does not cause significant side-effects. A target clinic blood pressure below 150/90mmHg is suggested for patients over 80 years
Isolated systolic hypertension Isolated systolic hypertension (systolic pressure ≥160 mmHg, diastolic pressure <90 mmHg) is common in patients over 60 years, and is associated with an increased cardiovascular disease risk; it

should be treated as for patients with both a raised systolic and diastolic blood pressure (see above). Patients with severe postural hypotension should be referred to a specialist.

Hypertension in diabetes For patients with diabetes, a target clinic blood pressure below 140/80mmHg is suggested. Most patients require a combination of antihypertensive drugs, antihypertensive treatment prevents macrovascular and microvascular complications. An ACE inhibitor (or an angiotensin-II receptor antagonist) may have a specific role in the management of diabetic nephropathy; in patients with type 2 diabetes, an ACE inhibitor (or an angiotensin-II receptor antagonist) can delay progression of microalbuminuria to nephropathy.

Hypertension in renal disease A target clinic blood pressure below 140/90mmHg is suggested (below 130/80 mmHg is advised in patients with chronic kidney disease and diabetes, or if proteinuria exceeds 1 g in 24 hours). An ACE inhibitor (or an angiotensin-II receptor antagonist) should be considered for patients with proteinuria; however, ACE inhibitors should be used with caution in renal impairment, high doses of loop diuretics may be required.

Hypertension in pregnancy
Labetalol is widely used for treating hypertension in pregnancy. Methyldopa is considered safe for use in pregnancy. Modified-release preparations of nifedipine for warnings on use during pregnancy. The following advice takes into account the recommendations of NICE Clinical Guideline 107 (August 2010).

Pregnant women are at high risk of developing preeclampsia if they have chronic kidney disease, diabetes mellitus, autoimmune disease, chronic hypertension, or if they have had hypertension during a previous pregnancy; these women are advised to take aspirin in a dose of 75mg once daily [unlicensed indication] from week 12 of pregnancy until the baby is born. Women with more than one moderate risk factor (first pregnancy, aged ≥40 years, pregnancy interval >10 years, BMI ≥35 kg/m2 at first visit, multiple pregnancy, or family history of pre-eclampsia) for developing pre-eclampsia are also advised to take aspirin 75mg once daily [unlicensed indication] from week 12 of pregnancy until the baby is born.

Women with gestational hypertension or pre-eclampsia who have been managed with methyldopa during pregnancy should discontinue treatment within 2 days of the birth. Women with a blood pressure of ≥160/110mmHg who require critical care during pregnancy or after birth should receive immediate treatment with either oral or intravenous labetalol, intravenous hydralazine, or oral modified-release nifedipine to achieve a target blood pressure of <150mmHg systolic, and diastolic 80–100 mmHg.

Hypertensive crisis
In hypertensive crisis prompt treatment with intravenous antihypertensive therapy is generally required. Over the first few minutes or within 2 hours, blood pressure should be reduced by 20–25%. When intravenous therapy is indicated, treatment options include sodium nitroprusside), labetalol, glyceryl trinitrate phentolamine, or esmolol; choice of drug is dependent on concomitant conditions and clinical status of the patient.
Severe hypertension (blood pressure ≥180/110 mmHg) without acute target-organ damage is defined as a hypertensive urgency; blood pressure should be reduced gradually over 24–48 hours with oral antihypertensive therapy, such as labetalol, or the calcium-channel blockers amlodipine, felodipine, or isradipine.
Use of sublingual nifedipine is not recommended.

See also Current recommendations for manage-ment of hypertension according

to Eighth Joint National Committee (JNC8)

3.2.1 ANGITOTENSIN-CONVERTING ENZYME INHIBITORS (ACE inhibitors)

ACE inhibitors inhibit the conversion of angiotensin I to angiotension II. They are effective and well tolerated.

Heart Failure. ACE inhibitors are very useful in all grades of heart failure, combined when appropriate with a diuretic and digoxin. Postassium supplements and potassium-sparing diuretics should be withdrawn before introducing an ACE inhibitor because of the risk of hyperkalaemia. First-dose phenomenon may occur when ACE inhibitors are introduced to patients with heart failure who are already taking a loop diuretic (e.g. furosemide 80 mg daily or more). At the start of treatment the ACE Inhibitor should therefore be at a very low dosage (e.g. captopril 6.25mg) with the patient recumbent and under close medical supervision.

Hypertension. ACE inhibitors are recommended for hypertension when thiazides and beta-blockers are contraindicated, not tolerated, or fail to control blood pressure. They are particularly indicated for hypertension in insulin-dependent diabetics with nephropathy. ACE inhibitors may cause very rapid fall of blood pressure in some patients who are taking diuretic. The first dose should preferably be at bed time.

Myocardial Infarction. ACE inhibitors are indicated for immediate and long-term management of patients who have had myocardial infarction.

Hospital Management. ACE inhibitor therapy for severe heart failure should be started in hospital. Indication in hospital is also recommended for patients-

- receiving more than 80 mg of furosemide daily or its equivalent;
- with palsma-sodium concentration below 130 mmol/litre;
- with pre-existing hypotension;
- with unstable heart failure;
- with plasma-creatinine concentration above 150 micromol/litre;
- receiving high-dose vasodilators;
- aged 70 years or more.

HEART FAILURE

The treatment of chronic heart failure aims to relieve symtoms to improve exercise tolerance, reduce the incidence of acute exacerbations and reduce mortality. An ACE inhibitor, given at an adequate dose, generally achieve these aims. **Digoxin** improves sympt-oms and exercise tolerance and reduces hospitalisation due to acute exacerbations but it does not reduce mortality. Diuretics are required to relieve symptoms in patients with fluid overlaod. Digoxin is given to patients with atrial fibrillation and also to those in sinus rhythm who remain symptomatic despite treatment with ACE inhibitor and diuretic.

A **thiazide diuretic** may be of benefit in patients with mild heart failure and good renal function but are ineffective in patients with poor renal function (estimated creatinine clearance less that 30 ml/minute), where a **loop diuretic** is prefered. If diuresis with a single diuretic is insufficient, a combina-tion of a loop diuretic and a thiazide diuretic may be tried. Addition of **metolazone** may also be considered but the resulting diuresis may be profound; in such case care is needed to avoid potentially dangerous electrolyte distur-bances.

The aldosterone antagonist **spironolactone** may be considered for patients with severe heart failure who are already receiving an ACE inhibitor and a diuretic and possibly also digoxin. Low doses of spironolactone (usually 25mg daily) have been shown to reduce symptoms and mortality in these patients. Close monitoring of serum creatinine and potassium is necessary with any change in treatment or in the patient's clinical condition.

Patients who cannot tolerate ACE inhibitors or in whom they are contra-indicated may be given **isosorbide**

dinitrate with **hydralazine,** but this combination may not be well tolerated. **Angiotension-II receptor antagonists** may be useful alternatives for patients who, because of symptoms such as cough cannot tolerate ACE inhibitors.

The beta-blockers **carvedilol** are of value in selected patients with stable heart failure and left-ventricular systolic dysfunction, **metoprolol** may also be beneficial. Treatment with a beta-blocker in heart failure should usually be initiated under specialist supervision.

Renal Effects. In patients with severe stenosis of the artery supplying a single functioning kidney ACE inhibitors are likely to cause severe and progressive renal failure; they are contraindicated in patients who have critical renovascular disease. Glomerular filtration is likely to be reduced in the affected kidney with the treatment by ACE inhibitor. Therefore, ACE inhibitors are not to be prescribed in patients with known or suspected renovascular disease, unless the blood pressure uncontrollable by other drugs. If they are used in these situations renal function tests are to be done regularly.

Renal function and electrolytes should be measured before initiating ACE inhibitors and monitored during treatment. Although ACE inhibitors now have some special role in some forms of renal disease they can occasionally cause renal impairment, which may lead to renal failure. The elderly are at particular risk. Concomitant treatment with NSAIDs increases the risk of renal damage, and the use of potassium sparing diuretics increase the risk of hyperkalaemia.

Cautions : May cause sharp fall of blood pressure especially in patients taking diuretics, on a low-sodium diet, on dialysis, dehydrated or with heart failure. They should also be given with caution in peripheral vascular disease or generalised atherosclerosis owing to risk of clinically silent renovascular disease. Renal function tests should be carried out before and during treatment and the dose should be reduced in renal impairment. The risk of agranulocytosis is possibly increased in collagen vascular disease. ACE inhibitors should be avoided in patients with a history of idiopathic or hereditary angiedema. ACE inhibitors should be prescribed with caution in breast-feeding. ACE inhibitors should also be given with caution in patients with peripheral vascular disease or those with severe generalised atherosclerosis.

Anaphylactoid Reactions. ACE inhibitors should be avoided during dailysis with dextran sulphate to prevent anaphylactoid reactions**.** They should also be withheld before deseusitization with bee venom. In the volume depleted patients diuretic should be discontiuned or the dose should be reduced significantly 2-3 days before initiation of an ACE inhibitor. If diuretic therapy cannot be stopped, clinical supervision is recommended for at least 2 hours after administration of the first dose of the ACE inhibitor or until the blood pressure has stabilized.

Contra-indications: ACE inhibitors are contraindicated in patients with hypersen-sitivity to ACE inhibitors (including angioedema) and in known or suspected renovascular disease, aortic stenosis or other outflow tract obstruction. ACE inhibitors should not be used in pregnancy

Side-effects: ACE inhibitors can cause profound hypotension and renal impairment. They may also cause angioedema, rashes, pruritus, urticaria, persistent dry cough, pancreatitis and upper respiratory tract symptoms such as sinusitis, rhinitis and sore throat. Gastrointestinal effects reported with ACE inhibitors include nausea, vomiting, dyspepsia, diarrhoea and constipation. Altered liver function tests, chloestatic jaundice and hepatitis have been reported. Blood dyscrasias including thrombocy-topenia, leucopenia, neutropenia and haemolytic anemia have also been reported.

CAPTOPRIL

Indications: mild to moderate essential hypertension alone or with thiazide therapy and severe hypertension resistant to other treatment; congestive cardiac failure; following myocardial infarction, diabetic nephropathy (microalbuminuria greater than 30mg/ day) in insulin-dependent diabetes

Cautions: *see notes above*

Contra-indications: *see notes above*

Interactions: *see Appendix-2*

Side-effects: *see notes above*; also tachycardia, serum sickness, weight loss, stomatitis, maculopapular rash, photosensitivity, flushing and acidosis

Dose: hypertension, used alone, initially 12.5 mg twice daily; if used in addition to diuretic, or in elderly, initially 6.25 mg two times daily (first dose at bedtime); usual maintenance dose 25 mg twice daily, max. 50 mg twice daily (rarely 3 times daily in severe hypertension)

Heart failure, initially 6.25-12.5 mg under close medical supervision *(see notes above);* usual maintenance dose 25mg 2-3 times daily, usual max. 150mg daily

Prophylaxis after infarction in clinically stable patients with asymptomatic or symptomaitc left ventricular dysfunction, initially 6.25mg starting as early as 1 day after infarction, then increased over several weeks to maximum tolerated level in divided doses

Diabetic nephropathy, 50-100mg daily in divided doses; if further blood press-ure reduction required, other antihypertensives may be used in conjunction with captopril; in severe renal impairment, initially 12.5mg twice daily (if concomitant diureitc therapy required, loop diuretic rather than thiazide should be chosen)

Proprietary Preparations
Acetor *(Drug Int),* Tab., 25 mg Tk. 3.00/Tab.
Capotril *(Alco)),* Tab., 25 mg Tk. 3.00/Tab.
Captopril *(Albion),* Tab., 25 mgTk. 3.00/Tab.
Cardopril *(Beximco),* Tab. 25 mg, Tk.3.01/Tab.

CILAZAPRIL

Indications: essential and renovascular hypertension (*see notes above)*; congestive heart failure (adjunct)

Cautions & Side-effects: same as for other ACE inhibitors

Interactions: *see Appendix-2*

Dose: initial dose is 0.5 mg daily; the first dose should be given preferably at bed-time. In the elderly, or those taking diuretics, the diuretic should be withdrawn 2-3 days before cilazapril is started. In the treatment of hypertension 1 to 1.25 mg once daily dose is needed

Proprietary Preparation
Inhibace[I] *(Roche),*Tab. 1mg not availavle

ENALAPRIL MALEATE [ED]

Indication: essential and renovascular hypertension (but *see notes above);* congestive heart failure, prevention of symptomatic heart failure and prevention of coronary ischaemic events in patients with left ventricular dysfunction

Cautions: *see notes above*

Contra-indications : *see notes above*

Interactions: *see Appendix-2*

Side-effects: *see notes above;* also palpitation, arrhythmias, angina, chest pain, syncope, cerebrovascular accident, myocardial infarction, anorexia, stomatitis, hepatic failure, erythema multiforme, Stevens-Johnson syndrome, toxic epider-mal necrolysis, exfoliative dermatitis and pemphigus, confusion, depers-sion, nervousness, asthenia, drowsiness, insomnia, blurred vision, tinnitus, sweating, flushing, impotence, alopecia, dyspnoea and muscle cramps

Dose: hypertension, used alone, initially 5mg once daily; if used in addition to diuretic, in ELDERLY patients, or in renal impairment, initially 2.5mg daily; usual maintenance dose 10-20mg once daily; in severe hypertension the dose may be increased to max. 40mg once daily. Heart failure (adjunct), asymptomatic left ventricular dysfunction, initially 2.5mg daily under close medical supervision;

usual maintenance dose 20mg daily in 1-2 divided doses

Proprietary Preparations
Anapril *(Eskayef),* Tab, 5 mg, Tk. 1.51/Tab.; 10 mg, Tk. 2.70/Tab.
Enalapril *(Albion),* Tab., 5 mg, Tk. 1.52/Tab.; 10 mg, Tk. 2.78/Tab.
Enaril *(Beximco),* Tab., 5 mg, Tk. 1.00/Tab.
Vasopril *(Square),* Tab., 5 mg, Tk. 1.25/Tab.; 10 mg, Tk. 2.26/Tab.

LISINOPRIL

Indications: essential and renovascular hypertension, congestive heart failure, following myocardial infarction in haemodynamically stable patients, diabetic nephropathy in normotensive insulin dependent and hypertensive noninsulin dependent diabetes mellitus

Cautions: *see notes above*

Contraindications: *see notes above*

Interactions: *see Appendix-2*

Side-effects: *see notes above;* tachycardia, cerebrovascular accident, myocardial infarction, dry mouth, confusion, mood change, asthenia, sweating, impotence and alopecia

Dose: hypertension, initially 2.5 mg daily, usual maintenance dose 10-20 mg daily, max. 40 mg daily, if used in addition to diuretic; *see notes above*

Heart failure (adjunct), initially 2.5 mg daily under close medical supervision, usual maintenance dose 5-20 mg daily

Prophylaxis after myocardial infarction, systolic blood pressure over 120 mmHg, 5mg within 24 hours followed by further 5mg, 24 hours later, then 10 mg after a further 24 hours, and continuing with 10 mg once daily for 6 weeks or continued; systolic blood pressure 100-120 mmHg initially 2.5 mg increasing to maintenance dose of 5mg once daily

Note. Should not be started after myocardial infarction if systolic blood pressure is less than 100 mmHg or less; to be withdrawn if prolonged hypotension (systolic blood pressure <90 mmHg) occurs for more than 1 hour.

Diabetic nephropathy, intially 2.5 mg daily adjusted to achieve a sitting diastolic blood pressure below 75 mmHg in normotensive insulin dependent diabetes and below 90 mmHg in hypertensive non-insulin dependent diabetes; usual dose, 10-20 mg daily

Proprietary Preparations
Acepril *(Drug Intl),* Tab., 5 mg, Tk. 7.00/Tab.
Lipril *(Acme),* Tab., 5 mg, Tk. 5.52/Tab.
Lispril *(Medimet),* Tab., 5 mg, Tk.2.25/Tab.
Nop *(Ambee),* Tab., 5 mg, Tk.3.55/ Tab
Stril *(ACI),* Tab., 5 mg, Tk. 3.01/Tab.

PERINDOPRIL

Indications: essential and renovascular hypertension, congestive heart failure

Cautions: inform the physician when there is swelling of the lips, face, tongue, and when there is difficulty in breathing and swallowing

Contraindications: *see notes above*

Interactions: *see Appendix-2*

Side-effects: *see notes above;* asthenia, flushing mood and sleep disturbances

Dose: hypertension, initially 2 mg daily (before food); usual maintenance dosage is 4mg once daily orally in the morning, max. 8mg daily, if necessary, after 1 month of treatment

Congestive heart failure: treatment should be under closed medical supervision, recommended initial dose is 2 mg daily orally in the morning which may be increased to 4 mg daily (once blood pressure acceptability has been demonstrated). In case of renal failure, the dosage of perindopril must be adjusted according to the degree of renal failure; periodic determination of serum potassium and creatinine levels recommended

Proprietary Preparations
Pendoril *(Renata),* Tab., 2 mg, Tk.9.00/Tab.; 4mg, Tk.14.00/Tab.; 8 mg, Tk.24.09/Tab.
Cadnyl *(Square),* Tab., 4 mg, Tk.12.05/Tab.
Versil *(Acme),* Tab., 4 mg, Tk.12.05/Tab.
Pericard *(Asiatic),* Tab.,2 mg, Tk.7/Tab.; 4 mg, Tk.12.00/Tab.

Perindopril Erbumine + Indapamide
Indapril *(Incepta),* Tab., 2 mg + 0.625 mg, Tk.7.00/Tab.; 4 mg + 1.25 mg, Tk. 12.00/Tab.
Midopril *(General),* Tab., 2 mg + 0.625 mg, Tk. 7.00/Tab.; 4 mg + 1.25 mg, Tk. 12.00/Tab.
Pendoril plus *(Renata),* Tab., 2 mg + 0.625mg, Tk. 10.00/Tab.; 4 mg + 1.25 mg, Tk.15.00/Tab.
Pericard Plus *(Asiatic),* Tab., 2 mg + 0.625mg, Tk. 7.00/Tab.; 4 mg + 1.25 mg, Tk.12.00/Tab.
Perindal Plus *(Opsonin),* Tab., 4 mg + 1.25mg, Tk. 9.06/Tab.; 2 mg + 0.625 mg, Tk.5.29/Tab.
Repres Plus *(Square),* Tab., 4 mg + 1.25 mg, Tk. 12.05/Tab.; 2 mg + 0.625 mg, Tk.7.02/Tab.

RAMIPRIL

Indications: mild to moderate hypertension, congestive heart failure (adjunct); following myocardial infarction in patients with clinical evidence of heart failure; prevention of myocardial infarction

Cautions: *see notes above*

Contraindications: *see notes above*

Interactions: *see Appendix-2*

Side-effects: *see notes above;* arrhythmias, angina, syncope, stomatitis, dry mouth, erythema multiforme and pemphigoid exanthema, precipitation or exacer-bation or Raynaud's syndrome, conjunctivitis, confusion, impotence, alopecia, bronchitis and muscle crapmps

Dose: hypertension, initially 1.25 mg daily, increased at intervals of 1-2 weeks; usual 2.5-5 mg once daily; max. 10 mg daily; for use along with diuretics *see notes above*

Heart failure (adjunct), initially 1.25 mg once daily under close medical supervision, increased if necessary at intervals of 1-2 weeks; max. 10 mg daily in single or 2 divided doses.

Prophylaxis after myocardial infarction (started in hospital 3 to 10 days after infarction), initially 2.5 mg twice daily, increased after 2 days to 5 mg daily, maintenance 2.5-5 mg twice daily.

Note. if initial 2.5 mg dose is not tolerated, give 1.25 mg twice daily for 2 days before increasing to 2.5 mg twice daily, then 5mg twice daily; withdraw if 2.5 mg twice daily not tolerated.

Proprietary Preparations
Acecard *(Healthcare),* Tab, 1.25 mg, Tk.3.00/Tab.; 2.5 mg, Tk. 5.00/Tab.; 5 mg, Tk.8.00/Tab.
Cartace *(Ad-din),* Tab., 2.5mg, Tk. 4.60/Tab.
Gepril *(Globe),* Tab., 5 mg, Tk. 8.00/Tab.
G-Ramipril *(Gonoshasthaya),* Tab., 2.5 mg, Tk. 2.50/Tab.; 5 mg, Tk. 4.00/Tab.
Mypril *(Eskayef),* Tab, 2.5 mg, Tk.5.00/Tab.; 5mg, Tk. 8.00/Tab.
Nuvace *(Orion),* Tab., 2.5 mg, Tk.5.00/Tab.; 5mg, Tk. 8.00/Tab.
Piramil *(Novartis),* Tab., 2.5 mg, Tk. 7.00/Tab.; 5 mg, Tk. 10.00/Tab.
Pricard *(White Horse),* Tab., 2.5 mg, Tk.4.00/Tab.;
Primace *(Beximco, Tongi),* Tab., 2.5 mg, Tk.5.00/Tab.; 5 mg, Tk. 8.00 /Tab.
Protace *(Unimed),* Tab., 2.5 mg, Tk.5.00/Tab.; 5 mg, Tk. 8.00/Tab.
Racard *(Pacific),* Tab., 1.25 mg, Tk. 1.88/Tab.; 2.5 mg, Tk. 3.46/Tab.; 5 mg, Tk. 6.02/Tab.
Ramace *(Opsonin),* Tab., 1.25 mg, Tk.1.89/Tab.; 2.5 mg, Tk. 3.77/Tab.; 5 mg, Tk.6.04/Tab.
Ramicard *(Drug Intl),* Tab., 1.25 mg, Tk.2.50/Tab.; 2.5 mg, Tk. 5.00/Tab.; 5 mg, Tk.8.00/Tab.
Ramil *(Popular),* Tab., 1.25 mg, Tk. 2.50/Tab.; 2.5 mg, Tk. 5.02/Tab.; 5 mg, Tk. 8.03/Tab.; 10mg, Tk. 12.00/Tab.
Ramilok *(Aristo),* Tab., 2.5 mg, Tk.5.00/Tab.; 5mg, Tk.8.00/Tab.
Ramipro *(General),* Tab., 2.5 mg, Tk.5.02/Tab.; 5 mg, Tk. 8.03/Tab.
Ramoril *(Incepta),* Tab., 1.25 mg , Tk.2.50/Tab.; 2.5 mg, Tk. 5.00/Tab.; 5 mg, Tk.8.00/Tab.; 10 mg, Tk. 12.00/Tab.
Rampril *(Rangs),* Tab., 2.5mg, Tk. 4.00/Tab.; 5 mg, Tk. 6.00/Tab.
Ripril *(Square),* Tab., 1.25 mg, Tk. 2.51/Tab.; 2.5 mg, Tk. 5.01/Tab.; 5 mg, Tk. 8.04/Tab.
R-P *(Biopharma),* Tab., 1.25 mg, Tk.3.01/Tab.; 2.5 mg, Tk.5.02/Tab.; 5 mg, Tk. 8.03/Tab.
Tritace *(Sanofi),* Tab., 2.5 mg, Tk. 9.50/Tab.; 5mg, Tk. 14.00/Tab.
Unipril *(Acme),* Tab., 1.25 mg , Tk. 2.50/Tab.; 2.5 mg, Tk. 5.01/Tab.; 5 mg, Tk. 8.04/Tab.

Ramipril + Hydrochlorothiazide
Ramicard Plus *(Drug Intl),* Tab., 2.5 mg + 12.5 mg, Tk 3.00/Tab.; 5 mg + 25 mg, Tk. 5.00/Tab.
Ramoril Plus *(Incepta),* Tab., 2.5 mg + 12.50 mg, Tk. 5.00/Tab; 5 mg + 25 mg, Tk. 8.00/Tab.
Protace H *(Unimed),* Tab., 2.5 mg + 12.50 mg, Tk. 5.00/Tab.

3.2.2 ANGIOTENSIN II RECEPTOR ANTAGONISTS (ARB)

Losartan and **valsartan** are specific angiotension-II receptor antagonists; their properties are similar to those of the ACE inhibitors. **Candesartan, eprosartan, irbesartan** and **telmisartan** have been intro-duced more recently. However, unlike ACE inhibitors, they do not cause the persistent dry cough, which is common with ACE inhibitors. They are useful alternatives for patients who have to discon-tinue an ACE inhibitor beacuse of persistent cough.

Cautions: angiotension-II receptor antagonists are to be used with caution in renal artery stenosis. It is advised that plasma-potassium concentration be monitored in the elderly and in patients with renal insufficiency; lower initial doses may be suitable in these patients.

Contraindications: angiotension-II receptor antagonists, should be avoided in pregnancy and bilateral renal artery stenosis.

Side-effects: Hypotension, hyperkala-emia and angioedema.

CANDESARTAN CILEXETIL

Indication : hypertension

Cautions: *see notes above,* mild to moderate hepatic impairment and renal impairment

Contraindications: *see notes above;* severe hepatic and renal impairment, cholestasis, breast-feeding and pregnancy

Interactions: *see Appendix-2*

Side-effects: *see notes above;* dizziness, myalgia, headache, nausea, abdominal pain, back pain, peripheral edema,rash and blood disorder.

Dose: initial dose is 4mg once daily. A lower initial dose of 2mg once daily is suggested for patient with renal impaiment. The dose should be adjusted according to response. The usual maintenance dose 4mg once daily with a maximum dose of 16mg once daily

Proprietary Preparations
Giran *(Aristo),* Tab., 8 mg, Tk. 6.00/Tab.; 16 mg, Tk. 11.00/Tab.
Candesa *(General),* Tab., 4 mg, Tk. 3.51/Tab.; 8 mg, Tk. 6.02/Tab.
Vesotan *(Rangs)*, Tab. 16 mg, Tk. 11.00/Tab.; 8 mg, Tk. 6.00/Tab.

IRBESARTAN

Indications: hypertension, diabetic nephropathy

Cautions: *see notes above*;

Contraindications: *see notes above;* breast-feeding and pregnancy

Interactions: *see Appendix-2*

Side-effects: *see notes above;* diarr-hoea, dyspepsia, dizziness, myalgia, asthenia, tinnitus, tachycardia, cough, rash, urticaria reported

Dose: initially 150mg once daily in hypertension, increased, if necessary, 300mg once daily

Proprietary Preparations
Arbitan *(Opsonin),* Tab., 75 mg, Tk. 4.53/Tab.; 150 mg, Tk. 9.06/Tab.
Cavapro *(Unimed),* Tab., 75 mg, Tk. 6.00/Tab.; 150 mg, Tk. 12.00/Tab.; 300 mg, Tk. 24.00/Tab.
Irbes *(Eskayef),* Tab, 75 mg, Tk. 5.00/Tab; 150 mg, Tk. 9.00/Tab.

Irbesartan+ Hydrochlorothiazide
Arbitan Plus *(Opsonin),* Tab., 12.50 mg + 150 mg, Tk. 9.06/Tab.; 12.50 mg + 75 mg, Tk. 4.53/Tab.

LOSARTAN POTASSIUM

Indication: hypertension

Cautions: *see notes above;* hepatic and renal impairment

Contraindications: *see notes above;* pregnancy and breast-feeding

Interactions: *see Appendix-2*

Side-effects: *see notes above;* diarrhoea, dizziness, taste disturbance, myalgia, migrane, urticaria, pruritus, rash, altered liver function tests.

Dose: usually 50mg once daily (elderly over 75 years, moderate to severe renal impairment, intravascular volume depletion, initially 25mg once daily); if necess-ary increase after several weeks to 100mg once daily

Proprietary Preparations
Acusan *(Concord),* Tab., 50 mg, Tk.8.00/Tab.
Angiloc *(Square),* Tab., 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 8.00/Tab.; 100 mg, Tk.12.00/Tab.
Angitan *(Chemist),* Tab. , 50 mg, Tk. 7.00/Tab.
Anin *(Delta),* Tab., 50 mg, Tk. 5.00/Tab.
Anreb *(General),* Tab., 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 8.00/Tab
Araten *(Unimed),* Tab., 50 mg, Tk. 8.00/Tab.
Arbium *(Asiatic),* Tab., 100 mg, Tk.10.00/Tab.; 25 mg, Tk. 3.50/Tab.; 50 mg, Tk.6.00/Tab.
Cardisan *(Beacon),* Tab., 50 mg, Tk.8.00/Tab.
Cardon *(Eskayef),* Tab., 25 mg, Tk.4.50/Tab.; 50 mg, Tk. 8.00/Tab
G-Losartan *(Gonoshasthaya),* Tab., 25 mg, Tk. 3.00/Tab.; 50 mg, Tk. 5.00/Tab.
Larb *(Opsonin),* Tab., 100 mg, Tk. 9.02/Tab.; 25 mg, Tk. 3.38/Tab.; 50 mg, Tk. 6.02/Tab.
LK *(Pacific),* Tab., 25 mg, Tk. 3.38/Tab.; 50 mg, Tk. 6.02/Tab.
Lok *(Globe),* Tab., 50 mg, Tk. 8.00/Tab.
Lopass *(Novartis),* Tab., 25 mg, Tk. 6.00/Tab.; 50 mg, Tk. 10.00/Tab.
Lopo *(Biopharma),* Tab., 25 mg, Tk.4.50/Tab.;50 mg, Tk. 8.00/Tab.
Losa *(Alco),* Tab., 25 mg, Tk. 3.50/Tab.;50mg, Tk. 6.00/Tab.
Losacor *(Healthcare),* Tab., 50 mg, Tk.8.00/Tab.
Losamax *(Veritas),* Tab., 50 mg, Tk. 8.00/Tab.
Losan *(Orion),* Tab., 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 8.00/Tab.
Losarcar *(Medimet),* Tab., 50mg, Tk.6.00/Tab.; 25mg, Tk.3.50/Tab.
Losardil *(Drug Int.),* Tab., 50 mg, Tk.8.00/Tab. 100 mg, Tk. 12.00/Tab; 25 mg, Tk. 4.50/Tab.
Losark *(Doctor TIMS),* Tab., 50 mg, Tk.8.00/Tab.
Losaron *(Amico),* Tab., 50 mg, Tk.5.00/Tab.;100 mg, Tk. 12.00/Tab.; 25 mg, Tk. 4.50/Tab.
Losart *(Acme),* Tab., 50 mg, Tk. 8.00/Tab.
Losartan *(Albion),* Tab., 100 mg, Tk.10.00/Tab.; 25 mg, Tk. 3.50/Tab.; 50 mg, Tk. 6.00/Tab.
Losartium *(Rangs),* Tab., 50mg, Tk. 8.00/Tab.
Losatan*(Popular),* Tab., 100 mg, Tk.10.04/Tab.; 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 8.00/Tab.
Losium *(Ibn Sina),* Tab., 25 mg, Tk. 3.50/Tab.; 50 mg, Tk. 8.00/Tab.
Lospil *(White Horse),* Tab. 50 mg, Tk.8.00/Tab.
Lotas *(Ambee) ,* Tab., 50mg, Tk. 5.69/Tab
Osartan *(Aristo),* Tab., 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 8.00/Tab.
Osartil *(Incepta),* Tab., 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 8.00/Tab.; 100 mg, Tk. 12.00/Tab.
Ostan *(Renata),* Tab., 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 10.00/Tab.;
Parten *(Jayson),* Tab., 50 mg, Tk. 5.02/Tab.
Pertilos *(Navana),* Tab., 50 mg, Tk. 8.00/Tab.
Prosan *(Beximco)*, Tab., 25 mg, Tk.5.00/Tab.; 50 mg, Tk. 8.00/Tab.
Raklok *(RAK),* Tab., 25 mg, Tk. 3.50/Tab.; 50mg, Tk. 8.00/Tab.
Renosart *(Leon),* Tab., 50 mg, Tk. 8.00/Tab.
Repace *(Sun),* Tab., 25 mg, Tk. 4.50/Tab.; 50mg, Tk. 8.00/Tab.
Taran *(Kemiko),* Tab., 25 mg, Tk. 4.50/Tab.; 50 mg, Tk. 8.00/Tab.
Xelotan *(Pharmasia),*Tab., 50 mg,Tk.6.00/Tab.

Losartan Potassium. + Hydrochlorothiazide
Acusan Plus *(Concord),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Angilock Plus *(Square),* Tab., 100 mg + 12.5mg, Tk. 11.00/Tab.; 100 mg + 25 mg, Tk.12.00/Tab.;50 mg + 12.50 mg, Tk.8.00/Tab.
Angitan plus *(Chemist),* Tab., 50 mg + 12.50 mg , Tk. 8.00/Tab.
Anin 50 Plus *(Delta),* Tab., 50 mg + 12.50mg, Tk. 6.00/Tab.
Anreb *(General),* Tab., 100 mg + 12.50 mg, Tk. 12.00/Tab.
Anreb Plus*(General),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Arbium Plus *(Asiatic),* Tab., 100 mg + 12.50mg, Tk. 10.00/Tab.; 100 mg + 25 mg,

Tk.10.00/Tab. ; 50 mg + 12.50 mg, Tk. 6.00/Tab.
Atsyrm Plus *(Unimed),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Cardisan Plus *(Beacon),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Cardoplus *(Eskayef),* Tab, 50 mg + 12.50mg, Tk. 8.00/Tab.
Larb Plus *(Opsonin),* Tab., 100 mg + 25 mg, Tk. 9.02/Tab.; 50 mg + 12.50 mg, Tk. 6.02/Tab.
LK Plus *(Pacific),* Tab., 50 mg + 12.50 mg, Tk. 6.02/Tab.
Lok-50 Plus *(Globe),* Tab., 50 mg + 12.5 mg, Tk. 6.00/Tab.
Lopass Plus *(Novartis),* Tab., 50 mg + 12.50mg, Tk. 10.00/Tab.
Lopo Plus *(Biopharma),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Losa Plus *(Alco),* Tab., 50 mg + 12.50 mg, Tk.8.00/Tab.
Losacor Plus *(Healthcare),* Tab., 50 mg + 12.50 mg, Tk. 8.00/Tab.
Losamax-H *(Veritas),* Tab., 100 mg + 25 mg, Tk. 12.00/Tab.; 50 mg + 12.50 mg, Tk.8.00/Tab.
Losan D *(Orion),* Tab., 50 mg + 12.50 mg, Tk. 8.00/Tab.
Losarcar plus *(Medimet),* Tab., 50 mg + 12.50, Tk.6.00/Tab.
Losardil Plus *(Drug Int.),* Tab., 100 mg + 12.50mg, Tk. 11.00/Tab.; 100 mg + 25 mg, Tk.12.00/Tab.; 25 mg + 12.50 mg, Tk.5.00/Tab.; 50 mg + 12.50 mg, Tk.8.00/Tab.
Losart Plus *(Acme),* Tab., 100 mg + 12.50mg, Tk. 12.00/Tab.; 100 mg + 25 mg, Tk. 12.00/Tab.; 50 mg + 12.50 mg, Tk. 8.00/Tab.
Losartan Plus *(Albion),* Tab., 50 mg + 12.50mg, Tk. 6.00/Tab.
Losartium-H *(Rangs),* Tab., 50 mg+12.50 mg, Tk. 8.00/Tab.
Losatan HZ *(Popular),* Tab, 50 mg+12.50 mg, Tk. 8.00/Tab.
Losium Plus *(Ibn Sina),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Lospil Plus *(White Horse),* Tab., 50 mg + 12.50 mg, Tk. 8.00/Tab.
Lotas plus *(Ambee) ,* Tab., 50 mg + 12.5 mg, Tk. 5.02 / Tab
Osartan-HZ *(Aristo),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Osartil Plus *(Incepta),* Tab., 100 mg + 25 mg, Tk. 12.00/Tab. ; 100 mg + 12.50 mg, Tk. 12.00/Tab.; 50 mg + 12.50 mg, Tk. 8.00/Tab.
Oscard *(Sharif),* Tab., 50 mg + 12.50 mg, Tk.6.00/Tab.
Ostan Plus *(Renata),* Tab., 100 mg + 25 mg, Tk. 8.00/Tab.
Parten Plus *(Jayson),* Tab., 50 mg + 12.50mg, Tk. 6.02/Tab.
Preslo-H *(Labaid),* Tab., 50 mg + 12.50 mg, Tk. 8.00/Tab.
Prosan HZ *(Beximco),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Reladol *(Globe),* 50 mg + 12.50 mg, Tk.6.00/Tab.
Renosart Plus*(Leon),* Tab., 50 mg + 12.50mg, Tk. 8.00/Tab.
Repace H *(Sun),* Tab., 50 mg + 12.50 mg, Tk.8.00/Tab.
Xelotan Plus 50 *(Pharmasia),* Tab., 50 mg + 12.50 mg, Tk. 6.00/Tab.

OLMESARTAN MEDOXOMIL

Indication: hypertension
Cautions: *see notes above*; hepatic impairment-dose should not exceed 20mg daily in moderate impairment
Contra-indications: *see notes above*; biliary obstruction, severe renal impairment
Interactions: *see Appendix- 2*
Side-effects: *see notes above;* also gastro-intestinal disturbances, chest pain, peripheral oedema, hypertriglyceridaemia, fatigue, influenza-like symptoms, cough, pharyngitis, urinary-tract infection, haematuria, hyperuricaemia, arthritis, myalgia, pruritis, urticaria
Dose: initially 10 mg once daily; if necessary increased to 20 mg once daily; max. 40 mg daily.
Reanal impairment-max. 20mg daily if eGFR 20-60mL/minutes/1.73m^3 ; avoid if eGFR less than 20mL/minutes/1.73m^3

Proprietary Preparations

Abetis *(ACI),* Tab. , 10 mg , Tk. 5.02/Tab.; 20mg , Tk. 8.03/Tab.; 40 mg , Tk. 15.06/Tab.
Olme *(Albion),* Tab. , 20 mg, Tk. 8.00/Tab.; 40 mg, Tk. 15.00/Tab.
Olmecar *(Square),* Tab. , 20 mg, Tk. 8.00/Tab.; 40 mg, Tk. 15.00/Tab.
Olmesan *(Beximco),* Tab. , 20 mg, Tk. 8.00/Tab.; , 40 mg, Tk. 15.00/Tab.
Olmesart *(Sharif),* Tab. 20 mg,Tk. 8/Tab.; 40 mg, Tk. 15.00/Tab.
Olmetic *(Drug Int.),* Tab. 20 mg, Tk.8.00/Tab.
Olmezest *(Sun),* Tab. , 10 mg, Tk. 5.00/Tab.; 20 mg, Tk. 8.05/Tab.; 40 mg, Tk. 15.00/Tab.
Olsart *(Opsonin),* Tab., 20 mg, Tk. 6.02/Tab.; 40 mg, Tk. 11.28/Tab.
Orbas *(Acme),* Tab., 20 mg, Tk. 8.00/Tab.; 40mg, Tk. 15.00/Tab.
Tenicar *(Unimed),* Tab. , 20 mg, Tk. 8.00/Tab.; 40 mg, Tk. 15.00/Tab.
Xyotil *(Incepta),* Tab. , 20 mg, Tk. 8.00/Tab. ; 40 mg, Tk. 15.00/Tab.

Olmesartan Medoxomil 20 mg + Hydrochlorothiazide 12.50 mg
Abetis Plus *(ACI),* Tab. Tk. 8.03/Tab.
Olmecar Plus *(Square),* Tab. Tk. 8.00/Tab.
Olme-H *(Albion),* Tab. Tk. 8.50/Tab.
Olmesan Plus *(Beximco),* Tab. Tk. 8.00/Tab.
Plmetic Plus *(Drug Int.),* Tab. Tk. 8.00/Tab.
Olmezest H *(Sun),* Tab. Tk. 8.50/Tab.
Olsart HZ *(Opsonin),* Tab.Tk. 6.02/Tab.;Tab., 40 mg + 12.50 mg, Tk. 11.32/Tab.
Tenizide *(Unimed),* Tab. Tk. 8.00/Tab.
Xyotil *(Incepta),* Tab.Tk. 8.00/Tab.

TELMISARTAN

Indication: hypertension
Cautions: *see notes above;* mild to moderate hepatic impairment and renal impairment
Contraindications: *see notes above;* biliary obstruction, breast-feeding
Interactions: *see Appendix-2*
Side-effects: *see notes above,* influenza like symptom, flatulence, anxiety, vertigo, increased sweating, blood disorder, increase in uric acid
Dose: usually 40mg once daily, increased if necessary after at least 4 weeks, to max. 80mg once daily.

Proprietary Preparations
Mitosan *(Novartis),* Tab., 40 mg, Tk.13.00/Tab.; 80 mg, Tk. 21.00/Tab.
Telcardis *(Unimed),* Tab., 40 mg, Tk.12.50/Tab.; 80 mg, Tk. 20.00/Tab.

Telmisartan + Hydrochlorithiazide
Mitosan Plus *(Novartis),* Tab., 40 mg + 12.50 mg, Tk. 13.00/Tab. ; 80 mg + 12.50 mg, Tk. 21.00/Tab.
Telcardis Plus *(Unimed),* Tab. , 80 mg + 12.50 mg, Tk. 20.00/Tab.; 40 mg + 12.50 mg, Tk. 12.50/Tab.

VALSARTAN

Indication : hypertension
Cautions: *see notes above;* mild to moderate hepatic impairment and renal impairment
Contraindications : *see notes above;* severe hepatic impairment, cirrhosis, biliary obstruction, breast-feeding
Interactions: *see Appendix-2*
Side-effects : *see notes above;* fatigue, neutropenia reported
Dose: usually 80 mg once daily (elderly over 75 years, mild to moderate hepatic impairment, severe renal impairment, intravascular volume depletion, initially 40 mg once daily); increase after at least 4 weeks to 160 mg once daily (80 mg daily in hepatic impairment)

Proprietary Preparations
Disys *(Healthcare),* Tab., 80 mg, Tk.10.00/Tab.; 160 mg, Tk. 18.00/Tab.
Arovan *(Aristo),* Cap., 80 mg, Tk. 10.00/Tab.
Valsartil *(Incepta),* Tab., 40 mg, Tk.5.00/Tab.; 80 mg, Tk. 9.00/Tab; 160 mg, Tk. 66.00/Tab.
Valset *(Orion),* Tab., 80 mg, Tk. 6.02/Tab.
Diovan *(Novartis),* Tab., 40 mg, Tk.34.00/Tab. 80 mg, Tk. 48.00/Tab.; 160 mg, Tk. 66.00/Tab.
Valtin *(Acme),* Tab., 80 mg, Tk. 9.00/Tab.; 160 mg, Tk. 16.00/Tab.
Cardival *(Drug Int.),* Tab., 80 mg, Tk.10.00/Tab.

Valsartan + Hydrochlorothiazide
Co-Diovan *(Novartis),* Tab., 160 mg + 12.50mg, Tk. 66.00/Tab;.Tab. , 160 mg + 25mg, Tk. 66.00/Tab.; 80 mg + 12.50 mg, Tk.48.00/Tab.
Cardival Plus *(Drug Intl),* Tab., 160 mg + 12.50 mg, Tk. 16.00/Tab.
Valsartil 80 Plus *(Incepta),* Tab., 80 mg + 12.50 mg, Tk. 9.00/Tab.; T160 mg + 25 mg, Tk. 16.00/Tab.
Valzide *(Renata),* Tab., 80 mg + 12.50 mg, Tk. 20.00/Tab. ; 80 mg + 12.50mg, Tk. 11.00/Tab.
Disys Plus *(Healthcare),* Tab., 80 mg + 12.50mg, Tk. 10.00/Tab.

Amlodipine + Valsartan
Amlosartan *(Incepta),* Tab. 10 mg + 160 mg, Tk. 16.00/Tab.; 5 mg + 160 mg, Tk. 16.00/Tab.; 5 mg + 80 mg, Tk. 9.00/Tab.
Amlovas VS *(Popular),* Tab.10mg +160mg, Tk. 16.0/Tab.; 5mg + 160mg, Tk. 16.06/Tab.; 5 mg + 80 mg, Tk. 9.03/Tab.
AV *(Drug Intl),* Tab.10 mg + 160 mg, Tk.10.00/Tab.; 5 mg + 160 mg, Tk. 8.00/Tab.
Avodil VI *(Opsonin),* Tab. 10 mg + 320 mg, Tk. 24.06/Tab.
Camoval *(Square),* Tab. 5 mg + 160 mg, Tk. 16.06/Tab.; 5 mg + 80 mg , Tk. 9.03/Tab.
Co-Disys *(Healthcare),* Tab. 5 mg + 80 mg, Tk. 10.00/Tab.; 5 mg + 160 mg, Tk. 18.00/Tab.; 10 mg + 160 mg, Tk. 19.00/Tab.
Co-Valtin *(Acme),* Tab. 5 mg + 160 mg , Tk. 16.00/Tab.; 5 mg + 80 mg , Tk. 9.00/Tab.

Exforge *(Novartis),* Tab. 10 mg + 160 mg, Tk. 78.85/Tab.; 5 mg + 160 mg, Tk. 70.54/Tab.; 5 mg + 80 mg, Tk. 50.35/Tab.

Amlodipine + Olmesartan Medoxomil
Abecab *(ACI),* Tab. 5 mg + 20 mg, Tk. 8.03/Tab.; 5 mg + 40 mg, Tk. 15.00/Tab.
Bizoran *(Beximco),* Tab. 5 mg + 20 mg, Tk. 8.00/Tab.; 5 mg + 40 mg, Tk. 15.00/Tab.
Calnor *(Opsonin),* Tab. 5 mg + 20 mg, Tk. 6.02/Tab.
Camlosart *(Square),* Tab. 5 mg + 40 mg, Tk. 15.00/Tab.; 5 mg + 20 mg, Tk. 8.00/Tab.
Disartan *(Drug Intl),* Tab. 5 mg + 20 mg, Tk. 8.00/Tab.
Olmezest AM *(Sun),* Tab. 5 mg + 20 mg, Tk. 8.50/Tab.
Orbapin *(Acme),* Tab. 5 mg + 20 mg, Tk. 8.00/Tab.
Tenivasc *(Unimed),* Tab. 5 mg + 20 mg, Tk. 8.00/Tab.

Amlodipine + Benazepril
Amlozep *(Beacon),* Cap., 5 mg + 10 mg, Tk. 6.00/Tab.
Amocal - BZ *(Opsonin),* Cap., 5 mg + 10 mg, Tk. 4.53/Tab
Benadip *(Incepta),* Cap., 5 mg + 10 mg, Tk. 6.00/Tab.; 2.5 mg + 10 mg, Tk. 4.00/Tab.; 5 mg + 20 mg, Tk. 8.00/Tab.
Camlopril *(Square),* Cap., 5 mg + 10 mg, Tk. 6.02/Tab.; 5 mg + 20 mg, Tk. 8.04/Tab.

Amlodipine + Telmisartan
Cardotel*(Pharmasia),* Tab. , 5 mg + 40 mg, Tk. 8.00/Tab.

3.2.3 RENIN INHIBITORS

Renin inhibitors inhibit renin directly; renin converts angiotensinogen to angiotensin I.
Aliskiren is the first in the class of renin blokers, Furthermore, renin inhibition decreases all the down-stream messengers leading to the receptors.
It may be preferred in renal disease.ACE inhibitors, ARBs, and diuretics all increase renin and plasma renin activity. By contrast, aliskiren neutralizes any compensatory increase in plasma renin activity even during combined therapy with a thiazide diuretic, an ACE inhibitor, or ARB and prevents the formation of both angiotensin I and angiotensin II. Aliskiren is licensed for the treatment of hypertension, either alone or in combination with other antihypertensives.

ALISKIREN

Indication: essential hypertension
Cautions: patients taking concomitant diuretics, on a low-sodium diet, or who are dehydrated (first doses may cause hypotension—initiate with care); renal artery stenosis, renal impairment; monitor plasma-potassium concentration and renal function in diabetes mellitus and heart failure, pregnancy and breast feeding.
Contraindications: concomitant use with ACE inhibitors or ARBs in patients with diabetes, pregnancy and lactation
Interactions: *see Appendix-2*
Side-effects: diarrhea, angioedema acute renal failure (reversible on discontinuation of treatment), anaemia, and hyperkalaemia also reported
Dose: ADULT over 18 years, 150 mg once daily, increased if necessary to 300 mg once daily

Proprietary Preparations
Rasilez(I) *(Novartis),* Tab. 150 mg, Tk. 62.50/Tab.; Tab., 300 mg, Tk. 78.00/Tab.

Aliskiren + Hydrochlorothiazide
Rasilez HCT(I) *(Novartis),* Tab., 150 mg + 12.5 mg, Tk. 62.50/Tab.

3.2.4 ALPHA ADRENOCEPTOR BLOCKING DRUGS

Prazosin which has post-synaptic alpha-blocking and vasodilator properties, causes a rapid reduction in blood pressure after the first dose and should be prescribed carefully; it rarely causes tachycardia. **Doxazosin, indoramin**, and **terazosin** have properties similar to those of prazosin. **Alfuzosin, doxazosin, indoramin, prazosin, tamsulosin** and **terazosin** are indicated for benign prostatic hyperplasia *(see also section 6.4.5).*

Phenoxybenzamine a powerful alpha-blocker with many side effects can be used with a beta-blocker for the short-term management of severe

hypertensive emergencies associated with phaeochromocytoma.

Phentolamine is a short-acting alpha-blocking drug used on rare occasions for a suppression test for phaechromo-cytoma.

PRAZOSIN

Indications : *see under dose*

Cautions: first dose may cause collapse due to hypotension (therefore should be taken on retiring to bed), elderly, renal impairment, hepatic impairment, pregnancy and breast feeding

Contraindications: not recomended for congestive heart failure due to mechanical obstruction (e.g. aoritic stenosis)

Interactions: *see Appendix-2*

Side-effects: postural hypotension, drowsiness, weakness, dizziness, headache, lack of energy, nausea, palpitati-ons, leucopenia, hepatitis, jaundice, urinary incontinence; cases of priapism and impotence reported

Dose: hypertension, 1 mg daily at bed-time (doubled after 7 days if necessary, usual maintenance dose 2-10 mg daily

Proprietary Preparations
Alphapress *(Renata),* Tab., 1 mg, Tk.4.00/Tab.; 2 mg, Tk. 6.00/Tab.
Minipress XL[I] *(Pfizer)*, Tab. 2.5 mg, Tk. 12.71/Tab.; 5 mg, Tk..21.18/Tab.
Prazopress *(Unimed),* Tab., 1 mg, Tk.4.00/Tab; 2 mg, Tk. 6.00/Tab.

TERAZOSIN

Indications: mild to moderate hypertension; benign prostatic hyperplasia
Cautions: first dose may cause collapse due to hypotension (within 30–90 minutes, therefore should be taken on retiring to bed) (may also occur with rapid dose increase), cataract surgery and breast feeding
Contraindications: history of postural hypotension and micturition syncope
Interactions: *see Appendix- 2*
Side-effects: drowsiness,postural hypotension, syncope, asthenia, headache, dry mouth, gastro-intestinal disturbances, oedema, blurred vision, intra-operative floppy iris syndrome, rhinitis, erectile disorders, tachycardia, and palpitations, rash, pruritus and angioedema; also reported weight gain, dsypnoea, paraesthesia, thrombocy-topenia and pain in extremities
Dose: hypertension, 1 mg at bedtime (compliance with bedtime dose important, see Cautions); dose doubled after 7 days if necessary; usual maintenance dose 2–10 mg once daily; more than 20 mg daily rarely improves efficacy

Proprietary Preparation
Terazon *(Incepta)*, Tab. 2 mg, Tk. 5.00/Tab.; 5mg, Tk. 8.00/Tab.

3.2.5 ADRENERGIC NEURONE BLOCKING DRUGS

Adrenergic neurone blocking drugs may cause postural hypotension. This group of drugs prevents the release of noradrenaline from postganlionic adren-ergic neurons. **Guanethidine,** a neurone blocker depletes the nerve endings of noradrenaline. Drugs of this group are rarely used now a day.

3.2.6 VASODILATOR ANTIHYPERTENSIVE DRUGS

Intravenous injection of **diazoxide** can be prescribed in hypertensive emergencies. **Hydralazine** given by mouth is a useful adjunct to other treatment; if used alone, it causes tachycardia and fluid retention; systemic lupus erythematosus (an important complication of hydrala-zine therapy) should be suspectted if there is unexplained weight loss, arthritis, or any other unexplained ill health.

Intravenous infusion of **sodium nitroprusside** is given in hypertensive emergencies on rare occasions when parenteral treatment is essential.

Minoxidil should be given when other antihypertensive drugs have failed to control severe hypertension; it can cause tachycardia and fluid retention. Because of this a beta-blocker and frusemide in high dosage must be given in combination with this vasodilator. Hypertrichosis renders this drug unsuitable for women.

Prazosin, doxazosin and terasozin (*see section 3.2.3)* have alpha-blocking, as well as vasodilator properties.

WARNING: Vasodilators, especially when used in combination with a beta-blocker and a thiazide may cause rapid fall in blood pressure precipitating a hypotensive crisis.

HYDRALAZINE HYDROCHLORIDE

Indications: moderate to severe hypertension, heart failure (with long-acting nitrate); hypertensive crisis (including that during pergnancy)

Cautions: hepatic impairment, coronary artery disease; test for antinuclear factor and for proteinuria every 6 months; pregnancy and breast-feeding

Contraindications: idiopathic systemic lupus erythematosus, severe tachycardia, high output heart failure, myocardial insufficiency due to mechanical obstruction, cor pulmonale, dissecting aortic aneurysm

Interactions: *see Appendix-2*

Side-effects : tachycardia, palpitations, flushing, hypotension, fluid retensio,gastrointestinal disturbances; headache; dizziness; systemic lupus erythematosus like syndrome after long-term therapy with over 100 mg daily fever, peripheral neuritis, nasal congestion, dyspnea, agitation, anxiety, anorexia, blood disorders, jaundice, raised plasma creatinine, proteinuria and haematuria

Dose: *by mouth*, hypertension, 25 mg twice daily increased to usual max., 50 mg twice daily

Heart failure (initiated in hospital) 25 mg 3-4 times daily, increased every 2 days if necessary. Usual maintenance dose 50-57 mg 4 times daily

By slow intravenous injection, hypertension with renal complications and hypertensive crisis, 5-10 mg diluted with 10 ml sodium chloride 0.9% may be repeated after 20-30 minutes

By intravenous infusion: hypertension with renal complications or hypertensive crisis initially 200-300 micrograms/ minute; maintenance usually 50-150 micrograms/ minute

Generic Preparation
Tablets . 50mg; 20mg

SODIUM NITROPRUSSIDE

Indications: hypertensive crisis, controlled hypotension in naesthesia, acute or chronic heart failure

Cautions: hypothyroidism, renal impairment, hyponatraemia, ischaemic heart disease, impaired cerebral circulation, elderly, hypothermia, monitor blood pressure and blood cyanide concentration and if treatment exceeds 3 days, also blood thiocyanate concentration; avoid sudden withdrawal; terminate infusion over 15-30 minutes; pregnancy and breast feeding

Contraindications: severe hepatic impairment severe vitamin B_{12} deficiency, compensatory hypertension

Interactions: *see Appendix-2*

Side-effects: over rapid reduction in blood pressure (reduce infusion rate), dizziness, nausea, retching, abdominal pain, perspiration, palpitations, acute transient phlebitis

Cyanide metabolites may cause tachycardia, sweating, hyperven-tilation, arrhythmias and marked metabolic acidosis

Dose: hypertensive crisis, *by intravenous infusion*, initially 0.5-1.5 micrograms/kg/ minute, then adjusted by increments of 0.5 micrograms/kg/ minute every 5 minutes within a range 0.5-8 microgram/kg/minute (lower doses in patients already receiving other antihyp-

ertensives); stop if marked response not obtained with max. dose in 10 minutes

Note. lower initial dose of 0.3 micrograms/kg/minute has been used.

For maintenance of blood pressure at 30-40% lower than pretreatment diaso-tolic blood presure, 20-400 microgram/ minute (lower dose for patients receiving other antihyperten-sives)

Controlled hypotension in surgery, *by intravenous infusion,* max. 1.5 micro-grams/kg/minute

Heart failure, *by intravenous infusion,* initially 10-15 micrograns/minute, increased every 5-10 minutes as necessary; usual range 10-200 micrograms/minute normally for max. 3 days

Generic Preparation
Injection (IV Infusion), 50 mg/ 5ml;

3.2.7 CENTRALLY ACTING ANTI-HYPERTENSIVE DRUGS

Methyldopa which is a centrally acting antihypertensive is safe in pregnancy, in asthmatics and in heart failure. The daily dose is to be kept below 1 g to minimize side-effects. **Clonidine** has the disadvantage that if suddenly withdrawn, it may cause a hypertensive crisis. Reserpine is no longer used because of adverse side-effects. **Moxonidine** a recently introduced centrally acting drug may have a role when thiazides, beta-blockers, ACE inhibitors and calcium-channel blockers are not suitable or have failed to control blood pressure.

CLONIDINE HYDROCHLORIDE

Indications: hypertension, migraine, menopausal flushing
Cautions; must be withdrawn gradually to avoid severe rebound hypertension; Raynaud's syndrome; history of depression, pregnancy and breast feeding; Driving-Drowsiness may affect performance of skilled tasks
Contraindications: any hypersensitivity to clonidine and avoid intravenous injection
Interactions: *seeAppendix- 2*
Side-effects: dry mouth, sedation, depression, fluid retention, bradycardia, Raynaud's phenomenon, headache, dizziness, euphoria, nocturnal unrest, rash, nausea, constipation, impotence
Dose: *by mouth,* 50–100 micrograms 3 times daily, increased every second or third day; usual max. dose 1.2 mg daily

Proprietary Preparation
Catapres *(Navana),*Tab.0.1mg, Tk.6.01/Tab

METHYLDOPA [ED]

Indications: hypertension, along with diuretics

Cautions: history of liver impairment; renal impairment; blood counts and liver function tests are advised; history of depression; positive direct Coombs' test in up to 20% of patients (may affect blood crossmathcing);

Note. Drowsiness may affect perform-ance of skilled tasks (e.g. driving);
Contraindications: depression, active liver disease, phaeochromocytoma

Interactions: *see Appendix-2*

Side-effects: dry mouth, stomatitis, bradycar-dia, exacerbation of angina, postural hypotension, sedation, dizzin-ess, myalgia, arthralgia, paraesthesia, nightmares, mild psychosis, parkinsonism, Bell's palsy, abnormal liver function tests, hepatitis, pancreatitis, haemolytic anemia, bone marrow depression, leucopenia, throm-bocytopenia, eosinophilia, lupus erythematosus like syndromes, drug

fever, myocarditis, nasal congestion, gynaceomastia, amenorrhoea

Dose: *by mouth*, Initially 250 mg 2-3 times daily, increased gradually at intervals of 2 or more days; max. 2 g daily; ELDERLY initially 125 mg twice daily, increased gradually; max. 2 g daily

Proprietary Preparations
Dopamet *(Opsonin),*Tab.,250 mg,Tk.2.32/Tab.
Dopegyt *(Ambee),* Tab. 250 mg, Tk. 3.09/Tab.
Sardopa *(Incepta),* Tab., 250 mg, Tk.3.08/Tab.

MOXONIDINE

Indication: mild to moderate essential hypertension
Cautions: avoid abrupt withdrawal (if concomitant treatment with beta-blocker has to be stopped, discontinue beta-blocker first, then moxonidine after a few days), severe coronary artery disease, unstable angina, first-degree AV block; moderate heart failure.
Contra-indications: sick sinus syndrome, sinoatrial block, second or third-degree AV block, bradycardia, severe heart failure, pregnancy and breast-feeding.
Interactions*: see Appendix-2*
Side-effects: dry mouth, diarrhoea, nausea, vomiting, dyspepsia, dizziness, somnolence, insomnia, back pain, rash, pruritus, less commonly bradycardia, tinnitus, angioedema, oedema, nervousness, neck pain
Dose: 200 micrograms once daily in the morning, increased if necessary after 3 weeks to 400 micrograms daily in 1–2 divided doses; max. 600 micrograms daily in 2 divided doses (max. single dose 400 micrograms)
Renal impairment- max. single dose 200 micrograms and max. daily dose 400 micrograms if eGFR 30–60 mL/minute/ 1.73m^2 ; avoid if eGFR less than 30 mL/ minute/1.73m^2;

Generic Preparations
Tablet 0.4 mg, 03 mg, 0.2 mg

3.3 NITRATES,CALCUIM-CHANNEL BLOCKERS AND OTHER ANTIANGINAL DRUGS

STABLE ANGINA. When patients have acute attacks, they should be treated immediately with sublingual glyceryl trinitrate. If attacks occur at definite intervals in a week, regular drug therapy is required. Aspirin in a dose of 75-150 mg daily must be given to patients with angina.

Patients with stable angina, who have normal left ventricular function, may be controlled effectively with sublingual glyceryl trinitrate and regular administration of a beta-blocker. A long-acting dihydropyridine calcuim-channel blocker may be added if it is necessary. For those without left ventricular dysfunction and in whom beta-blockers are contraindicated, diltiazem or verapamil may be given and a long-acting nitrate may be added if symptom control is not adequate. For those intolerant of standard treatment or where standard treatment has failed, nicorandil may be tried.

For patients with left ventricular dysfunction a long-acting nitrate should be used and a long-acting dihydro-pyridine calcium-channel blocker may be added if necessary. A statin should be considered for those with an elevated plasma cholesterol concentration.

3.3.1 NITRATES

Nitrates as vasodilators play a beneficial role in angina. They are potent coronary vasodilators, but their main benefit is due to reduction in venous return, which reduces left ventricular work. Flushing, headache, and postural hypotension are

the main unwanted side-effects of nitrate preparations.

Glyceryl trinitrate given sublingually is a most effective drug to provide rapid relief of pain in angina, but the effect lasts only for 20 to 30 minutes. The aeorsol spray is an alternative method for rapid pain relief of angina for those who have difficulty to dissolve sublingual formulation. The shelf-life of the aerosol is also much longer. Modified release and transdermal formulation provide prolonged duration of action but in this case tolerance may develop.

Isosorbide dinitrate is a stable sublingual preparation for those who do not have to use nitrates frequently. It is orally effe-cttive for prophylaxis. The effective may persist for several hours; duration of action for modified release preparations is up to 12 hours. **Isosorbide mononitrate**, the active metabolite of isosorbide dinitrate is also available for pain relief or prophylaxis.

Intravenous injection of glyceryl trinitrate and isosorbide mononitrate is useful in the treatment of acute left ventricular failure.

TOLERANCE: Many patients on long-acting or transdermal nitrates rapidly develop tolerance. If tolerance is suspected to transdermal patches they should not be applied for several consecutive hours in each 24 hour; in case of modified release tablet of isosorbide dinitrate, the second can be given after about 8 hours rather than after 12 hours. Standard formulation of isosorbide mononitrate should not to be given more than twice daily unless small doses are used; modified preparations should only be given once daily.

GLYCERYL TRINITRATE [ED]

Indications: prophylaxis and treatment of angina, left ventricular failure

Cautions: severe hepatic or renal impairment, hypothyroidism, malnutrition, or hypothermia, recent history of myocardial infarction, metal containing transdermal systems should be removed before cardioversion or diathermy; tolerance

Contraindications : hypersensitivity of nitrates, hypotensive conditions and hypovolaemia, hypertrophic obstructive cardio-myopathy, aortic stenosis, mitral stenosis, marked anemia, head trauma, cerebral haemorrhage, closed angle glaucoma

Interactions: *see Appendix-2*

Side-effects: throbbing headache, flushing, dizziness, postural hypotension, tachycardia

Specific side-effects following injections include severe hypotension, nausea and itching, diaphoresis, apprehension, restlessness, muscle twitching retorsternal discomfort, palpitations, abdominal pain, syncope. Prolonged administration has been associated with methaemoglobinaemia

Dose: *sublingually*, 0.3-1 mg repeated as required

By intravenous infusion, 10-2000 micrograms/minut.

Proprietary Preparations

Angicard *(Drug Int.),* Tab., 0.5 mg, Tk.3.00/Tab.
Angist *(Acme),* Tab., 0.5 mg, Tk. 4.01/Tab.
Anril *(Square),* Spray, 400 microgram/spray, Tk. 215.80/200Puffs; Sublingual Tab., 0.5 mg, Tk. 3.01/Tab; SR Tab., 2.6 mg, Tk. 4.01/Tab; IV Injection, 5 mg/ml, Tk. 75.28/Vial
GTN *(Eskayef),* Tab, 2.6 mg, Tk. 4.00/Tab.
Nidocard *(Drug Int.),* SR Tab., 2.6 mg , Tk.4.00/Tab.; Tab., 6.4 mg, Tk. 7.00/Tab.; Inj., 5 mg/ml, Tk. 100.00/Vial
Nitrodil *(Medimet),* Cap. 2.6 mg, Tk. 4.65/Cap.
Nitrin *(Healthcare),* SR Tab., 2.6 mg, Tk.5.00/Tab.
NitroCap *(Orion),* Cap., 2.6 mg, Tk. 5.02/Cap.
Nitrocard *(Aristo),* Spray, 400microgram/spray, Tk. 250.00/Spray; Tab. , 2.6mg, Tk. 4.00/Tab.
Nitrocontin *(Mundipharma),* CR Tab, 2.6 mg, Tk. 5.36/Tab.; CR Tab., 6.4 mg, Tk. 8.00/Tab.
Nitrofix *(Opsonin),* SR Tab., 2.6 mg, Tk.3.01/Tab.
Nitrosol *(Beximco),* Spray, 400microgram/spray, Tk. 225.00/200 MD
Nlitro *(Unimed),* SR Tab. , 2.6 mg, Tk.4.00/Tab.
Nitrovas *(Popular),* SR Tab., 2.6mg, Tk.4.02/Tab.

Pactorin *(ACI),* Tab. , 2.6 mg , Tk. 4.02/Tab.
Rectocare *(Square),* Oint., 0.40%, Tk.65.25/15gm
Trocer *(Incepta),* SR Tab., 2.6 mg, Tk.4.00/Tab.; Spray, 400 microgram/spray, Tk. 225.00/Spray; SR Cap., 2.6 mg, Tk.4.00/Cap.
Xynocard *(White Horse),* SR Tab., 2.6 mg, Tk. 3.00/Tab.

ISOSORBIDE DINITRATE [ED]

Indications: prophylaxis and treatement of angina, left ventricular failure

Cautions, Contraindications, Side-effect: *see under Glyceryl trinitrate*

Interactions: *see Appendix-2*

Dose: *sublingually*, 5-10 mg

By mouth, daily in divided doses; angina, 30-120 mg, left ventricular failure, 40-160 mg up to 240 mg if required;

By intravenous infusion, 2-10 mg/hour, higher doses up to 20 mg/hour may be required in some cases

Generic Preparation
Tablet, 10mg

ISOSORBIDE MONONITRATE

Indications: prophylaxis of angina, adjunct in congestive heart failure

Cautions : *see under Glyceryl Trinitrate*

Contraindications, Side-effect: *see under Glyceryl Trinitrate*

Interactions: *see Appendix-2*

Side-effects: *see under Glyceryl Trinitrate*

Dose: initially 20 mg 2-3 times daily or 40 mg twice daily (10 mg twice daily in those who have not previously received nitrates); up to 120 mg daily in divided doses if required

Proprietary Preparations
A-Card *(Acme),* Tab., 20 mg, Tk. 1.42/Tab.
Angifix *(Incepta),* Tab. 20 mg, Tk. 1.42/Tab.
Esmo *(Square),* Tab., 20 mg, Tk. 1.42/Tab.; LA Cap., 50 mg, Tk. 7.02/Cap.
ISM *(Aristo),* Tab. 20 mg, Tk. 1.40/Tab.
Moniten *(ACI),* Tab.20 mg, Tk. 1.42/Tab.; 40mg, Tk. 2.32/Tab.
Monocard *(Drug Intl),* Tab.20 mg, Tk.1.42/Tab.; SR Cap. 50 mg, Tk. 7.00/Cap.
Monotrate *(Sun),* Tab. 20 mg, Tk. 1.42/Tab. OD Tab. 50 mg, Tk. 4.13/Tab.
Unicard *(Sonear)*, 20 mg, Tk. 1.43/Tab.

3.3.2 CALCIUM-CHANNEL BLOCKERS

Calcium-channel blockers interfere with the inward movement of calcium ions through the slow channels of the active myocardial cell membranes within the specialized conducting systems of the heart and the cells of vascular smooth muscle. These drugs depress the contractility of myocardium, the formation and propagation of electrical impulses within the heart, and diminish coronary or systemic vascular tone. Calcium-channel blockers differ in their pharmacological actions. There are important differences between verpamil, diltiazem and the dihydropyridine calcium-channel blockers (amlodipine, felodipine, isradipine**,** lacidipine, nicardipine, nifidipine, nimodipine). **Verapamil** is a negatively inotropic calcium channel-blocker indicated in angina, hypertension and arrhythmias; decreases cardiac output, slows the heart rate, and impairs atroventricular conduction. It may precipitate heart failure, and should not be used with beta-blokcers. Constipation is a common side effect.

Nifedipine, a coronary and peripheral arterieolar vasodilator acts by relaxing vascular smooth muscle. It has more influence on the blood vessels and has no antiarrhythmic activity. **Nicardipine** has effects similar to those of nifedipine and may produce less reduction of myocardial contractility. **Amlodipine** and **felodipine** also have similar effects like that of nifedipine and nicardipine and do not have effect on myocardial contractility; they do not produce clinical deterioration in heart failure. They have a longer half-life and can be given once daily. Nifedipine, nicardipine and felodipine can be prescribed for the treatment of angina or hypertension. All are valuable in forms of angina

associated with coronary vasospasm. Side effects are flushing, headache and swellings of ankles.

Isradipine and **lacidipine** have similar effects to those of nifedipine and nicerdipine. Isradipine and lacidipine are only indicated for hypertension whereas **nisoldipine** is indicated for angina and hypertension. **Nimodipine** is indicated only for prevention of vascular spasm follwing subarachnoid haemorrhage.

Diltiazem is effective in angina; the longer-acting preparation can be prescribed in hypertension. It may be used in patients for whom beta-blockers are contraindicated or ineffective. It has a less negative inotropic effect than verapamil and significat myocardial depression occurs rarely. It should be used with caution in association with beta-blockers.

Verapamil and diltiazem depress cardiac function and may cause clinically significant deterioration of heart failure; and is absolutely contraindicated in heart failure.

WITHDRAWAL: There are evidences that sudden withdrawal of calcium-channel blockers may be associated with an exacerbation of stable angina

AMLODIPINE BESYLATE[ED]

Indications: hypertension, prophylaxis of angina

Caution: hepatic impairment

Contraindications: cardiogenic shock, significant aortic stenosis, pregnancy and breast-feeding

Interactions: *see Appendix-2*

Side-effects: headache, edema, fatigue, nausea, flushing, dizziness, gum hyper-plasia, rashes, dry mouth, palpitations, dyspnoea, muscle cramps, myalgia, arthralgia, impotence, jaundice, hyperglycaemia, thromboc-ytopenia, angioedema, alopecia, gynaecomastia

Dose: hypertension or angina, initially 5 mg once daily, max. 10 mg once daily

Proprietary Preparations

Acudipin *(Concord),* Tab., 5 mg, Tk. 5.00/Tab.
Amdin *(Alco),* Tab., 5 mg, Tk. 4.00/Tab.; 10mg, Tk. 6.00/Tab.
Amdocal *(Beximco),* Tab., 5 mg, Tk.5.00/Tab.; 10 mg, Tk. 7.00/Tab.
Amedin *(Sonear),* 5 mg, Tk. 5.00/Tab.
Amlocard *(Drug Intl),* Tab., 5 mg, Tk.4.50/Tab.; 10 mg, Tk. 7.00/Tab.
Amlodipine *(Albion),* Tab., 5 mg, Tk.4.00/Tab.; 10 mg, Tk.6.00/Tab.
Amlopin *(Acme),* Tab., 5mg, Tk.5.00/Tab.; 10mg, Tk. 7.00/Tab.
Amlosun *(Sun),* Tab., 5 mg, Tk. 5.00/Tab.
Amlotab *(Incepta),* Tab., 5 mg, Tk. 5.00/Tab.;
Amlovas *(Popular),* Tab., 5mg, Tk. 3.51/Tab.; 10mg, Tk. 6.02 /Tab.
Amlowide *(Beacon),* Tab., 5 mg, Tk. 3.00/Tab.
Amocal *(Opsonin),* Tab., 5 mg, Tk. 3.76/Tab.; 10 mg, Tk. 4.53/Tab.
Ampil *(White Horse),* Tab., 5 mg, Tk.5.00/Tab.
Cab *(ACI),* Tab., 5mg, Tk. 5.00/Tab.
Calchek *(General),* Tab., 5 mg, Tk. 5.00/Tab
Calock *(Medimet),* Tab., 10mg, Tk.3.75/Tab.; Tab., 5mg, Tk.4.00/Tab.
Calpin *(Globe),* Tab., 5 mg, Tk. 3.50/Tab.
Calpress *(Asiatic),* Tab., 5mg, Tk. 4.00/Tab.; 10 mg, Tk. 6.00/Tab.
Calvasc *(Unimed),* Tab., 5 mg, Tk. 5.00/Tab; 10 mg, Tk. 8.00/Tab.
Camlodin *(Square),* Tab., 5 mg, Tk. 5.00/Tab; 10 mg, Tk. 6.02/Tab.
Cardipin *(Renata),* Tab., 5 mg, Tk. 5.00/Tab
Cardolab *(Labaid),* Tab., 5 mg, Tk. 5.00/Tab
Cardosia *(Pharmasia),* Tab., 5 mg, Tk.4.00/Tab.
Ccb *(Orion),* Tab., 5 mg, Tk. 3.01/Tab.
Cvnor *(Navana),* Tab., 5 mg, Tk. 4.02/Tab.
Dipicard *(Leon),* Tab., 5 mg, Tk.5.00/Tab; 10mg, Tk. 7.00/Tab.
Dipinol *(Supreme),* Tab., 5mg, Tk. 5.00/Tab.
Diplor *(Ibn Sina),* Tab., 5 mg, Tk. 5.00/Tab.
Emlon *(Biopharma),* Tab., 5 mg, Tk 5.00/Tab.; 10 mg, Tk. 7.00/Tab.
G-Amlo *(Gonoshasthaya),* Tab. 5 mg, Tk.2.50/Tab.; 10 mg, Tk. 4.00/Tab.
Hipre *(Pacific),* Tab., 5 mg, Tk. 3.76/Tab.; 10mg, Tk. 5.26/Tab.
Ipin *(Chemist),* Tab. , 5 mg, Tk. 4.00/Tab.
Locard *(Jayson),* Tab., 5 mg, Tk. 3.05/Tab.
Lodical *(Somatec),* Tab., 5 mg, Tk. 5.00/Tab
Lodipin *(Aristo),* Tab., 5mg, Tk. 5.00/Tab
Nelod *(Kemiko),* Tab., 5 mg, Tk. 5.00/Tab; 10mg, Tk. 8.00/Tab.
Nopidin *(Ad-din),* Tab., 5 mg, Tk. 3.00/Tab.
Raklopin *(RAK),* Tab., 5 mg, Tk. 4.00/Tab.; 10mg, Tk. 6.00/Tab.
Sidopin *(Eskayef),* Tab, 5 mg, Tk. 5.00/Tab.
Ticard *(Doctor TIMS),* Tab., 5 mg, Tk.5/Tab.
Vesocal *(Rangs),* Tab., 5mg, Tk. 5.00/Tab.; 10mg, Tk. 8.00/Tab.
Xelcard *(Healthcare),* 5mg, Tk. 5.00/Tab.

Amlodipine + Atenolol

Acudipin Plus *(Concord),* Tab., 5 mg + 50mg, Tk.6.00/Tab.
Aloten *Kemiko),* Tab. , 5 mg + 25 mg, Tk.4.24/Tab.
Aloten Forte *(Kemiko),* Tab. , 5 mg + 50mg, Tk. 4.50/Tab.
Amdin Plus *(Alco),* Tab. , 5 mg + 50mg, Tk.4.50/Tab.
Amdocal Plus *(Beximco),* Tab., 5 mg + 25 mg, Tk. 5.25/Tab.; 5 mg + 50mg, Tk. 6.00/Tab.
Amlobet *(Sun),* Tab. , 5 mg + 50mg, Tk.6/Tab.
Amlocard Plus *(Drug Intl),* Tab., 5 mg + 25mg, Tk.5.00/Tab.; 5 mg + 50 mg, Tk.6.00/Tab.
Amlocom *(Beacon),* Tab. , 5 mg + 50 mg, Tk.4.50/Tab.
Amlodipine Plus *(Albion),* Tab. , 5 mg + 50mg, Tk. 4.50/Tab.; 5 mg + 25 mg, Tk.4.25/Tab.
Amloten *(Acme),* Tab., 5 mg + 25 mg, Tk.5.25/Tab.; 5 mg + 50 mg, Tk. 6.00/Tab.
Amlovas AT *(Popular),* Tab., 5 mg + 50 mg, Tk. 4.02/Tab.
Amocal-AT *(Opsonin),* Tab., 5 mg + 50 mg, Tk. 4.51/Tab.
Ampil Plus *(White Horse),* Tab., 5 mg + 50mg, Tk. 6.00/Tab.
Angical *(Apex),* Tab., 5 mg + 50 mg, Tk.6/Tab.
Apodin *(Globe),* Tab., 5 mg + 50 mg, Tk. 4.50/Tab.
Betacal *(Orion)* Tab. , 5 mg + 50 mg, Tk. 6.00/Tab.
Betanol-A *(Sanofi),* Tab., 5 mg + 25 mg, Tk.5.25/Tab.; 5 mg + 50 mg, Tk.6.00/Tab.
Bpnol Plus *(Delta),* Tab. , 5 mg + 50 mg, Tk.4.00/Tab.
Calbeta *(Unimed),* Tab. , 5 mg + 50mg, Tk.6.00/Tab.
Calchek Plus *(General),* Tab., 5 mg + 50mg, Tk. 6.00/Tab.
Calock plus *(Medimet),* Tab., 5 mg + 25 mg, Tk.5.00/Tab.; 5 mg + 50 mg, Tk.4.50/Tab.
Calpin plus *(Globe),* Tab., 5 mg + 50 mg, Tk. 4.50/Tab.
Camlodin Plus *(Square),* Tab, 5 mg + 50 mg, Tk. 6.00/Tab.; 5 mg + 25 mg, Tk. 5.00/Tab.
Cardipin Plus *(Renata),* Tab., 5 mg + 50 mg, Tk. 6.00/Tab.
Cardosia Plus *(Pharmasia),* Tab., 5 mg + 50mg, Tk.5.00/Tab.
Combicard *(Healthcare),* Tab.5 mg + 50 mg, Tk. 6.00/Tab.
Cvnor-A *(Navana),* Tab., 5 mg + 25 mg, Tk.5.00/Tab.
Dipicard Plus *(Leon),* Tab., 5 mg + 50mg, Tk.6.00/Tab.
Diplor Plus *(Ibn Sina),* Tab., 5 mg + 25 mg, Tk. 4.00/Tab.; 5 mg + 50 mg, Tk. 6.00/Tab.
Emlon Plus *(Biopharma),* Tab., 5 mg + 50 mg, Tk. 6.00/Tab.
Fixocard *(Incepta),* Tab. 5 mg + 25 mg, Tk.5.25/Tab.; 5 mg + 50mg, Tk. 6.00/Tab.
Hipre Plus *(Pacific),* Tab. 5 mg + 50mg, Tk.4.51/Tab.
Ipin plus *(Chemist),* Tab., 5 mg + 50 mg, Tk. 6.00/Tab.
Locard Plus *(Jayson),* Tab. 5 mg + 50mg, Tk.3.02/Tab.
Lodical Plus *(Somatec),* Tab. 5 mg + 50mg, Tk. 6.00/Tab.
Lodicard *(Aristo),* Tab. 5 mg + 50 mg, Tk.6.00/Tab.
Nopirol *(Ad-din),* Tab., 5 mg + 25 mg, Tk. 4.00/Tab.
Sidoplus *(Eskayef),* Tab. 5 mg + 25 mg, Tk.5.25/Tab.; 5 mg + 50mg, Tk. 6.00/Tab.
Tenocab *(ACI),* Tab. 5 mg + 25 mg, Tk.5.25/Tab.; 5 mg + 50 mg, Tk. 6.00/Tab.
Tenodin *(Asiatic),* Tab. 5 mg + 25 mg, Tk.4.20/Tab.; 5 mg + 50 mg, Tk.4.50/Tab.
Tenopin *(Sharif),* Tab. 5 mg + 50 mg, Tk.4.50/Tab.
Ticard Plus *(Doctor TIMS),* Tab. 5 mg + 50mg, Tk. 6.00/Tab.
Veridipin Plus *(Veritas),* Tab. 5 mg + 50mg, Tk. 6.00/Tab.
Vesocal plus *(Rangs),* Tab., 5 mg + 50 mg, Tk. 6.00/Tab.

DILTIAZEM HYDROCHLORIDE

Indications: prophylaxis and treatment of angina; hypertension

Cautions: reduce dose in hepatic and renal impairment, heart failure or singificantly impaired left ventricualr function, bradycardia, first degree AV block or prolonged PR interval

Contraindications: severe bradycardia, left ventricualr failure, second-or third-degree AV block (unless pacemaker fitted) sick sinus syndrome, pergnancy and breast-feeding

Interactions: *see Appendix-2*

Side-effects: bradycardia, sino-atrial block, AV block, palpitations, dizziness, hypotension, malaise, asthenia, headache, hot flushes, gastrointestinal disturbances, ankle edema, photosensitivity, altered liver function tests, hepatitis, gynaecomastia, gum hyperplasia, extrapyramidal symptoms, depression reported

Dose: angina, 30 to 60 mg 3 times daily (elderly initially twice daily); increased if necessary to 360 mg daily

Proprietary Preparations
Cardil *(Ibn Sina),* Tab., 30 mg, Tk. 2.25/Tab.
Cardisef *(Supreme),* Tab., 30 mg, Tk.3/Tab.; 60 mg, Tk. 5.00/Tab.
Cardizem *(Drug Intl),* Tab., 30 mg, Tk.3.00/Tab; 60 mg, Tk. 5.00/Tab. ; SRTab. , 90 mg, Tk. 6.00/Tab.; *SR* Tab., 120 mg, Tk. 8.00/Tab.
Diltiazem *(Albion),* Tab., 30 mg, Tk. 2.00/Tab. Tab., 60 mg, Tk. 3.80/Tab.**;** *SR* Tab., 90 mg, Tk. 5.61/Tab.

LACIDIPINE

Indication: hypertension

Cautions: cardiac conduction abnormalities, poor cardiac reserve, hepatic impairment; withdraw if ischaemic pain occurs shortly after initating treatment or if cardiogenic shock develops

Contraindications: aortic stenosis, pregnancy and breast-feeding; avoid within 1 month of myocardial infarction.

Interactions: *see Appendix-2*

Side-effects: headache, flushing, edema, dizziness, palpitations, gum hyperplasia, muscle cramps, polyuria, chest pain, mood disturbances

Dose: initially 2 mg as a single daily dose, preferably in the morning, increased after 3-4 weeks to 4 mg daily, then if necessary to 6 mg daily

Proprietary Preparations
Lacicard *(Aristo),* Tab., 4 mg, Tk. 6.00/Tab.; 2mg, Tk. 4.00/Tab.
Laciten *(Square),* Tab., 4 mg, Tk. 6.00/Tab.; 2mg, Tk. 4.00/Tab.
Lacidip *(Incepta),* Tab., 2 mg, Tk. 4.00/Tab.; 4mg, Tk. 6.00/Tab.
Lacitab *(Acme),* Tab., 2 mg, Tk. 4.01/Tab.; 4mg, Tk. 6.02/Tab.
L-cardin (*Drug Int.)* Tab., 2 mg, Tk. 3.00/Tab

LERCANIDIPINE HYDROCHLORIDE

Indications: mild to moderate essential hypertension

Cautions: sick sinus syndrom (if pacemaker not fitted) hepatic and renal impairment, left ventricular dysfunction

Contraindications: aortic stenosis, pregnancy and breast-feeding, avoid within 1 month of myocardial infarction unstable angina, uncontrolled heart failur

Interactions: *see Appendix-2*

Side-effects: headache, flushing, edema, dizziness, palpitations, rash, gum hyperplasia, muscle cramps, polyuria, chest pain, mood disturbances

Dose: initially 10 mg as once daily before food, increased if necessary after at least 2 weeks to 20mg daily

Proprietary Preparations
Canider *(ACI),* Tab., 10 mg, Tk. 5.02/Tab.
Lotensyl *(Sun),* Tab., 10 mg, Tk. 5.55/Tab.
Larcadip *(Incepta),* Tab., 10 mg, Tk. 5.00/Tab.

NIFEDIPINE [ED]

Indications: prophylaxis of angina (preferably used with beta-blockers); hypertension; Raynaud's phenomenon

Cautions: withdraw if ischaemic pain occurs or existing pain worsens shortly after starting treatment, poor cardiac reserve, heart failure or singificantly impaired left ventricualr function, severe hypotension; reduce dose in hepatic impairment, diabetes mellitus; may inhibit labour; pregnancy; breast-feeding

Contraindications: cardiogenic shock, advanced aortic stenosis; within 1 month of myocardial infarction; unstable or acute attacks of angina

Interactions: *see Appendix-2*

Side-effects: headache, flushing, dizziness, tachycardia, palpitation, short-acting preparations may induce an exaggerated fall in blood pressure and reflex tachycardia which may lead to myocardial or cerebrovascular ischae-mia, gravitational edema, rash (erythema multiforme reported), pruritus, urticaria,

nausea, constipation or dirrhoea, increased frequency of micturition, eye pain, visual disturba-nces, gum hyperplasia, paraesthesia, myalgia, tremor, impotence, gynaecom-astia; depression, telangiectasia reported

Dose: mild to moderate hypertension and angina prophylaxis, 10 to 20 mg twice daily adjusted according to response to 40 mg twice daily. In Raynaud's phenomenon, initially 5 mg three times daily, adjusted according to response to 20 mg 3 times daily

Proprietary Preparations
Nifedipine *(Albion),* Tab., 10 mg, Tk.0.34/Tab.
Nifin *(Acme),* Tab., 10 mg, Tk. 0.34/Tab.
Nifecap *(Drug Intl),* Cap., 10 mg, Tk. 2.10/Cap.
Nidipine SR *(Square),* SR Tab., 20 mg, Tk.0.64/Tab.

NIMODIPINE

Indications: prevention and treatment of ischaemic neurological deficits following aneurysmal subarachnoid haemorrhage
Cautions: cerebral oedema or severely raised intracranial pressure; hypotension; avoid concomitant administration of nimodipine tablets and infusion, other calcium-channel blockers, or beta-blockers; hepatic and renal impairment, pregnancy and brest feeding.
Contra-indications: within 1 month of myocardial infarction; unstable angina; acute porphyria
Interactions: *see Appendix-2*
Side-effects: hypotension, variation in heart-rate, flushing, headache, nausea, sweating and feeling of warmth, thrombocytopenia
Dose: prevention, by mouth, 60 mg every 4 hours, starting within 4 days of aneurysmal subarachnoid haemorrhage and continued for 21 days. Treatment, by intravenous infusion via central catheter, initially 1 mg/hour (up to 500 micrograms/
hour if body-weight less than 70 kg or if blood pressure unstable), increased after 2 hours to 2 mg/hour if no severe fall in blood pressure; continue for at least 5 days (max. 14 days); if surgical intervention during treatment, continue for at least 5 days after surgery; max. total duration of nimodipine use 21 days

Proprietary Preparations
Nimocal (*Square),*Tab., 30mg, Tk.5.01/Tab.

VERAPAMIL HYDROCHLORIDE[ED]

Indiactions: *see under dose and preparation*

Cautions: first-degree AV block, acute phase of myocardial infarction (avoid if bradycardia, hypotension, left ventricular failure), patients taking beta-blockers, hepatic impairment and breast-feeding

VERAPAMIL AND BETA-BLOCKDRS. It has been suggested that after verapamil injection has been given first, an interval of 30 minutes is sufficient before giving a beta-blockers. It may also be hazardous to give verapamil and a beta-blocker together by mouth

Contraindications: hypotension, brady-cardia, second and third degree AV block, sick sinus syndrome, cardiogenic shock, sinoatrial block, history of heart failure or singificantly impaired left ventricular function, atrial flutter or fibrillation compli-cating Wolff-Parkinson-White syndrome, porphyria, patient recently treated with beta blockers.

Interactions: *see Appendix-2*

Side-effects: constipation, less comm-only nausea, vomiting, flushing, headache, dizziness fatigue, ankle edema, erythema, pruritus, urticaria, angiedema, Stevens-Johnson syndrome, myalgia, arthralgia, paraesthesia, increased prolactin concentration, hypotension, bradycardia, heart block and asystole

Dose: *by mouth*, supraventricular arrhyt-hmias (but see also Contraindications*),* 40-120 mg 3 times daily

Angina, 80-120 mg times daily

Hypertension, 240-480 mg daily in 2-3 divided doses or once daily with sustained release preparations

By slow intravenous injection over 2 minutes (3 minutes in elderaly), 5-10 mg (preferrably with ECG monitoring); in paroxysmal tachyarrhythmias a further 5 mg after 5-10 minutes if required

Proprietary Preparations
Angimil *(Medimet),* Tab., 80 mg, Tk.4.25/Tab.; 40 mg, Tk.2.25/Tab.; 240 mg, Tk.7.00/Tab.
Veracal *(Incepta),* Inj., 5 mg/2 ml, Tk. 30.00/2ml; SR Tab., 120 mg, Tk. 7.00/Tab. ; SR Tab., 180 mg, Tk. 6.00/Tab.; Tab., 40 mg, Tk. 2.25/Tab.; 80 mg, Tk. 3.00/Tab.
Veramil *(Rangs),* SR Tab., 240 mg, Tk. 7.00/Tab.; Tab., 80 mg, Tk. 3.00/Tab.
Verapamil *(Albion),* Tab. 80 mg, Tk. 3.00/Tab.

3.3.3 OTHER ANTIANGINAL DRUGS

Nicorandil, a potassium-channel activator, has both arterial and venous vasodilating properties and is indicated for the prevention and long-term treatment of angina. When added to other antianginal drugs in refractory unstable angina, it may produce additional benefit.

Ivabradine selectively inhibits the pacemaker; reduces cardiac pacemaker activity, slowing the heart rate and allowing more time for blood to flow to the myocardium. Its antianginal potency is similar to that of beta-blokade and amlodipine.

Ranolazine is used as adjunctive therapy in patients who are inadequately controlled or intolerant of first line antianginal drugs. It may be used in combination with amlodipine, beta-blockers, or nitrates. The mechanism is inhibition of the slow inward sodium current whereby sodium enters the ischemic cells, then dragging in calcium ions by sodium-calcium exchange with their proischemic effects.
Trimetazidine is a partial inhibitor of fatty acid oxidation without hemodynamic effects.

NICORANDIL

Indications: prophylaxis and treatment of angina

Cautions: hypovolaemia, acute pulmonary edema, acute myocardial infarction with acute left ventricular failure, pregnancy and breast-feeding

DRIVING: patients should be warned not to drive or operate machinery until it is establised that their performance is unimpaired

Contraindications: cardiogenic shock, left ventricular failure with low filling pressures, hypotension

Interactions: *see Appendix-2*

Side-effects: headache, flushing, nausea, dizziness, weakness, reduction in blood pressure and/or increase in heart rate; angiedema, hepatic dysfunction also reported

Dose: initially 10 mg twice daily (if susceptible to headache 5 mg twice daily) usual dose 10-20 mg twice daily, up to 30 mg twice daily may be used

Proprietary Preparations
Corangi *(Unimed),* Tab. 10mg, Tk. 3.50/Tab., 20mg, Tk. 7/Tab
Nicor *(Orion),* Tab. 10mg, Tk. 3/Tab

IVABRADINE

Indications: stable angina pectoris in patients with normal sinus rhythm, who have a contraindication to or intolerance to beta blockers, inappropriate sinus tachycardia.
Cautions: mild heart failure including asymptomatic left ventricular dysfunction; monitor for atrial fibrillation or other arrhythmias (treatment ineffective), hypotension, retinitis pigmentosa; pregnancy and breast-feeding
Contra-indications: for angina, if heart rate below 60 beats per minute; for heart failure, if heart rate below 75 beats per minute; unstable or acute heart failure; cardiogenic shock; acute myocardial infarction; unstable angina; immediately after cerebrovascular accident; sick-sinus
syndrome; sino-atrial block; patients dependent on pacemaker; second- and

third-degree heart block; congenital QT syndrome, hepatic and renal impairment
Interactions: *see Appendix- 2*
Side-effects: bradycardia, first-degree heart block, ventricular extrasystoles, headache, dizziness, visual disturbances, nausea, palpitations, supraventricular extrasystoles, dyspnoea, vertigo, muscle cramps, eosinophilia, hyperuricaemia, and raised plasma-creatinine concentration
Dose: **i**nitially 5 mg twice daily, increased if necessary after 3–4 weeks to 7.5 mg twice daily (if not tolerated reduce dose to 2.5–5 mg twice daily); ELDERLY initially
2.5 mg twice daily
Note. Ventricular rate at rest should not be allowed to fall below 50 beats per minute

Proprietary Preparations
Corabid *(Unimed),* Tab., 5 mg, Tk. 35.00/Tab.; 7.5 mg, Tk. 50.00/Tab.
Ivanor *(Square),* Tab., 5 mg, Tk. 25.00/Tab.; 7.5 mg, Tk. 35.00/Tab.
Ivaprex *(Incepta),* Tab., 5 mg, Tk. 30.00/Tab.; 7.5 mg, Tk. 45.00/Tab.
Ivaten *(Drug Intl),* Tab., 5 mg, Tk. 2.50/Tab.; 7.5 mg, Tk. 3.50/Tab.

RANOLAZINE

Indications: as adjunctive therapy in the treatment of stable angina in patients inadequately controlled or intolerant of first-line antianginal therapies
Cautions: moderate to severe congestive heart failure; QT interval prolongation; elderly; body-weight less than 60 kg; hepatic and renal impairmen; pregnancy and breast-feeding; renal impairment use with caution if eGFR 30–80 mL/minute/ 1.73m^2 ; avoid if eGFR less than 30 mL /minute/1.73m^2
Interactions: *see Appendix- 2*
Side-effects: constipation, nausea, dizziness, headache, asthenia; weight loss, dry mouth, dyspepsia, flatulence, hot flush, hypotension, prolonged QT interval, peripheral oedema, dysponea, epistaxis, hypoaesthesia, tremor, anxiety, anorexia, dysuria, haematuria, dehydration, pain in extremities, muscle cramp, joint swelling, visual disturbance, tinnitus, pruritus, sweating, cold extremities, disorientation, erectile dysfunction, parosmia, urticaria, rash
Dose: ADULT over 18 years, initially 375 mg twice daily, increased after 2–4 weeks to 500 mg twice daily and then adjusted according to response to max. 750 mg twice daily (reduce dose to 375–500 mg twice daily if not tolerated)

Proprietary Preparations
Ranolin *(Square),* XR Tab.,500 mg, Tk. 16.00/Tab.; 1 gm, Tk. 25.00/Tab.
Ranola *(General),* ER Tab.,500 mg , Tk. 16.00/Tab.
Ralozine *(Incepta),* SR Tab.,500 mg, Tk. 16.00/Tab.

TRIMETAZIDINE

Indication: angina pectoris

Cautions: pregnancy and breast feeding

Contraindication: hypersensitivity to trimetazidine

Interactions: *see Appendix-2*
Side-effects: gastrointestinal disturbance, nausea, vertigo
Dose: 40 to 60mg given daily by mouth in divided doses. 35 mg tablet preparations : 35 mg at meal times in the morning and evening.

Proprietary Preparations
Angimet *(Orion),* MR Tab., 35 mg, Tk. 5.02/Tab.; Tab., 20 mg, Tk. 3.01
Anginox *(General),* Tab., 20 mg, Tk. 3.00/Tab.
Angirid *(Acme),* MR Tab., 35 mg, Tk.5.01/Tab.
Angivas *(Popular),* Tab, 20 mg, Tk.3.00/Tab.; MR Tab., 35 mg, Tk. 5.00/Tab.
Antoris *(Opsonin),* MR Tab., 35 mg, Tk.4.51/Tab.
Feelnor *(Incepta),* MR Tab., 35 mg, Tk.5.00/Tab.; Tab., 20 mg, Tk. 3.00/Tab.
Metavas *(Nipro JMI),* MR Tab., 35 mg, Tk. 5.00/Tab.
Trimet *(Drug Int.),* Tab., 20 mg, Tk. 3.00/Tab.; MR Tab., 35 mg, Tk. 5.00/Tab.
Vascare *(Doctor TIMS),* Tab., 20 mg, Tk.3.00/Tab.
Vastadin *(Sharif),* MR Tab., 35 mg, Tk.5.00/Tab.
Vestar *(Healthcare),* MR Tab., 35 mg, Tk.6.00/Tab.

3.3.4 PERIPHERAL AND CEREBRAL VASODILATORS & NEUROSENSORY OXYGENATOR DRUGS

Intermittent claudication, a serious peripheral vascular complication is due to occlusion of vessels. Cessation of smoking and exercise are conservative measures in the management of intermittent claudication. Low-dose aspirin (75-300 mg daily) may be considered if serum total cholesterol is elevated. **Naftidrofuryl** 200 mg 3 times daily may improve moderate intermittent claudication; but the effect of the drug on the outocme of the disease is uncertain. Patients receiving naftidrofuryl should be assessed for improvement after 3-6 months. **Cilostazole** is used in Intermittent claudication to improve walking distance in patient without peripheral tissue necrosis and who do not have pain at rest.**Nifedipine** is useful for reducing the frequency and severity of vasopastic attacks. **Naftidrofuryl** may also produce symptomatic improvement; **Inositol nicotinate,** a nicotinic acid derivative may also be considered. **Oxpentifylline** (pentoxyfylline), cinnari-zine and prazocin have been used but are not established as effective.

Almitrine & Raubasine is a combination formula of two components, available as-almitrine bismesylate 30 mg & raubasine 10 mg in tablet form. This combined product acts as a neurosensory oxygenator drug and effective in the treatment of cerebral insufficiency.

ALMITRINE & RAUBASINE

Indications: disorders of memory, lack of concentration ,hearing loss, dizziness, buzzing sounds in the ear

Cautions: abnormal sensation in the lower limbs, weight loss

Contraindications: known allergy to the drug; severe liver disease

Side-effects: nausea, sensations of heaviness and burning in the stomach, diarrhea, or constipation, agitation, dizziness; palpitations; sensation of 'pins and needles', stinging, weight loss

Dose: 1 tablet once or twice daily. In case of missing dose, the next dose at the normal time

Proprietary Preparations

Albasine *(Drug Int.),* Tab. Tk. 12.00/Tab.
Truxil *(Square),* Tab. Tk. 10.00/Tab.

CILOSTAZOL

Indication: intermittent claudication in patients without rest pain and no peripheral tissue necrosis

Cautions: atrial or ventricular ectopy, atrial fibrillation, atrial flutter; diabetes mellitus (higher risk of intra-ocular bleeding)

Interactions: *see Appendix -2*

Contraindications: active peptic ulcer, haemorrhagic stroke in previous 6 months, surgery in previous 3 months, proliferative diabetic retionpathy, poorly controlled hypertension

Side-effects: diarrhoea, headache, nausea, vomiting, dyspepsia, flatulence, abdominal pain, tachycardia, palpitation, angina, arrhythmia, dizziness, ecchymosis, puritus, edema, asthenia

Dose: 100 mg twice daily (30 minutes before or 2 hours after food)

Proprietary Preparations

Cilosta *(Square),* Tab., 100 mg, Tk.12.05/Tab.
Inclaud *(ACI),* Tab., 100 mg, Tk. 12.00/Tab.
Vasocil*(Ibn Sina),* Tab. , 100 mg, Tk.12.00/Tab.; 50 mg, Tk. 7.00/Tab.
Zocil *(Beximco),* Tab., 100 mg, Tk.12.00/Tab. 50 mg, Tk. 7.00/Tab.

INOSITOL NICOTINATE

Indications: peripheral vascular disease, hyperlipidaemia

Cautions: cerbrovascular insufficiency and unstable angina

Contraindications: recent myocardial infraction,acute phase of cerbrovascular accident,pregnancy

Interactions: *see Appendix-2*

Side-effects: flushing, dizziness nausea, vomiting
Dose: 3g daily in 2-3 divided doses; max 4g daily

Proprietary Preparation
Nicosit *(Incepta),* Tab. 500mg, Tk. 5/Tab.; 750mg, Tk. 7/Tab

OXPENTIFYLLINE / PENTOXIFYLLINE

Indication: peripheral vascular disease
Cautions: hypotension, coronary artery disease, renal impairment, severe hepatic impairment
Contraindications: cerebral haemorrhage, extensive retinal haemorrhage, acute myocardial infarction, pregnancy and breast-feeding
Interactions: *see Appendix-2*
Side-effects: gastrointestinal disturbances headache, sleep disturbances, headache, tachycardia, angina, hypotension, thrombocytopenia, intrahepatic cholestasis, hypersensitivity reactions.
Dose: 400 mg 2-3 times daily

Proprietary Preparations
Oxifyl CR *(Square),* Tab., 400 mg, Tk. 7.02/Tab.
Trental Dragee *(Sanofi),* Tab., 400 mg, Tk. 15.06/Tab.

VINPOCETINE

Indications: acute ischaemic stroke due to cerebral thrombosis, cerebral embolism; acute circulatory disorder, hypertensive crisis, the acute cerebrovascular disorder, ischemic neurological deficit, multi infarct dementia, cerebral arteriosclerosis, hypertensive encaphalopathy
Contraindication: pregnancy
Interactions: *see Appendix-2*
Side-effects: transient hypotension and tachycardia
Dose: 15mg-30mg in divided dose

Proprietary Preparations
Avintol *(ACI),* Tab., 5mg, Tk. 4.00/Tab.
Camiton *(Drug Int),* Tab., 5 mg, Tk. 4.00/Tab.
Caviton *(Opsonin),* Tab., 5 mg, Tk. 2.26/Tab.
Cerenin *(Ambee),* Tab. 5 mg, Tk. 3.55/Tab.
Cereton *(General),* Tab., 5 mg, Tk.4.02/Tab.; Inj., 10mg/2 ml, Tk. 40.00/2 ml
Cerevas *(Square),*Tab., 5 mg, Tk. 4.01/Tab.
Cerivin *(Beximco),* Tab., 5 mg, Tk. 4.02/Tab.
Cognitol *(Sun),* Tab., 5 mg, Tk. 4.05/Tab.
Vincet *(Eskayef),* Tab, 5 mg, Tk. 4.00/Tab.
Vinsetine *(Incepta),* Tab., 5 mg, Tk. 4.00/Tab.
Vinton *(Aristo),*Tab., 5mg, Tk. 4.00/Tab.

3.4 POSITIVE INOTROPIC DRUGS

Cardiac Glycosides, phosphodies-terase inhibitors and sympathomime-tics with inotropic activity are positive inotropic drugs.

CARDIAC GLYCOSIDES

Cardiac glycosides are still widely used for the treatment of cardiac failure in association with rapid atrial fibrillation, but the effectiveness of ACE inhibitors in prolonging survival in patients with heart failure has led to decreased use of Cardiac glycosides in patients in sinus rhythm. **Digoxin,** the most widely used cardiac glycoside slows ventricular rate in rapid atrial fibrillation and is most useful in the treatment of atrial fibrillation. Digoxin increases the force of myocardial contraction and reduces conductivity within the atrioventricular (AV) node; it is prescribed for patients with heart failure who remain symptomatic despite optimal use of diuretics.
Digoxin has a long half-life and the maintenance dose needs to be given only once daily. Renal function is the most important determinant of digoxin dosage though its elimination from the body depends on metabolism in the liver.
Digitoxin is also long-acting and eliminates through bile excretion; it can be given in renal failure.
Side-effects: depend both on the plasma concentration of the cardiac glycoside and on the sensitivity of the conduction system or of the myocardium. Cardiac glycosides should be used with special care in the elderly. Hypokalaemia predisposes to toxicity; therefore regular monitoring of plasma potassium concen-tration is needed and

potassium sparing diuretics or foods rich in potassium should be given.
Toxicity can often be managed by withdrawing digoxin and hypokalaemia to be corrected if required; severe conditions require emergency specialist management. **Digoxin-specific antibody fragments** can be used for life-threatening over dosages as a measure beyond the withdrawal of the cardiac glycoside and correction of any electrolyte abnormality.
CHILD: the dose is based on body-weight; they require a relatively larger dose of digoxin than adults.
***Note*.** the bioavailability of the tablet form of digoxin or digitoxin is pharma-cologically very important beca-use of the critical nature of the product.

DIGOXIN [ED]

Indications: heart failure, supraventricular arrhythmia (particularly in atrial fibrillation)
Cautions: recent infarction; sick sinus syndrome; thyroid disease; elderly, pregnancy
Contraindications:renal impairment, rapid intravenous administration,heart block,hypokalamia
Side-effects: usually associated with excessive dosage; anorexia, nausea, vomiting, headache, fatigue, drowsiness, confusion, delirium, hallucination, depression, arrhythmia, heart block, intestinal ischaemia; gynaecomastia on long-term use; thrombocytopenia reported
Interactions: *see Appendix-2*
Dose: *by mouth*, rapid digitalization, 1-1.5 mg in divided doses over 24 hours; less urgent digitalization, 250-500 micrograms daily (higher dose may be divided)
Maintenance, 62.5-500 micrograms daily (higher dose may be divided) according to renal function and, in atrial fibrillation, on heart-rate response; usual range, 125-250 micrograms daily (lower dose may be appropriate in elderly).
Emergency loading dose *by intravenous infusion,* total dose of 0.5-1 mg given in divided doses with about half of the total dose given over 10-20 minutes, followed by further fractions of the total dose (also given over 10-20 minutes) at intervals of 4-8 hours according to response.
Note. the above doses may need to be reduced if digoxin (or another cardiac glycoside) has been given in the preceding 2 weeks. For plasma concentration monitoring, blood should be taken at least 6 hours after a dose

Proprietary Preparations
Agoxin *(Aristo),* Tab. , 250 mcg, Tk. 1.09/Tab.
Centoxin *(Opsonin),* Tab., 250 mcg, Tk. 0.82/Tab.; Elixir, 250 mcg/5 ml, Tk. 56.60/Tab.
Digoxen*(DrugInt.)*,Cap.0.1mg,Tk.0.94/Cap; 0.2mg,Tk.1.34/Cap.

PHOSPHODIESTERASE INHIBITORS

Enoximone and milrinone are selective Phosphodiesterase inhibitors that exert most of their effects on the myocardium after administration but there is no evidence of any beneficial effect on survival.

3.5 DIURETICS

Thiazides act by inhibiting the sodium and chloride cotransporter in the distal convoluted tubule. The main side effects are hypokalaemia and metabolic alkalosis. They are given in chronic heart failure to relieve edema and are widely used in lower doses to treat mild to moderate hypertension.
Loop diuretics inhibit the sodium potassium chloride co-transporter in the thick ascending loop. The main unwanted effects are hypokalaemia, metabolic alkalosis and hypovolemia. They are prescribed in left ventricular failure and in patients with chronic heart failure to reduce pulmonary edema.

Combination diuretic therapy may be prescribed in patients with edema who do not respond to the treatment with one diuretic.
ELDERLY: initially diuretics should be used in low dose in the elderly. The dose is to be adjusted according to renal function. Diuretics should not be used on a long-term basis.
POTASSIUM LOSS: both thiazides and loop diuretics may cause hypokalaemia which may be fatal in coronary heart disease and in those patients who are being treated with cardiac glycosides. Potassium supplements are not needed when thiazide diuretics are given in combi-nation with potassium sparing diuretics
Potassium supplements are not usually essential when thiazides are used alone in the treatment of hypertension.

3.5.1 THIAZIDES AND RELATED DIURETICS

Thiazides and related diuretics are moderately potent. The onset of action of diuresis of this group starts within 1 to 2 hours of oral administration and the action lasts for 12 to 24 hours. They are to be given early in the morning so that the diuresis does not interfere with normal sleep pattern.
Bendroflumethiazide (Bendrofluazide), a thiazide diuretic is widely used; a low dose of 2.5 mg daily is routinely prescribed in the treatment of hypertension. Higher doses of thiazides cause increased level in plasma uric acid, glucose, and lipids and decreased level in plasma potassium. Bendroflu-methiazide (Bendrofluazide) is randomly used for heart failure and for the treatment of mild hypertension or with other drugs in severe hypertension.
Chlorthalidone, a thiazide related compound may be given on alternate day to relieve edema. It is also useful if acute retention is liable to be precipitated by a more rapid diuresis.

Other thiazides and related diuretics (including **benzthiazide**, **clopamide**, **cyclopenthiazide,hydrochlorothiazide**, **hydroflumethiazide** and **polythiazide**) are more expensive than the longer established thiazides, but have no special advantages.

Metolazone is especially effective when combined with a loop diuretic; it can be given even in renal failure. The patient needs to be monitored carefully due to profound diuresis.

Xipamide and Indapamide are structurally similar to chlorthalidone. Indapamide can cause less metabolic disturbances, particularly less impair-ment of glucose intolerance.

BENDROFLUMETHIAZIDE/ BENDROFLUAZIDE

Indications: edema, hypertension

Cautions : diabetes and gout pregnancy and breast-feeding

Contraindications: severe hepatic and renal impairment, postural hypotension, elderly,

Interactions: *see Appendix-2*

Side effect: hypokalaemia, hypomagnes-aemia, hyponatraemia, hypercalcaemia, hypochloraemic alkalosis hyperurica-emia, gout, hyperglycemia, neutron-penia and thrombocy-topenia, pancreatitis, intrahepatic cholestasis, hyper-sensitivity reactions and SLE

Dose: edema, initially 5-10 mg in the morning daily or on alternate days; maintenance, 5-10mg 1-3 times weekly.

Hypertension, 2.5 mg in the morning; higher doses rarely necessary

Generic Preparation
Tablet, 2.5mg

CHLORTHALIDONE

Indications: edema hypertension; under close supervision it can be given in patients having ascites due to cirrhosis and nephrotic syndrome; mild to moderate chronic heart failure, diabetes insipidus
Cautions : *see under Benedrofluazide.*

Contraindications: *see under benedrofluazide*
Interactions: *see Appendix-2*
Side-effects: *see under benedrofluazide*
Dose: edema, up to 50 mg daily for limited period; hypertension, 25 mg in the morning increased to 50 mg if necessary; heart failure, 25-50 mg in the morning; increased if necessary to 100-200 mg daily

Generic Preparation
Thalidone *(Popular),* Tab., 25 mg, Tk.5.02/Tab.

HYDROCHLOROTHIAZIDE [ED]

Indication: edema, hypertension
Cautions: *see under benedrofluazide.*
Contraindications: *see under benedrofluazide*
Interactions: *see Appendix-2*
Side-effects: *see under benedrofluazide*
Dose: hypertension, 25 mg daily, increased to 50 mg daily if necessary
ELDERLY: in some elderly patients an initial dose of 12.5 mg daily may be sufficient

Proprietary Preparations
Acuren *(Incepta),* Tab., 25 mg, Tk. 0.70/Tab.
Acuren *(Incepta),* Tab., 50 mg, Tk. 1.00/Tab.
HTZ *(Unimed),* Tab., 25 mg, Tk. 0.70/Tab.
Hypezide *(Pacific),* Tab., 50 mg, Tk. 0.75/Tab.

INDAPAMIDE

Indication: essential hypertension
Cautions: renal impairment, gout, hyperparathyroidism (discontinue if hypercalcaema); hyperaldosteronism; pregnancy and breast-feeding
Contraindications: recent cerebrovascular accident, severe liver disease
Interactions: *see Appendix-2*
Side-effects: hypokalaemia, , dizziness, fatigue, muscular cramps, anorexia, dyspepsia, rashes, increase in liver enzymes, blood disorder, hyponatraemia, metabolic alkalosis, hyperglycemia, increased plasma urate concentrations, paraesthesia, photosensitivity, impotence, renal impairment
Dose : 2.5 mg daily in the morning

Proprietary Preparations
Dihert *(Novartis),* SR Tab., 1.5 mg, Tk.8.00/Tab.
Idatix *(Incepta),* SR Tab., 1.5 mg, Tk.5.00/Tab.
Indamid *(Sharif),* SR Tab., 1.5 mg, Tk.5.00/Tab.
Indapa *(Drug Int.),* SR Tab., 1.5 mg, Tk.5.00/Tab.
Indelix *(Beximco),* SR Tab., 1.5 mg, Tk.6.00/Tab.
Indimide *(Healthcare),* SR Tab., 1.5 mg, Tk.6.50/Tab.
Ipide *(Renata),* Tab., 1.5 mg, Tk. 5.00/Tab.
Repres *(Square),* SR Tab., 1.5 mg, Tk.5.01/Tab.
Xelix *(Aristo),* SR Tab., 1.5 mg, Tk. 5.00/Tab.

METOLAZONE

Indications: oedema, hypertension
Cautions: electrolytes should be monitored, particularly with high doses, long-term use, or in renal impairment; mayexacerbate diabetes, gout, and systemic lupus erythematosus; nephrotic syndrome, hyperaldoste-ronism, and malnourishment; avoid in severe liver disease, hypokalaemia pregnancy and breast feeding
Contraindications: refractory hypokalaemia, hyponatraemia and hypercalcaemia, symptomatic hyperuricaemia and Addison's disease.
Interactions: see Appendix-2
Side-effects: mild gastro-intestinal disturbances, postural hypotension, altered plasma-lipid concentrations, metabolic and electrolyte disturbances including hypokalaemia, hyponatraemia, hypomagnesaemia, hypercalcaemia, hyperglycaemia, hypochloraemic alkalosis, hyperuricaemia and gout
Dose: oedema, 5-10 mg daily in the morning, increased if necessary to 20 mg daily in resistant oedema, max. 80 mg daily. Hypertension, initially 5 mg daily in the morning; maintenance 5 mg on alternate days.

Generic Preparation
Tablet, 500 mcg, 5 mg

3.5.2 LOOP DIURETICS

Loop diuretics are the most efficacious oral diuretic agent; inhibit reabsorption from the ascending limb of the loop of Henle in the renal tubule; useful for the treatment of acute episodes of pulmonary edema due to left ventricular failure; intravenous administration produces relief of breathlessness and reduces pre-load very rapidly. Loop diuretics are also effective for edema in patients with long-standing heart failure, cirrhosis and renal failure; diuretic resistant edema can be treated with a loop diuretics combined with thiazides or related diuretic .

Loop diuretics are sometimes used to lower blood pressure in those with chronic renal failure (in whom thiazides may by ineffective). Hypoklaemia may develop; and constant monitoring is needed to avoid hypotension. If there is an enlarged prostate, urinary retention may occur. **Furosemide** and **bumetanide** are similar in activity, both act within 1 hour of oral administration and diuresis is complete within 6 hours so that, if necessary, they can be given twice in one day without interfering with sleep. Transient deafness is a risk if potentially ototoxic drugs (e.g. aminoglycoside) are given concomitantly. **Bumetanide** may cause myalgia. In patients with impaired renal function larger doses may be needed.

BUMETANIDE

Indication: oedema
Cautions: hypovolaemia and hypotension should be corrected before initiation of treatment; electrolytes should be monitored during treatment; can exacerbate diabetes mellitus and gout and prostate enlargement
Contra-indications: severe hypokalaemia, severe hypona-traemia, anuria, comatose and precomatose states associated with liver cirrhosis and in renal failure
Intercactions: *see Appendix-2*
Side-effects: *see under Furosemide*; also gynaecomastia, breast pain, musculos-keletal pain
Dose: *by mouth,* 1 mg in the morning, repeated after 6–8 hours if necessary; severe cases, 5 mg daily increased by 5 mg every 12–24 hours according to response; ELDERLY, 500 micrograms daily may be sufficient
By intravenous injection, 1–2 mg, repeated after 20 minutes if necessary; ELDERLY, 500 micrograms daily may be sufficient
By intravenous infusion, 2–5 mg over 30–60 minutes; ELDERLY, 500 micrograms daily may be sufficient
By intramuscular injection, 1 mg initially then adjusted according to response; ELDERLY, 500 micrograms daily may be sufficient

Proprietary Preparations
Bumecard *(Incepta),* Inj., 0.05 gm/100 ml, Tk. 30.00/vial; Tab., 1 mg, Tk. 5.00/Tab; Tab., 5mg, Tk. 18.00/Tab.
Conart *(ACI),* Tab., 1 mg, Tk. 5.00/Tab.
Urinide *(Navana),* Tab., 5 mg, Tk. 10.00/Tab.

FRUSEMIDE/ FUROSEMIDE [ED]

Indications: edema, oliguria due to renal failure

Cautions: pregnancy and breast-feeding, hypotension, liver failure, enlarged prostate; hypovolaemia to be corrected before using in oliguria

Contraindications: precoma state associated with liver cirrhosis and renal failure with anuria

Interactions: *see Appendix-2*

Side-effects: hyponatraemia, hypokalaemia and hypomagnesa-emia, hypoch-loraemic alkalosis, increased calcium excretion, hypotension, hyperuricaemia; temporary increase in plasma cholesterol and triglyceride concentrations and bone marrow depression, pancreatitis, deafress and myalgia

Dose : *by mouth*, edema, initially 40 mg in the morning; maintenance 20 mg daily or 40 mg on alternate days, increased in resistant edema to 80 mg daily or 40 mg

on alternate days; increased in resistant edema to 80 mg daily or more

In oliguria, initially 250 mg daily; if necessary larger doses, increasing in steps of 250 mg, may be given every 4-6 hours to a maximum of a single dose of 2 g (rarely used)

CHILD: 1-3 mg/kg daily, max, 40 mg daily.

By intramuscular injection or slow intravenous injection initially 20-50mg

CHILD: 0.5-1.5 mg/kg to a max. daily dose of 20 mg

By intravenous infusion (by syringe pump if necessary), in oliguria, initially 250 mg over hour (rate not exceeding 4 mg/min). If satisfactory urine output not obtained in the subsequent hour further 500 mg over 2 hours, then if no satisfactory response within subsequent hour, further 1 g over 4 hours; if no response obtained dialysis probably required; effective dose (up to 1 g) can be repeated every 24 hours

Proprietary Preparations
Frudema *(Pacific),* Tab., 40 mg, Tk 0.40/Tab.
Frusemide *(Albion),* Tab., 40 mg, Tk.0.53/Tab.
Frusin *(Opsonin),* Inj., 20 mg/2 ml, Tk.6.02/amp.; Inj., 20 mg/2 ml, Tk. 6.02/amp.; Tab., 40 mg, Tk. 0.4/Tab.;
Syrup 40 mg/5 ml, Tk. 64.15/60 ml
Fusid *(Square),* Tab., 40 mg, Tk. 0.64/Tab.; Inj., 20 mg/2 ml, Tk. 8.00/amp.
G-Furosemide *(Gonoshasthaya),* Inj., 20mg/2ml, Tk. 3.00/amp.; Tab., 40 mg, Tk.0.50/Tab.
Lasix *(Sanofi),* Tab., 40 mg, Tk. 0.64/Tab.; Inj., 20 mg/2 ml, Tk. 8.00/amp.
Trofurit *(Ambee) ,* Inj. , 20 mg / 2ml , Tk. 5.53 /2 ml Amp; Tab., 40 mg , Tk. 0.53/Tab.

TORASEMIDE

Indications: edema associated with heart failure including pulmonary edema with renal and hepatic disorder, hypertesion
Cautions: *see under Furosemide,* hepatic impairment, renal inpairment, prgnancy
Contra-indications: see under Furosemide
Interactions: *see Appendix-2*
Side-effects: *see under Furosemide*, also dry mouth, paraesthesia
Dose: edema, uasual dose 5mg once daily, increased according to response to 20mg once daily; usual max.40mg daily

Proprietary Preparations
Dilast *(Incepta),* Tab. 20 mg, Tk.8.00/Tab.
Dytor *(Unimed),* Tab.2.5 mg, Tk. 6.00/Tab.; 5mg, Tk. 11.00/Tab.
Luretic*(Drug Int.)* Tab. 2.5 mg, Tk. 2.00/Tab.; 5mg, Tk. 3.50/Tab.

3.5.3 POTASSIUM-SPARING DIURETICS

Triamterene and **Amiloride** are used in combination with other diuretics for the treatment of hypertension. They cause retention of potassium and are therefore used as a more convenient alternative to giving potassium supplements along with thiazides or loop diuretics.

Spironolactone is a potassium-sparing diuretic and a competitive antagonist of aldosterone which is effective in the treatment of the edema due to cirrhosis of liver. Low doses of spironolactone may be beneficial in severe heart failure; this diuretic is also indicated in primary hyperaldosteronism. Potassium supplements should not be given with potassium sparing diuretics. The diuretic should not be prescribed to a patient receiving an ACE inhibitor; the concomitant use can cause severe hyperkalaemia.

AMILORIDE HYDROCHLORIDE

Indications: edema, potassium conservation with thiazide and loop diuretics
Cautions: pregnancy and breast-feeding, monitor in renal impairment ,diabetes mellitus, elderly
Contraindications: hyperkalaemia, renal failure
Interactions: *see Appendix-2*
Side-effects: include gastrointestinal disturbances, rashes, confusion, postural

hypotension, hyperkalaemia, hyponatraemia

Dose: used alone, initially 10 mg daily, adjusted according to response; max. 20 mg daily

With other diuretics, congestive heart failure and hypertension, initially 5-10 mg daily; cirrhosis with ascites, initially 5 mg daily

Proprietary Preparation
see under hydrochlorothiazaide

POTASSIUM-SPARING DIURETICS WITH OTHER DIURETICS

It is preferred to prescribe thiazides and potassium sparing diuretics as individual diuretics. The use of fixed combinations may be rational if there is a problem of compliance. Potassium-sparing diuretics are not usually needed in the routine treatment of hypertension unless hypokalaemia develops.

ALDOSTERONE ANTAGONISTS

EPLERENONE

Indications: adjunct in stable patients with left ventricular dysfunction with evidence of heart failure, following myocardial infarction (start therapy within 3–14 days of event)
Cautions: elderly, hepatic impairment- renal impairment- increased risk of hyperkalaemia—close monitoring required; avoid if eGFR less than 50 mL/ minute/ 1.73m2; pregnancy
Interactions: *see Appendix-2*
Contra-indications: hyperkalaemia; concomitant use of potassium-sparing diuretics or potassium supplements
Side-effects: diarrhea, nausea, hypotension; dizziness; hyperkalaemia; rash; flatulence, vomiting, atrial fibrillation, postural hypotension, arterial thrombosis, dyslipidaemia, gynaecomastia, pyelonep-hritis, hyponatraemia, dehydration, eosinophilia, asthenia, leg cramps, azotaemia, sweating and pruritus

Dose: initially 25 mg once daily, increased within 4 weeks to 50 mg once daily; CHILD not recommended

Proprietary Preparations
Aldonist*(Unimed),* Tab., 25 mg, Tk.45/Tab.; 50 mg, Tk. 85/Tab.
Epleron *(Incepta),* Tab., 25 mg, Tk.45/Tab.

SPIRONOLACTONE [ED]

Indications: it is used as an adjunct to other diuretics to reduce the loss of potassium in the management of refractory edema such as that associated with ascites in cirrhosis of the liver, malignant ascites and nephrotic syndrome. The drug is also indicated in congestive heart failure, primary hyperaldosteronism

Cautions: hepatic impairment, severe renal impairment, and electrolytes to be monitored to prevent hyperkalaemia

Contraindications: acute renal insufficiency, hyperkalaemia, pregnancy and breast-feeding; Addision's disease; the drug should not be given in combination with another potassium sparing diuretic

Interactions: *see Appendix-2*

Side-effects: diarrhea, gynaecomastia, menstrual irregularities, hirsutism, lethargy, mental confusion, hyperkal-aemia, hyponatraemia

Dose: 100-200 mg daily, increased up to 400 mg if required. CHILD: initially 3 mg/kg daily in divided doses

Proprietary Preparations
Inospiron *(Incepta),* Tab., 25 mg, Tk.5.00/Tab.
Spiretic *(Drug Int.),* Tab., 25 mg, Tk.5.00/Tab.
Spirocard *(Popular),* Tab., 100 mg, Tk.18.07/Tab.; Tab., 25 mg, Tk. 5.02/Tab.

Spironolactone + Frusemide
Dilup *(ACI),* Tab., 50 mg + 40 mg, Tk.8.03/Tab.; Tab., 50 mg + 20 mg, Tk.6.02/Tab.
Diretic *(Drug Int),* Tab., 50 mg + 20 mg, Tk.6.00/Tab.; DS Tab., 50 mg + 40 mg, Tk.8.00/Tab.
Edeloss *(Incepta),* Tab., 50 mg + 20 mg, Tk.6.00/Tab.

Edeloss Plus *(Incepta),* Tab., 50 mg + 40mg , Tk. 8.00/Tab.
Edemide *(Acme),* Tab., 50 mg + 40 mg, Tk.10.00/Tab.; 50 mg + 20 mg, Tk. 8.00/Tab.
Edenil *(Eskayef),* Tab., 50 mg + 40 mg, Tk.8.00/Tab.; 50 mg + 40 mg, Tk. 6.00/Tab.
Frulac *(Orion),* Tab., 50 mg + 40 mg, Tk.10.00/Tab.; 50 mg + 20 mg, Tk. 8.00/Tab.
Frunal *(Ad-din),* Tab., 20mg + 50mg, Tk. 6.00/Tab.
Fruselac *(Aristo),* Tab., 50 mg + 20 mg, Tk.6.00/Tab.;
Fruselac Plus *(Aristo),* Tab., 50 mg + 40 mg, Tk. 8.00/Tab.
Frusin Plus *(Opsonin),* Tab., 50 mg + 20 mg, Tk. 4.53/Tab.; 50 mg + 40 mg , Tk. 6.04/Tab.
Frusiton *(Globe),* Tab., 40 mg + 50 mg, Tk. 8.00/Tab.; 20 mg + 50 mg, Tk. 6.00/Tab.
Fruson *(Ibn Sina),* Tab., 50 mg + 20 mg, Tk.6.00/Tab.
Furo Plus *(Beacon),*Tab., 50 mg + 20 mg, Tk.6.00/Tab.
Fuseton *(Alco),*Tab., 50 mg + 40 mg, Tk.5.00/Tab.
Fusid *(Square),*Tab. 50 mg + 40 mg, Tk.10.00/Tab.
Fusid Plus *(Square),* Tab., 50 mg + 20 mg, Tk. 8.00/Tab.
Lacitone *(General),* Tab., 50 mg + 20 mg, Tk. 6.02/Tab.
Lasilactone *(Sanofi),* Tab., 50 mg + 20 mg, Tk. 6.02/Tab.
Laxicon *(White Horse),*Tab. 50 mg + 20 mg, Tk. 6.00/Tab.
Laxur *(Healthcare),* Tab. 50 mg + 20 mg, Tk. 8.00/Tab.
Redema *(Rangs),* Tab., 20mg + 50mg/Tab, Tk. 6.00/Tab.; 40mg + 50mg, Tk. 8.00/Tab.
Resitone *(Beximco),* Tab., 50 mg + 20 mg, Tk. 6.02/Tab.
Resitone Plus *(Beximco),*Tab., 50 mg + 40mg, Tk. 8.00/Tab.
Spirocard Plus *(Popular),*Tab., 50 mg + 20mg, Tk. 6.02/Tab.
Tonemide *(Pacific),* Tab., 50 mg + 20 mg, Tk.4.51/Tab.
Uritone *(Renata),* Tab., 50 mg + 20 mg, Tk.6.00/Tab.; 50 mg + 40 mg, Tk.8.00/Tab.
Urospin *(Biopharma),*Tab., 50 mg + 20 mg, Tk.6.02/Tab.

3.5.4 OSMOTIC DIURETICS

Osmotic diuretics are used to reduce cerebrospinal fluid (CSF) pressure causing cerebral edema; these drugs are filtered at the glomerulous, which do not markedly influence sodium and chloride excretion. Osmotic diuretics are not used in heart failure as they may expand the blood volume. **Mannitol** is used in cerebral edema; a typical dose is 1 g/kg as a 20% solution given by rapid intravenous infusion.

MANNITOL [ED]

Indications: *see notes above;* also in glaucoma (*see section 10.4.3*) for transient reduction of intraocular fluid pressure

This diuretic is indicated prophylactically for acute renal failure in situations such as cardiovascular operations, treatment with nephrotoxic anticancer agents, severe traumatic injury and management of haemolytic transfusion reactions.

Cautions: extravasation causes inflammation and thrombophlehitis

Contraindications: congestive cardiac failure, pulmonary edema

Side-effects: chills, fever, hyperos-molality and hyponatremia may occur during treatment of renal failure

Interactions: *see Appendix-2*

Dose: *by intravenous infusion* for diuresis, 50-200 g over 24 hours, preceded by a test dose of 200 mg/kg by slow intraven-ous injection; in cerebral edema (*see notes above)*

Proprietary Preparations
Manisol *(Orion Infusion),* I.V. Infusion, 20%, Tk. 125/500ml
Mannisol A(I) *(Human Serum Ins),* I.V. Infusion 10%, Tk.142.64/500ml
Osmosol *(Beximco),* I.V Infusion, 20%, Tk.126.40/500ml

3.5.5 CARBONIC ANHYDRASE INHIBITORS

The carbonic anhydrase inhibitors are weak diuretics and have been replaced by thiazides. These are used for prophylaxis against mountain sickness but are not the substitutes for acclimatization.

Acetazolamide and eye drops of **dorzolamide** inhibit the formation aqueous humour and are used in

glaucoma *(see section 10.4.3);* also used in petit mal epilepsy as an anticonvulsant; in the treatment of salicylates or barbiturate poisoning to alkalinize the urine; side-effects include drowsiness, paraesthesia, blood dyscrasias and allergic skin rashes.

3.6 ANTIARRHYTHMIC DRUGS.

Anti-arrhythmic drugs can be classified clinically into those that act on supraventricular arrhythmia e.g. verapamil and those that act on ventricular arrhythmia e.g. lignocaine.

CAUTIONS: The negative inotropic effects of antiarrythmic drugs tend to be additive. Therefore special care should be taken if two or more are used especially if myocardial function is impaired. Most or all drugs that are effective in countering arrythmias can also provoke them in some circumstances; moreover hypokalaemia enhances the pro arrhythmic effect of many drugs.

Drugs for **supraventricular arrhythmias** include adenosine, cardiac glycosides and verapamil. **Adenosine** is usually the treat-ment of choice of paroxysmal supraven-tricular tachycar-dia. It has a very short duration of action, but prolonged in those who are taking dipyridamole. **Verapamil** is preferred to adenosine in asthma. Verapamil is very much effective for supraventricular tachycardia. An initial intravenous dose may be followed by oral treatment. Hypotension may occur with larger doses. It should not be used for tachyarrhythmias where the QRS complex is a broad complex. It is also contra-indicated in Wolff-Parkinson-White syndrome. It is contraindicated in CHILD. Some supra-ventricular arrythmias in childhood can be accelerated by verapamil with fatal consequences.

Oral administration of **digoxin** is the treatment of choice in cases of atrial fibrillation and atrial flutter. Intravenous digoxin, prefer-ably infused slowly, is occasionally required if the ventricular rate needs rapid control. Cardiac glycosides are contra-indicated in supraventricular arrhythmia associated with Wolff-Parkinson-White syndrome.

Drugs for **both supraventricular and ventricular arrhythmias** include amio-darone, beta-blockers, disopyramide, flecai-nide, procainamide, propafenone and quinidine. **Amiodarone** is a highly effective drug; its main action is to suppress atrial and ventricular re-entrant rhythms and is the drug of choice for the treatment of life threatening ventricular tachycardia especially when other drugs are not effective or contraindicated. It may be given in paroxysmal supraventricular, nodal and ventricular tachycardias, atrial fibrillation and flutter, and ventricular fibrillation. Amiodarone has an extremely long plasma life of about several weeks and once daily dose is needed; side effects are numerous and important; they include photosensitive skin rashes, corneal deposits, and abnormal thyroid function (both hypothyroidism and hyperthy-roidism may occur); higher doses may cause anorexia, nausea and vomiting. Most patients taking amiodarone are adv-ised to shield the skin from light and to use a wide-spectrum sunscreen to protect against ultraviolet and visible light.

Laboratory tests should be performed before treatment and every 6 months. A raised T_3 and T_4 with very low or undetectable TSH concentration suggest the development of thyrotoxicosis which may be very refractroty needing amiodarone to be withdrawn at least temporarily to achieve control this condition; treatment with carbimazole may also be required. Hypothyroidism can be treated with replacement therapy without with-drawing amiodarone if it is essential. Pneumonitis should always be suspected if new or progressive shortness of breath or cough develops in a patient taking amiodarone. Fresh neurological symptoms should raise the possibility of peripheral neuropathy. Amiodarone is also associated with hepatotoxicity, and treatment should be discontinued if severe liver function

abnormalities or clinical signs of liver disease develop.

Beta-blockers act as anti-arrhythmic drugs principally by attenuating the effects of the sympathetic system on automatcity and conductivity within the heart. Intravenous administration of a beta-blocker such as **esmolol** or **propranolol**, can achieve rapid control of ventricular rate.

Disopyramide may be given by intravenous injection to control arrhythmias after myocardial infarction (including those not responding to lidocaine but it impairs cardiac contractility. Oral administration of disopyramide is useful but it has an antimuscarinic effect, which limits its use in patients with glaucoma or prostatic hypertrophy.

Flecanide belongs to the same general class as lidocaine. It may be of value in serous symptomatic ventricular arrhyth-mias. It may also be indicated for junctional re-entry tachycardias and for paroxysmal atrial fibrillation. As with quinidine it may precipitate serious arrhy-thmias in a small minority of patients.

Procainamide can be given by intravenouse injection to control ventricular arrhythmias, but prologed oral use can cause a syndrome resembling systemic lupus erythematosus.

Propafenone is used for the propylaxis and treatment of ventricular arrhythmais and also for some supraventricular arrhythmias and It has a complex mechanism of action, including weak beta-blocking activity (therefore caution is needed in obstructive airways diseases; contra-indicated if severe).

Quinidine may be effective in supp-ressing supraventricular and ventricular arrhythmais. It may itself precipitate rhythm disorders, and is better if used on specialist advice only. It can cause hypersensitivity reactions and gastroin-testinal upsets.

Durgs for ventricular arrhythmias include **bretylium, lidocaine**, **mexiletine** and **phenytoin**. Bretylium is only used as an antiarrhymic drug in resuscitation; it can cause severe hypotension. Mexiletine may be given as a slow intravenous injection if lignocaine is ineffective, it has a similar action. Adverse cardiovascular and central nervous system effects may limit the dose; nausea and vomiting may prevent an effective dose being given by mouth.

ADENOSINE

Indications: rapid reversion to sinus rhythm of paroxysmal supraventricular tachycardias, including those associated with accessory conducting pathways (e.g.
Wolff-Parkinson-White syndrome); aid to diagnosis of broad or narrow complex supraventricular tachycardias

Cautions: monitor ECG and have resuscitation facilities available; atrial fibrillation or flutter with accessory
pathway (conduction down anomalous pathway may increase); first-degree AV block; bundle branch block; left main coronary artery stenosis; uncorrected hypovolaemia; stenotic valvular heart disease; left to right shunt; pericarditis; pericardial effusion; autonomic dysfunction; stenotic carotid artery disease with cerebrovascular insufficiency; recent myocardial infarction; heart failure; heart transplant;

Contra-indications: second- or third-degree AV block and sick sinus syndrome (unless pacemaker fitted); long QT syndrome; severe hypotension; decompensated heart failure; chronic obstructive lung disease (including asthma)and pregnancy

Interactions: *see Appendix-2*

Side-effects: nausea; arrhythmia (discontinue if asystole or severe bradycardia occur), sinus pause, AV block, flushing, angina (discontinue), dizziness; dyspnoea; headache; less commonly metallic taste; palpitation, hyperventilation, weakness, blurred vision, sweating; very rarely transient worsening of intracranial hypertension, bronchos-pasm, injection-site reactions; also reported vomiting, syncope, hypotension (discontinue if severe), cardiac arrest, respiratory failure (discontinue), and convulsions

Dose: *by rapid intravenous injection* into central or large peripheral vein, 6 mg over 2 seconds with cardiac monitoring; if necessary followed by 12 mg after 1–2 minutes, and then by 12 mg after a further 1–2 minutes; increments should not be given if high level AV block develops at any particular dose Important Patients with a heart transplant are very sensitive to effects of adenosine and should receive initial dose of 3 mg over 2 seconds, followed if necessary by 6 mg after 1–2 minutes, and then by 12 mg after a further 1–2 minutes. Also, if essential to give with dipyridamole reduce adenosine dose to a quarter of the usual dose

Proprietary Preparation
Adecard*(Popular)* Inj.,6mg/2ml,Tk 150/Amp

AMIODARONE HYDROCHLORIDE

Indications: *see notes above* (should be initiated in hospital or under specialist supervision)
Cautions: liver function and thyroid function tests required before treatment and then every 6 month *(see notes above for tests of thyroid function);* chest x-ray required before treatment; heart failure; renal impairment; elderly; severe brady-cardia and conduction disturbances in excessive dosage; intravenous use may cause moderate and transient fall in blood pressure
Contraindications: sinus bradycardia, sino-atrial heart block, unless pacemaker fitted, avoid in severe conduction disturbances or sinus node disease, history of thyroid dysfunction, pregnancy and breast-feeding, avoid intravenous use in severe respiratory failure, circulartory collapse, severe arterial hypotension
Interactions: *see Appendix-2*
Side-effects: reversible corneal micro-deposits, peripheral neuropathy and myopathy, phototoxicity, skin discoloration, hypothyroidism, hyperthyroidism, diffuse pulmonary alveolitis, pneumonitis and fibrosis, janudice, hepatitis and cirrhosis reported, tremor, nightmares, vertigo headache, sleeplesssness, fatigue, alopecia, paraesthesia, benign raised intracranial pressure, impotence, epididymoorchitis, ataxia, vasculitis, renal involvement and thrombocytopenia, anaphylaxis on rapid injection, also bronchospasm or apnoea
Dose: *by mouth*, 200 mg 3 times daily for 1 week reduced to 200 mg twice daily for a further week; maintenance, usually 200 mg daily or the minium required to control the arrhythmia *by intravenous infusion*, 5 mg/kg over 20-120 minutes with EGC monitoring, max.1.2 g in 24 hours
Doses may need to be reduced to avoid convulsion, depression of the central nervous system or depression of the cardiovascular system

Proprietary Preparations
Cardiron *(Drug Intl),* Tab., 200 mg, Tk.7.00/Tab.
Pacet *(Beximco),* Tab., 100 mg, Tk. 5.02/Tab.; 200 mg, Tk. 10.04/Tab.

DISOPYRAMIDE

Indications: is used in the management of supraventricular and ventricular arrhythmias. It also has antimuscarine and negative inotropic properties
Cautions: discontinue if ventricular tachycardia, ventricular fibrillation, hypotension, hypoglycemia develop; atrial flutter or tachycardia with partial block, bundle branch block, heart failure (avoid if severe); prostatic enlargment; glaucoma; hepatic and renal impairment (*see Appendix-4*); pregnancy and breast-feeding (*see Appendix-5 & 6*)
Interactions: *see Appendix-2*
Contraindications: complete heart block or cardiogenic shock and sinus node dysfuction (unless pacemaker fitted)
Side-effects: antimuscarinic effect include dry mouth, blurred vision, urinary retaintion; gastrointestinal irritation other side effects include psychosis, cholestatic jaundice, hypoglycemia, elevated liver enzyme. It also has cardiac depressant properties and may induce cardiac arrhythmias particularly tachycardia and ventricular fibrillation,

heart block, heart failure, and hypotension (see caution above)
Dose: *by mouth* 300-800mg daily in divided dose.
By slow Intravenous injection, 2mg/kg over at least 5minutes to a max of 150mg,at a rate not exceeding 30 mg per minute; with ECG monitoring, followed immediately either by 200mg by mouth, then 200mg every 8 hours for 24 hours or 400microgram/kg/hour by intravenous infusion; max.300mg in first hour and 800mg daily

Proprietary Preparation
Norbit *(Incepta),* Cap. 100 mg.Tk.8/Cap.

LIDOCAINE HYDROCHLORIDE/ LIGNOCAINE HYDROCHLORIDE (ED)

Indications: ventricular arrhythmias, especially after myocardial infarction
Cautions: congestive cardiac failure, in hepatic failure and following cardiac surgery; elderly
Contraindications: sino-atrial disorders, all grades of atrioventricular block, severe myocardial depression
Side-effects: dizziness, paraesthesia or drowsiness ,confusion, respiratory depression and convulsions; hypotension and bradycar-dia (may lead to cardiac arrest)
Dose: *by intravenous injection*, in patients without gross circulatory impairment 100 mg as a bolus over a few minutes (50 mg in lighter patients or those whose circu-lation is severely impaired), followed immediately by infusion of 4 mg/minute for 30 minutes; 2 mg/minute for 2 hours, then 1 mg/minute; reduce concentration further if infusion continued beyond 24 hours (ECG monitoring and specialist advice needed for infusion)
IMPORTANT**:** following intravenous injection lignocaine has a short duration of action (lasting for 15-20 minutes). If an intravenous infusion is not immediately available the initial intravenous injection of 50-100 mg can be repeated if necessary once or twice at intervals of not less than 10 minutes *(see also section 8.2)*

Proprietary Preparations
Jasocaine *(Jayson)*, Inj. 4%, Tk. 3.54/2ml amp; Inj. 1%,Tk.16.88/50ml; 2%, Tk. 28.65./50ml

PROPAFENONE HYDROCHLORIDE

Indications: ventricular arrhythmias; paroxysmal supraventricular tachy-arrhythmias which include paroxysmal atrial flutter or fibrillation and paroxysma re-entrant tachycardias involving the AV node or accessory pathway, where standard therapy ineffective or contra-indicated
Cautions: heart failure; elderly; pacemaker patients; potential for conversion of paroxysmal atrial fibrillation atrial flutter with 2:1 or 1:1 conduction block; obstructive airways disease; hepatic impairment, pregnancy, breast-feeding,driving
Contra-indications: uncontrolled congestive heart failure, cardiogenic shock (except arrhythmia induced), severe bradycardia, electrolyte disturbances, severe obstructive pulmonary disease, marked hypotension, myasthenia gravis; unless adequately paced avoid in sinus node dysfunction, atrial conduction defects, second degree or greater AV block, bundle branch block or distal block
Interactions: *see Appendix-2*
Side-effects: QRS prolongation; gastro-intestinal disturbances, dry mouth, bitter taste, anorexia, jaundice, cholestasis, chest pain, bradycardia, sino-atrial, atrioventricular, or intraventricular blocks, hypotension, dizziness, syncope, pro-arhythmic effects; anxiety, confusion, ataxia, restlessness, headache, sleep disorders, paraesthesia, fatigue, seizures, extrapyramidal symptoms; impotence, reduced sperm count, blood disorders, lupus syndrome; blurred vision; hypersensitivity
Dose: body-weight 70 kg and over, initially 150 mg 3 times daily after food under direct hospital supervision with ECG monitoring and blood pressure control (if QRS interval prolonged by more than 20%, reduce dose or

discontinue until ECG returns to normal limits); may be increased at intervals of at least 3 days to 300 mg twice daily and, if necessary, to max. 300 mg 3 times daily; body-weight under 70 kg, reduce dose; ELDERLY may respond to lower doses

Proprietary Preparation
Rythmosin *(Unimed),* Tab. 150mg, Tk.15/Tab.

3.7 SYMPATHOMIMETICS

The properties of sympathomimetics vary according to whether they act on alpha or on beta adrenergic receptors. **Adrenaline** (epinephrine) acts on both alpha and beta recepotrs and increases both heart rate and contractility ($beta_1$ effect); it can cause peripheral vasodilation (a $beta_2$ effect) or vasoconstriction (an alpha effect).

3.7.1 INOTROPIC SYMPATHOMIMETICS

The cardiac stimulants **dobutamine** and **dopamine** act on $beta_1$ receptors in cardiac muscle, and increase contractibility with little effect on rate. Dosage of dopamine is critical since although low doses induce vasodilatation and increase renal perfusion, higher doses (more that 5 micrograms/kg per minute) lead to vasoconstriction and may exacerbate heart failure.
Dopexamine acts on $beta_2$ receptors in cardiac muscle to produce its positive inotropic effect, and on peripheral dopamine receptors to increase renal perfusion; it is reported not to induce vasconstriction.
Isoprenaline is less selective and increases both heart rate and contractility. It may prevent Strokes Adams attacks, but insertion of a pacemaker is preferable. It is now only used as a short-term emergency treatment of heart block or severe bradycardia.
SHOCK. Shock is a medical emergency associated with a high mortality. The underlying cause of shock such as haemorrhage, sepsis or myocardial insufficiency should be corrected. The pro-found hypotension of shock must be treated promptly to prevent tissue hypoxia and organ failure. Volume replacement is essential to correct the hypovolaemia associated with haemorrhage and sepsis but may be detrimental in cardiogenic shock. Depending on haemodynamic status, cardiac output may be improved by the use of sympathomimetic inotropic drugs such as **adrenaline, dobutamine** or **dopamine**. In septic shock, when fluid replacement and inotropic support fail to maintain blood pressure, the vasconstrictor **noradrenaline** may be considered. In cardiogenic shock peripheral resistance is frequently high and to raise it further may worsen myocardial preformance and exacerbate tissue ischaemia. The use of sympathomimetic intoropics and vasoconstrictors should preferably be confined to the intensive care setting in a hospital and undertaken with invasive haemodynamic monitoring.

DOBUTAMINE

Indications: inotropic support in infarction, cardiac surgery, cardiomyopathies, septic shock and cardiogenic shock

Caution: severe hypotension complicating cardiogenic shock

Interactions: *see Appendix-2*

Side-effects: tachycardia and marked increase in systolic blood pressure indicate overdosage

Dose: *by intravenous infusion*, 2.5-10 micrograms/kg/minute, adjusted according to response

Proprietary Preparations
Dobumin *(ACI),* Inj., 250 mg/vial, Tk.250.94/Vial

Dobutin *(Incepta),* Inj., 250mg/vial, Tk.250.00/Vial
Dobuject[I] ***(Bayer)*** Inj., 250mg/amp, Tk.278.49/Vial

DOPAMINE HYDROCHLORIDE [ED]

Indications: cardiogenic shock in infarction or cardiac surgery

Cautions: correct hypovolaemia, low dose in shock due to acute myocardial infarction, *see notes above*

Contraindications: tachyarrhythmia, pha-eochromocytoma

Interactions: *see Appendix-2*

Side-effects: nausea and vomiting, peripheral vasconstriction, hypoten-sion, hypertension, tachycardia
Dose:. *by intravenous infusion*, 2–5 micrograms/kg/minute initially, *see notes above*

Proprietary Preparations
Cardopa *(ACI),* Inj.,(IV Infusion),.40 mg/ ml, Tk.45.17/5mlVial
D-Dopamine *(Drug Int),* Inj.,(IV Infusion), 40mg/ml,, Tk. 45.00/5mlVial
Dopamin HC[I]*(Rotex medica*) Inj., (IV Infusion), 40 mg/ml,Tk. 63.40/5mlVial
Myomine *(Incepta),* Inj.,(IV Infusion), 40 mg/ ml,, Tk. 45.00/5mlVial

ISOPRENALINE HYDROCHLORIDE

Indications: heart block, severe bradycardia

Cautions: ischaemic heart disease, diabetes mellitus, hyperthyroidism

Interactions: *see Appendix-2*

Side-effects: tachycardia, arrhythmias, hypotension, sweating, tremor, headache

Dose: *by intravenous infusion*, 0.5-10 micrograms/minute

Generic Preparations
Injection, 0.2%; Tab.30 mg; 20 mg

3.7.2 VASOCONSTRICTOR SYMPATHOMIMETICS

Vasoconstrictor sympathomimentics raise blood pressure transiently by constricting peripheral blood vessels acting on alphaadrenergic receptor. They are sometimes used as an emergency method of elevating blood pressure where other measures have failed.

The danger of vasoconstrictors is that although they raise blood pressure they do so at the expense of perfusion of vital organs such as the kidney.

Spinal and epidural anaesthesia may result in sympathetic block by causing hypotension. Management may include intravenous fluids (which are usually given prophylactically), elevation of the legs, oxygen, and injection of a pressor drug such as ephedrine or methoxamine. **Ephedrine** constricts preipheral vessels and also accelerates the heart rate (by acting on beta-receptors). Use is made of this dual action of ephedrine to manage associated bradycardia (although intravenous injection of atropine sulphate 400 to 600 micrograms may also be required if bradycardia persists). When hypotension occurs in association with tachycardia, the pure alpha-adrenergic stimulant action of **methoxamine** is more appropriate.

EPHEDRINE HYDROCHLORIDE

Indications: *see under Dose*

Cautions: hyperthyroidism, diabetes mellitus, ischaemic heart disease, hypertension, angleclosure glaucoma, elderly, pregnancy may cause acute urine retention in prostiatic hypertrophy

Contraindications: breast-feeding

Interactions: *see Appendix-2*

Side-effects: nausea, vomiting, anorexia, tachycardia, arrhythmias, anginal pain, vasoconstriction with hypertension, vasodilation with hypotension, dizziness and flushing, dyspnoea, headache, anxiety, restlessness, confusion, psychoses, insomnia, tremor, difficulty in micturition, urine retention, sweating,

hypersalivation; changes in blood-glucose concentration

Dose: reversal of hypotension from spinal or epidural anaesthesia, *by slow intravenous injection* of a solution containing ephedrine hydrochloride 3 mg/ml, 3-6 mg (max. 9 mg) repeated very 3-4 minutes to max. 30 mg. *(see also section 4.7.3)*

Proprietary Preparations

Ephedrine hydrochloride 25 mg/5 ml
Ephidin *(Popular),* Inj., Tk.12.05/Amp.
Epidron *(Renata),* Inj.,Tk.12.05/Amp.
Fedrin *(Jayson),* Inj., Tk.12.05/Amp.
G-Ephedrine *(Gonoshasthaya),* Inj.,Tk. 12.00/Amp.
Nordrine *(Incepta),* Inj.,Tk.12.00/Amp.

3.7.3 DRUGS USED IN CARDIOPULMONARY RESUSCITTATION

Cessation of cardiac function results in rapid depletion of oxygen in vital organs. After 6 minutes of pulseness, brain damage can be expected to occur. For this reason early cardiopulmonary resucitation (CPR) within 4 minutes and rapid cardiac life support (ACLS) with attempted defibrillation within 8 minutes are essential for imporving survival and neurological recovery rates. The sequence of steps in the performance of CPR is recommended as the ABC's: Airway, Breathing and Circulation.
The AHA's (American Heart Association) 2000 guideline for CPR and emergency cardiac care adopted a new classification for therapeutic recommendation.

Drug Therapy during CPR

Catecholamines are used in cardiac arrest to: (1) increase arterial and coronary perfusion during and following CPR, (2) stimulate contraction during asystole, and (3) act as an ionotropic agent.

Epinephrine increases brain and heart blood flow by two mechanisms : (1) it prevents carotid artery collapse and raises arterial pressure. During both chest compression and release phase of chest compression (i.e. systole and diastole). (2) It preferentially reduces blood flow to the external carotid, renal and splanchic beds thereby redirecting flow toward brain and heart. In cardiac arrest **adrenaline** (**epinephrine**) 1 in 10000 (1 mg per 10 ml) is recommended in a dose of 10 ml by intravenous injection through a central vein or in an upper extremity and should be repeated every 5 minutes.

If the peripheral line is used, the drug should be used rapidly, then flushed with 20 ml **sodium chloride** 0.9% injection (to expedite entry into the circulation). It should not be administered in same IV line as that use of alkaline solution.

If IV line has not been established, the endotracheal route may be used.

Intracardiac route should be avoided because it may cause serious complication such as intramyocardial damage, coronary perforation and pneumothorax.

Other durgs used in **cardiopulmonary** resuscitation include **norepinephrine**, **sodium bicarbonate atropine** and **calcium chloride**.

Norepinephrine *(see also section 3.7.1)* is a potent vesoconstrictor and generally produces a rise in blood pressure. Its disadvantage is renal and mesenteric vasoconstriction. It should not be used in initial phase of resuscitation

Atropine is no longer recommended in the treatment of asystole or pulse less electrical activity.

Calcium chloride (5 to 10 mg/kg) enhances the contractile state of the heart and is indicated in treating severe hypotension due to overdose of **calcium channel blocker** or **hyperkalemia**. It is no longer recommended for use in asystole or electromechanical dissociation.

Anti-arrhythmic drugs are used in the treatment of various arrhythmias during cardiac arrest.

ADRENALINE/ EPINEPHRINE [ED]

Indications: *see notes above*

Cautions: heart disease, diabetes mellitus, hyperthyrodism, hypertension, arrhythmias, cerebrovascular disease, angle-closure glaucoma, second stage of labour

Interactions: *see Appendix-2*

Side-effects: anxiety, tremor, tachycardia, headache, cold extremities; in over dosage arrhythmias, cerebral haemorrhage, pulmonary edema; nausea vomiting, sweating, weakness, dizziness and hyperglycaemia also reported

Dose : *see notes above*

Proprietary Preparations

Adrin *(Gaco)*, Inj., 1 mg/ml, Tk. 25.00/Amp
Adrinor *(Incepta),* Inj.1 mg/ml, Tk. 25.00/Amp.

ATROPINE SULPHATE [ED]

Indications:bradycardia,cardiopulmonary resuscitation,premedication, intra-perative bradycardia; with anticholinesterases for reversal of nondepolarising neuromuscular block; antidote to organophosphorous poisoning; symptomatic relief of gastro-intestinal disorders characterised by smooth muscle spasm; cycloplegia, anterior uveitis

Cautions: should be used with caution in Down's syndrome, in children and in the elderly; gastro-oesophageal reflux disease, diarrhoea, ulcerative colitis, autonomic neuropathy, acute myocardial infarction,hypertension, tachycardia (including hyperthyroidism, cardiac insufficiency, cardiac surgery), pyrexia, and in individuals susceptible to angle-closure glaucoma; pregnancy

Contra-indications: myasthenia gravis (but may be used to decrease muscarinic side-effects of anticholinesterases), paralytic ileus, pyloric stenosis, toxic megacolon, and prostatic enlargement.

Interactions: *see Appendix-2*.

Side-effects: constipation, transient bradycardia (followed by tachycardia, palpitation and arrhythmias), reduced bronchial secretions, urinary urgency and retention, dilatation of the pupils with loss of accommodation, photophobia, dry mouth, flushing and dryness of the skin. confusion, giddiness, angle-closure glaucoma may occur

Dose: arrhythmias after myocardial infarction, 500 micrograms of atropine sulfate given intravenously; the dose may be repeated every 3–5 minutes if necessary up to a maximum total dose of 3 mg.

Premedication, by intravenous injection, 300–600 micrograms immediately before induction of anaesthesia;

By subcutaneous or intramuscular injection, 300–600 micrograms 30–60 minutes before induction of anaesthesia;

Intra-operative bradycardia, by intravenous injection, 300–600 micrograms (larger doses in emergencies);

Control of muscarinic side-effects of neostigmine in reversal of competitive neuromuscular block, by intravenous injection, 0.6–1.2 mg;

Proprietary Preparations

Atropine *(Chemist),* Inj., 1mg/ml, Tk. 2.52/1 ml Amp
Atropine-Jayson *(Jayson),* Inj., 0.6 mg/1ml, Tk. 5.00/1 ml Amp.
Atropine-Jayson *(Jayson),* Inj., 0.6 mg/1ml, Tk. 5.00/amp.
G-Atropine *(Gonoshasthaya),* Inj., 0.6 mg/1ml, Tk. 3.01/1ml Amp.

3.8 ANTICOAGULANTS AND PROTAMINE

Anticoagulants are indicated for prophylaxis and treatment of deep vein thrombosis in the legs; they are also used to prevent thrombi forming on prosthetic heart valves. Anticoagulants prevent the formation of thrombus in the venous circulation and are not useful for preventing thrombus formation in arteries.

3.8.1 PARENTERAL ANTICOAGULANTS

HEPARIN [ED]

The drug acts rapidly but the duration of action is short. For the treatment of deep vein thrombosis and pulmonary embolism heparin is to be given as an IV loading dose; it is to be followed by continuous IV infusion or by subcutaneous injection at regular intervals; daily laboratory monitoring of Activated Partial Thromboplastin Time (APTT) is essential. Heparin is also given for the management of myocardial infarction, the management of unstable angina, and the management of acute peripheral arterial occlusion.

Indications: prophylaxis and treatment of venous thrombosis and pulmonary embolism; treatment of myocardial infarction and arterial embolism; prophylaxis in arterial and heart surgery; cerebral and venous thrombosis; as anticoagulant in blood transfusions; extracorporeal circu-lation and dialysis

Cautions: elderly, pregnancy, post surgical patients, advanced hepatic and renal disease, jaundice, hypersensitivity to heparins; spinal or epidural anaesthesia

Interactions: *see Appendix-2*

Contraindications: haemorrhagic diseases, thrombocytopenia, haemo-philia, subacute bacterial endocarditis, peptic ulcer, severe hypertension; patient who has recently undergone surgery at site where hemorrhage is special risk

Side-effects: bleeding, thrombocyto-penia, hyperkalaemia, transient alopecia, diarrhoea; osteoporosis, occasionally hypersensitivity reactions

Dose: for the treatment of deepvein thrombosis and pulmonary embolism, *by intravenous injection* of loading dose of 5000 units (10,000 units in severe pulmonary embolism) followed by continuous infusion of 1000-2000 units/hour 25 units /kg/hour or *by subcutaneous injection* of15000 units every 12 hours (laboratory monitoring essential, preferably on a daily basis, and dose adjusted accordingly)

In unstable angina and in acute peripheral arterial occlusion, intravenous regimen as for the treatment of deepvein thrombosis and pulmonary embolism (see above) to be followed.

For acute myocardial infarction or unstable angina: 5000units intravenous bolus, followed by 1000unit/hour in patients weighing, > 80kg and 800 units/hour in < 80kg, maintained for 48 hours or more, with adjustment according to the APTT

Haemodialysis: loading intravenous dose of 5000 units at the commencement of dialysis, followed by further continuous infusion to be completed 1 hour before completion of dialysis

Low dose prophylaxis : In high risk patients who are undergoing surgery intravenous injection or by subcutaneous injection of 5000 units 8-12 hours before operation, and to be continued post operatively for 7 days until patient is mobile to prevent post-operative deep vein thrombosis or pulmonary embolism; in this regimen laboratory monitoring is not required

CHILD: the loading dose to be lower; 15-25 units/kg/hour by Intravenous infusion

Proprietary Preparations
Heparin(l) *(Rotexmedica),* Inj., 5000 IU/ml. Tk.325.33/5mlVial
Heparin Leo (l) *(Leo),* Inj., 5000 IU/ml. Tk.704.00/5mlVial

LOW MOLECULAR WEIGHT HEPARINS

Low molecular weight Heparins are salts of fragments of heparin produced by chemical on enzymatic depolymerisation of the heparin molecule. Common low molecular weight heparins are: **enoxaparin, dalteparine** and **tinzaparin**. Commercially available low-molecular weight heparins differ in their method of production, molecular weight range and degree of sulphation. Like Heparin, these compounds enhance the activity of antithrombin III. They have no significant effect on blood coagulation tests such as APTT. They have longer duration of action than unfractional heparin.

They are used for the management of venous thromboembolism and unstable angina. They are also used for prophylaxis, particularly during surgery, and for treatment of established thromboembolism.

DALTEPARIN SODIUM

Indication : *see notes above*

Side effects, Contraindications and **Caution**: *see under Heparin*

Dose: in unstable angina and Non Q wave myocardial infraction, given subcuta-neously in a dose of 200 units/kg 12 hourly for 5-8 days (max.10,000 units every 12 hours) and low dose aspirin should be given concomitantly

For tratment of deep vein thrombosis and pulmonary embolism, *subcutaneously*, in a dose of 200 units /kg daily for at least 5 days (max 18000 units daily).
For prophylaxis of venous thromboembolism during surgical procdure, started pre-operatively for patients at moderate risk, 25,000 units given subcutaneously 1 to 2 hours before the procedure, followed by 2500units once daily for 5-7 days or until the patient is ambulant; for those at high risk, 2500 units are given 1 to 2 hours before procedure and 8-10 hours after procedure followed by 5000 units daily

For prevention of clotting in the extracorporeal circulation during haemodialysis or haemofiltration in adult with chronic renal failuer an intravenous injection of dalteparin 30 to 40 unit per kg followed by an intravenous infusion of 10 to 15 unit/kg/hour

Proprietary Preparations
Fragmin(l) *(Pfizer),* Inj. 5000 IU/0.2 ml, Tk. 337.50/0.2 ml Syringe;7500IU Tk. 631.48/0.3ml Syringe

ENOXAPARIN SODIUM

Indications : *see notes above*

Side-effects; cautions; contraindications: *see under Heparin*

Dose: in unstable angina and non Q wave myocardial infarction, given *subcutenously* in a dose of 1mg (100 units) per kg 12 hourly for 5-8 days; low dose aspirin should be given concomitantly

In the prophylaxis of venous thrombosis during surgical procedures, given *subcutaneously*; patients with mild to moderate risk are given 20mg (2000units) 2 hours pre-operatively and then 20mg (2000 units) once daily for 7-10 days. Patients at high risk are given 40mg (4000 units) 12 hours before

operation and then 40mg (4000 units) once daily for 7-10 days.

For the treatment of deep vein thrombosis enoxaparin is given *subcutaneously* in a dose of 1mg (100 units) per kg body weight 12 hourly or 1.5mg (150 units) per kg once daily for 5 days or until oral anti-coagUlation is established.

For the prophylaxis of thromboembolism in immobilized patients, the dose is 40mg (4000 units) once daily for at least 6 days. Treatment should be continued (max. 14 days) until patients are ambulant.

Proprietary Preparations

Cardinex *(Drug int)* Inj.(P.F Syringe), 40 mg/0.4 ml , Tk. 350.00/Syringe; 60 mg/0.6 ml, Tk. 525.00/ Syringe; 80 mg/0.8 ml, Tk. 575.00/ Syringe
Claxo *(General),* Inj.,(P.F Syringe), 40 mg/0.4 ml, Tk. 350.00 Syringe; 60 mg/0.6 ml, Tk. 525.00/ Syringe
Cleven *(Beximco)*, Inj.,(P.F Syringe), 20 mg/0.2 ml, Tk. 200.00/ Syringe; 40 mg/0.4 ml, Tk. 350.00/ Syringe; 60 mg/0.6 ml, Tk. 500.00/ Syringe; 80 mg/0.8 ml, Tk. 550.00 /Syringe
Clexane *(Sanofi,),* Inj. (P.F Syringe), 20 mg/0. 2 ml, Tk. 270.00/ Syringe;40 mg/0.4 ml, Tk. 460.00/ Syringe ; 60 mg/0.6 ml, Tk. 650.00/ Syringe ; 80 mg/0.8 ml, Tk. 800.00/ Syringe
Clotinex *(Square),* Inj., (P.F Syringe) 40 mg/0.4 ml, Tk. 450.00/ Syringe; 60 mg/0.6 ml, Tk. 575.00 Syringe;80 mg/0.8 ml, Tk. 650.00/ Syringe
Enoparin *(Popular),* Inj., (P.F Syringe) 40 mg/0.4 ml, Tk. 450.00/ Syringe; 60 mg/0.6 ml, Tk. 500.00/ Syringe;80 mg/0.8 ml, Tk. 550.00/ Syringe
Eparin *(Beacon),* Inj. (P.F Syringe), 60 mg/0.6 ml, Tk. 575.00/ Syringe
Intravas*(Aristo),* Inj., (P.F Syringe) 40 mg/0.4 ml, Tk. 350.00/ Syringe;Inj., 60 mg/0.6 ml, Tk. 525.00/ Syringe; 80 mg/0.8 ml, Tk. 550.00/ Syringe
Parinox *(Incepta),* Inj., (P.F Syringe) 40 mg/0.4 ml, Tk. 350.00/ Syringe;Inj., 60 mg/0.6 ml, Tk. 500.00/ Syringe; 80 mg/0.8 ml, Tk. 525.00/ Syringe

3.8.2 ORAL ANTICOAGULANTS

Oral anticoagulants inhibit the formation of active form of vitamin K. The onset of action of oral anticoagulant is delayed. It takes 48-72 hours for anticoagulation action; for immediate effect heparin must be given. **Warfarin** is the only oral anticoagulant that is used in deep vein thrombosis, in pulmonary embolism, in patients with atrial fibrillation who can develop emboli and to prevent formation of emboli on prosthetic heart valves; in rheumatic heart disease; and transient ischaemic attacks.

Rivaroxaban, a direct inhibitor of activated factor X, is given orally for prophylaxis of venous thromboembolism in adults after hip or knee replacement surgery. It is well tested in chronic nonvalvular atrial fibrillation. It does not require therapeutic monitoring. The common side-effects are nausea and haemorrhage, and patients should be monitored for signs of bleeding or anaemia; treatment should be stopped if severe bleeding occurs.

RIVAROXABAN

Indications: *see notes above*
Cautions: *see notes above*; also bleeding disorders; concomitant use of drugs that increase risk of bleeding; severe hypertension; active or recent gastro-intestinal ulceration; vascular retinopathy; anaesthesia with postoperative indwelling epidural catheter (risk of paralysis—monitor neurological signs and wait at least 18 hours after rivaroxaban dose before removing catheter and do not give next dose until at least 6 hours after catheter removal); recent surgery; hepatic impairment- ,pregnancy and breast feeding moderate hepatic and renal impairment; renal impairment- use with caution if eGFR 15–29 mL/minute/ 1.73m^2 or if eGFR 30–49 mL/minute/1.73m^2 and concomitant use of drugs that increase plasma-rivaroxaban concentration; avoid if eGFR less than 15 mL/minute/1.73m^2; pregnancy and breast feeding
Contra-indications: active bleeding
Interactions: *see Appendix-2*
Side-effects: nausea; haemorrhage (*see notes above)*; dyspepsia, dry mouth, vomiting, hypotension, oedema, tachycardia, thrombocythaemia,

syncope, dizziness, headache, renal impairment, pain in extremities, pruritus, and rash; jaundice also reported
Dose: prophylaxis of venous thromboembolism following knee replacement surgery, ADULT over 18 years, 10 mg once daily for 2 weeks starting 6–10 hours after surgery.
Prophylaxis of venous thromboembolism following hip replacement surgery, ADULT over 18 years, 10 mg once daily for 5 weeks starting 6–10 hours after surgery

Proprietary Preparations
Rivarox *(Eskayef)* Tk.25.00/Tab.

WARFARIN[ED]

Indications: *see notes above*
Cautions: hepatic or renal disease, recent surgery
Contraindications: pregnancy, peptic ulcer, severe hypertension, bacterial endocarditis
Interactions: *see Appendix-2*
Side-effects: haemorrhage; alopecia, hypersensitivity, hepatic dysfunction, rashes
Dose: usual ADULT dose is 10 mg daily for 2 days at the start of treatment. Afterwards the dose is adjusted according to the prothrombin time; the maintenance dose is 3 to 9 mg daily

Proprietary Preparations
Farevan *(Gaco)* Tab., 5 mg, Tk. 3.04/Tab.
Warin *(Incepta),* Tab., 5 mg, Tk. 3.00/Tab.

3.8.3 PROTAMINE SULFATE[ED]

Indications: to stop bleeding in case of heparin overdosage

Contraindications: history of allergic reactions to protamine insulin; infertility in men; men who have had a vasectomy

Interactions: *see Appendix-2*

Side-effects: hypersensitivity reactions, vomiting, dyspnoea, and bradycardia

Dose: *by intravenous injection* for about 3 minutes, 1 mg neutralizes 80-100 units heparin when given within 15 minutes of heparin; if longer time, less protamine needed because heparin is rapidly excreted; max. 50 mg

Generic Preparation
Injection, 10mg/ml

3.9. ANTIPLATELET DRUGS

These drugs inhibit thrombus formation by decreasing platelet aggregation. **Aspirin** 75-300 mg daily may be given routinely to prevent recurrent attack of thrombotic cerebrovascular or cardiovascular disease. Aspirin 300 mg should be given immediately after the diagnosis of ischaemic heart disease. Aspirin decreases mortality after myocardial infarction. Low doses of aspirin (75 mg or 100 mg) are to be prescribed following bypass surgery and post myocardial infarction. Aspirin has also been used in atrial fibrillation, stable angina and for intermitent claudication. **Ticlopidine** inhibits platelet aggregation and clot retraction; it has currently been used for prevention of thrombosis in cerebral vascular and coronary heart disease. **Clopidogrel** is an analogue of ticlopidine with similar action and uses. **Dipyridamole** inhibits embolization from prosthetic heart valves in combination with warfarin, and reduces thrombosis in patients with thrombotic disease.
Ticlopidine is limited by the need to take the drug twice daily, by poor tolerability, notably gastrointestinal distress, but most important by severe side effects, including bone marrow aplasia. The antiplatelet effects of clopidogrel have a delayed onset (several hours after ingestion), and there is substantial variability in response among patients. **Prasugrel** is a novel third- generation thienopyridine that irreversibly inhibits the $P2Y_{12}$ receptor at the same site as clopidogrel. Compared with clopidogrel, prasugrel is more potent, faster in onset, and more consistent in inhibiting platelets- but at a price of more bleeding.
Glycoprotein IIb/IIIa inhibitors prevent platelet aggregation by blocking the binding of fibrinogen to receptors on platelets. **Abciximab** is a monoclonal antibody which binds to glycoprotein

IIb/IIIa receptors and to other related sites; it is licensed as an adjunct to unfractionated heparin and aspirin for the prevention of ischaemic complications in high-risk patients undergoing percutaneous transluminal coronary intervention. Abciximab should be used once only (to avoid additional risk of thrombocytopenia). **Eptifibatide** and **tirofiban** also inhibit glycoprotein IIb/IIIa receptors; they are licensed for use with unfractionated heparin and aspirin to prevent early myocardial infarction in patients with unstable angina or non-ST-segment-elevation myocardial infarction. Abciximab, eptifibatide and tirofiban should be used by specialists only.

ASPIRIN

Indications: prophylaxis against arterial thrombotic events including cerebrovascular disease and myocardial infarction (*see also section 7.5.2.2)*

Cautions: asthma, uncontrolled hypertension, renal and hepatic impairment; pregnancy

Contraindications: active peptic ulcer; haemophlia ,gout, asthma or history of bronchospasm, children below 12 years and in breast-feeding

Interactions: *see Appendix-2*

Side-effects: bronchospasm, gastrointestinal bleeding, Rey's syndrome

Dose : *see notes above*

Proprietary Preparations
see section 7.5.2.2

CLOPIDOGREL

Indications: for reduction of atherosclerotic events (e.g. myocardial infarction, ischaemic stroke, or established peripheral arterial disease)

Cautions: *see under Ticlopidine*

Contraindications: the presence of active bleeding and hypersensitivity to the drug

Interactions: *see Appendix-2*

Side-effects: *see under Ticlopidine*. The incidence of blood dyscrasiais is reported to be lower with Clopidogrel.

Dose: *by mouth* 75 mg once daily with or without fail. In acute coronary syndromes, initial dose is 300 mg and then 75 mg once daily. In coronary stenting, the combination of clopidogrel with aspirin is as effective as ticlopidine with aspirin, except that non cardiac events are better reduced by clopidogrel

Proprietary Preparations
Anclog *(Square),* Tab. 75 mg, Tk. 12.00/Tab.
Anlet *(Globe),* Tab., 75 mg, Tk. 10.00/Tab.
Anplat *(RAK),* Tab. 75 mg, Tk. 10.00/Tab.
Antiplet *(Rangs),* Tab., 75mg , Tk. 10.00/Tab.
Apt *(Sharif),* Tab. 75 mg, Tk. 10.00/Tab.
Clognil *(Orion),* Tab. 75 mg, Tk.11.00/Tab.
Clogrel *(Ad-din),* Tab., 75mg, Tk. 9.00/Tab.
Clont *(Opsonin),* Tab. 75 mg, Tk. 9.02/Tab.
Clopid *(Drug Intl),* Tab. 75 mg, Tk. 12.00/Tab.
Clopidol *(Alco),* Tab. 75 mg, Tk. 10.00/Tab.
Clopigel *(Pacific),* Tab. 75 mg, Tk. 6.84/Tab.
Clopilet *(Sun),* Tab. 75 mg, Tk. 11.05/Tab.
Clorel *(ACI),* Tab. 75mg, Tk. 12.00/Tab.
Dclot *(Acme),* Tab. 75 mg, Tk. 10.04/Tab.
Dogrel *(Astra),* Tab. 75 mg, Tk. 10.00/Tab.
Dorel *(General),* Tab. 75 mg, Tk. 10.04/Tab.
Gevit *(Globe),* Tab. 75 mg, Tk.10.00/Tab.
Livocard *(White Horse),* Tab. 75 mg, Tk.10.00/Tab.
Lopirel *(Incepta),* Tab. 75 mg, Tk. 12.00/Tab.
Loplate *(Kemiko),* Tab. 75 mg, Tk. 10.00/Tab.
Noclog *(Eskayef),* Tab. 75 mg, Tk. 12.00/Tab.
Odrel *(Beximco),* Tab. 75 mg, Tk. 12.00/Tab.
Pladex *(Unimed),* Tab. 75 mg, Tk. 12.00/Tab.
Plagrin *(Renata),* Tab. 75 mg, Tk.10.04/Tab.
Platrel *(Novartis),* Tab. 75 mg, Tk. 12.50/Tab.
Plavix *(Navana),* Tab. 75 mg, Tk. 10.04/Tab.
Preclot *(Popular),* Tab. 75 mg, Tk. 12.00/Tab.
Replet *(Healthcare),* Tab.75mg, Tk.10.00/Tab.

Clopidogrel 75mg + Aspirin75mg
Anclog Plus *(Square),* Tab., Tk.12.00/Tab.
Asclop *(Biopharma),* Tab., Tk.12.50/Tab.
Aspin Plus *(Aristo),* Tab., Tk. 11.00/Tab.
Clas *(Delta),* Tab., Tk. 8.00/Tab.
Clognil Plus *(Orion),* Tab., Tk.12.00/Tab.
Clontas *(Opsonin),* Tab., Tk.8.3/Tab.
Clopicard Plus *(Veritas),* Tab.,Tk.12.00/Tab.
Clopid-AS *(Drug Intl),* Tab. Tk.12.00/Tab.
Clopidol Plus *(Alco),* Tab., Tk.12.00/Tab.
Clopigel Plus *(Pacific),* Tab., Tk. 7.52/Tab.
Clopilet A *(Sun),* Tab., Tk.11.00/Tab.
Clorel-A *(ACI),* Tab., Tk. 12.00/Tab.
Combiplat *(Beacon),* Tab., Tk.11.00/Tab.
Dogrel Plus *(Astra),* Tab., Tk. 11.00/Tab.
Dorel Plus *(General),* Tab., Tk.11.04/Tab.
Ecosprin Plus *(Acme),* Tab., Tk.11.04/Tab.

G-Co-Aspirin *(Gonoshasthaya),* Tab, Tk.6.50/Tab.
Livocard Plus *(White Horse),* Tab., Tk.11.00/Tab.
Lopirel Plus *(Incepta),* Tab., Tk.12.00/Tab.
Loplate Plus *(Kemiko),* Tab., Tk.11.00/Tab.
Noclog Plus *(Eskayef),* Tab, Tk.12.00/Tab.
Odrel Plus *(Beximco),* Tab., Tk.12.00/Tab.
Pladex-A *(Unimed),* Tab., Tk.12.50/Tab.
Plagrin Plus *(Renata),* Tab., Tk.11.04/Tab.
Plavix-Plus *(Navana),* Tab., Tk.12.05/Tab.
Preclot AS *(Popular),* Tab., Tk.12.00/Tab.
Replet Plus *(Healthcare),* Tab., Tk. 11.00/Tab.

DIPYRIDAMOLE

Indications : *see notes above*

Cautions : recent myocardial infarction, severe angina and heart failure

Side-effects: throbbing headache, increasing bleeding during or after surgery, hot flushes, tachycardia and gastro-intestinal effects

Interactions: *see Appendix-2*

Dose: *by mouth* 300-600 mg daily in 3-4 divided doses before food
By Intravenous injection, for diagnostic use only

Proprietary Preparations
Pyrintin *(Opsonin),* Tab. 100mg, Tk.1.10/Tab.
Santinal MR *(Unimed),* Tab. 200mg, Tk.10.00/Tab.

EPTIFIBATIDE

Indications: coronary angioplasty, non-ST-segment elevation myocardial infarction
Cautions: risk of bleeding, concomitant drugs that increase risk of bleeding—discontinue immediately if uncontrolled serious bleeding; measure baseline prothrombin time, activated partial thromboplastin time, platelet count, haemoglobin, haematocrit and serum creatinine; monitor haemoglobin, haematocrit and platelets within 6 hours after start of treatment then at least once daily; discontinue if thrombolytic therapy, intra-aortic balloon pump or emergency
cardiac surgery necessary; hepatic impairment- avoid in severe liver disease—increased risk of bleeding; renal impairment- reduce infusion to 1 microgram/kg/minute if eGFR 30–50 mL/minute/1.73m^2 ; avoid if eGFR less than 30 mL/minute/1.73m^2; pregnancy and breast-feeding
Contra-indications: abnormal bleeding within 30 days, major surgery or severe trauma within 6 weeks, stroke within last 30 days or any history of haemorrhagic stroke, intracranial disease (aneurysm, neoplasm or arteriovenous malformation), severe hypertension, haemorrhagic diathesis, increased prothrombin time or INR, thrombocytopenia, significant hepatic impairment; if serum creatinine > 4 mg/dl.
Interactions: *see Appendix-2*
Side-effects: bleeding manifestations; anaphylaxis and rash
Dose: initially by intravenous injection, 180 micrograms/kg, then by intravenous infusion, 2 micrograms/kg/minute for up to 72 hours (up to 96 hours if percutaneous coronary intervention during treatment

Proprietary Preparations
Integril *(Incepta),* Inj., 0.002gm/ml, Tk.3,000.00/10 ml ; 0.075gm/100ml, Tk.9,000.00/100 ml

PRASUGREL

Indications: prevention of atherothrombotic events in patients with ACS undergoing primary or delayed coronary angioplasty
Cautions: recent trauma, surgery, gastro-intestinal bleeding, or active peptic ulcer disease, concomitant use of drugs that increase risk of bleeding; discontinue at least 7 days before elective surgery if antiplatelet effect not desirable; elderly; body-weight less than 60 kg; increased risk in patients likely to undergo CABG; premature discontinuation increases the risk of stent thrombosis; hepatic and renal impairment,pregnancy and breast-feeding
Contra-indications: active pathological bleeding, history of stroke or transient ischaemic attack, severe hepatic impairment and hypersensitivity to drug
Interactions: *see Appendix -2*
Side-effects: haemorrhage (including gastro-intestinal and intracranial), haematoma, haematuria, anaemia, rash
Dose: ADULT over 18 years, initially 60 mg as a single dose then body-weight over
60 kg, 10 mg once daily or body-weight under 60 kg or ELDERLY over 75 years, 5 mg once daily with or without food.

Proprietary Preparations
Apagrel *(Healthcare),* Tab., 5 mg, Tk.12.00/Tab.; 10 mg, Tk. 10.00/Tab.
Asurel *(Navana),* Tab., 5 mg, Tk. 20.00/Tab.;
Efigrel *(Square),* Tab., 5 mg, Tk. 12.00/Tab.; 10 mg, Tk. 20.00/Tab.
Efirel *(Opsonin),* Tab., 10 mg, Tk.15.04/Tab.**;** Tab., 5 mg, Tk. 9.02/Tab.
Hemagrel *(ACI),* Tab., 5 mg, Tk. 12.00/Tab.; 10 mg Tk. 20.00/Tab.
Opagrel *(Orion),* Tab., 10 mg , Tk. 15.00/Tab.; 5 mg, Tk. 8.00/Tab.
Prapid *(Drug Int.),* Tab., 5 mg, Tk. 12.00/Tab.; 10 mg, Tk. 20.00/Tab.
Prasulet *(Beacon),* Tab., 5 mg, Tk.11.95/Tab;.10 mg, Tk. 19.95/Tab.
Prasurel *(Incepta),* Tab., 10 mg, Tk.20.00/Tab.; 5 mg.Tk. 12.00/Tab.
Prasuva *(Beximco),* Tab., 5 mg, Tk.12.00/Tab.

TICLOPIDINE HYDROCHLORIDE

Indications : *see notes above*

Cautions: renal impairment, hepatic impairment; there is an increased risk of bleeding due to concomitant administration of other drugs; to be withdrawn immediately if there is serious bleeding

Interactions : *see Appendix-2*

Side-effects: bleeding, nausea diarrhoea, severe neutropenia

Dose: 250mg twice daily

Generic Preparation
Tablet, 250mg

3.10 FIBRINOLYTIC AGENTS

Acute coronary syndromes encompass a spectrum of conditions which include unstable angina, and myocardial infarction with or without ST-segment elevation. Patients with different acute coronary syndromes may present similarly; definitive diagnosis is made on thebasis of clinical presentation, ECG changes, and measurement of biochemical cardiac markers.

Unstable angina and non-ST-segment elevation myocardial infarction (NSTEMI) are related acute coronary syndromes that fall between the classifications of stable angina and ST-segment elevation myocardial infarction (STEMI). They usually occur as a result of atheromatous plaque rupture, and are often characterised by stable angina that suddenly worsens, recurring or prolonged angina at rest, or new onset of severe angina. Patients with unstable angina have no evidence of myocardial necrosis, whereas in NSTEMI, myocardial necrosis (less significant than with STEMI) will be evident. There is a risk of progression to STEMI
or sudden death, particularly in patients who experience pain at rest.

ST-segment elevation myocardial infarction (STEMI) is an acute coronary

syndrome where atheromatous plaque rupture leads to thrombosis and myocardial ischaemia, with irreversible necrosis of the heart muscle, often leading to long-term complications.
STEMI can also occasionally occur as a result of coronary spasm or embolism, arteritis, spontaneous thrombosis, or sudden severe elevation in blood pressure.

Management of unstable angina and non-ST-segment elevation myocardial infarction (NSTEMI)

These conditions are managed similarly; the aims of management are to provide supportive care and pain relief during the acute attack and to prevent further cardiac events and death. For advice on the management of patients with acute ST-segment elevation myocardial infarction (STEMI), see below.

Initial management Oxygen should be administered if there is evidence of hypoxia, pulmonary oedema, or continuing myocardial ischaemia; hyperoxia should be avoided and particular care is required in patients with chronic obstructive airways disease.

Nitrates are used to relieve ischaemic pain. If sublingual glyceryl trinitrate is not effective, intravenous or buccal glyceryl trinitrate or intravenous isosorbide dinitrate is given. If pain continues, diamorphine or morphine can be given by slow intravenous injection; an antiemetic such as metoclopramide should also be given.

Aspirin (chewed or dispersed in water) is given for its antiplatelet effect in a dose of 300mg. If aspirin is given before arrival at hospital, a note saying that it has been given should be sent with the patient. Clopidogrel in a dose of 300mg (or 600 mg [unlicensed] if used prior to percutaneous coronary intervention) should also be given. **Prasugrel**, in a dose of 60 mg, is an alternative to clopidogrel in certain patients undergoing percutaneous coronary intervention. **Ticagrelor**, in a dose of 180 mg, is also an alternative to Clopidogrel. Patients should also receive either **unfractionated heparin,** a **low molecular weight heparin**, or **fondaparinux**. Patients without contra-indications should receive beta blockers which should be continued indefinitely. In patients without left ventricular dysfunction and in whom beta-blockers are inappropriate, Diltiazem or verapamil can be given.
The glycoprotein IIb/IIIa inhibitors **eptifibatide** and tirofiban can be used (with aspirin and unfractionated heparin) for unstable angina or for NSTEMI in patients at a high risk of either myocardial infarction or death.
In intermediate- and high-risk patients, abciximab, eptifibatide, or tirofiban can also be used with aspirin and unfractionated heparin in patients undergoing percutaneous coronary intervention, to reduce the immediate risk of vascular occlusion. In intermediate- and high-risk patients in whom early intervention is planned, bivalirudin can be considered as an alternative to the combination of a glyocprotein IIb/IIIa inhibitor plus a heparin.
Revascularisation procedures are often appropriate for patients with unstable angina or NSTEMI
Long-term management The need for long-term angina treatment or for coronary angiography should be assessed. Most patients will require standard angina treatment to prevent recurrence of symptoms.
Prevention of cardiovascular events Patients with unstable angina, or NSTEMI should be given advice and treatments to reduce their cardiovascular risk. The importance of life-style changes, especially stopping smoking, should be emphasised. **Aspirin** should be given indefinitely in a dose of 75mg daily. Antihypertensive treatment should be initiated if appropriate, and a statin should also be given.
In patients with unstable angina or NSTEMI, Clopidogrel is given, in combination with aspirin, for up to 12

months—most benefit occurs during the first 3 months. Prasugrel or ticagrelor are alternatives to Clopidogrel in certain patients. An ACE inhibitor should also be given.

Management of ST-segment elevation myocardial infarction (STEMI)

The aims of management of STEMI are to provide supportive care and pain relief, to promote reperfusion and to reduce mortality. Oxygen, nitrates, and diamorphine or morphine can provide initial support and pain relief; aspirin and percutaneous coronary intervention or thrombolytics promote reperfusion; anticoagulants help to reduce re-occlusion and systemic embolisation; long-term use of aspirin, beta-blockers, ACE inhibitors, and statins help to reduce mortality further.

Initial management Oxygen should be administered if there is evidence of hypoxia, pulmonary oedema, or continuing myocardial ischaemia; hyperoxia should be avoided and particular care is required in patients with chronic obstructive airways disease.

The pain (and anxiety) of myocardial infarction is managed with slow intravenous injection of diamorphine or morphine; an antiemetic such as metoclopramide (or, if left ventricular function is not compromised, cyclizine) by intravenous injection should also be given.

Aspirin (chewed or dispersed in water) is given for its antiplatelet effect; a dose of 300mg is suitable. If aspirin is given before arrival at hospital, a note saying that it has been given should be sent with the patient. **Clopidogrel**, in a dose of 300 mg (or 600 mg [unlicensed] if used prior to percutaneous coronary intervention), should also be given. **Prasugrel**, in a dose of 60 mg, is an alternative to Clopidogrel in certain patients undergoing percutaneous coronary intervention. **Ticagrelor**, in a dose of 180 mg, is also an alternative to clopidogrel.

Patency of the occluded artery can be restored by percutaneous coronary intervention or by giving a **thrombolytic drug,** unless contra-indicated. Percutaneous coronary intervention is the preferred method; a **glycoprotein IIb/IIIa inhibitor** can be used to reduce the risk of immediate vascular occlusion in intermediate- and high-risk patients. Patients undergoing percutaneous coronary intervention should also receive either unfractionated heparin or a low molecular weight heparin (e.g. enoxaparin); **bivalirudin** is an alternative to the combination of a glycoprotein IIb/IIIa inhibitor plus a heparin. In patients who cannot be offered percutaneous coronary intervention within 90 minutes of diagnosis, a thrombolytic drug should be administered along with either unfractionated heparin (for maximum 2 days), a low molecular weight heparin (e.g. enoxaparin), or fondaparinux.

Patients who do not receive reperfusion therapy (with percutaneous coronary intervention or a thrombolytic) should be treated with either fondaparinux, enoxaparin, or unfractionated heparin. Prescribers should consult product literature and local protocols (where they exist) for details of anticoagulant dose and duration.

Nitrates are used to relieve ischaemic pain. If sublingual glyceryl trinitrate is not effective, intravenous glyceryl trinitrate or isosorbide dinitrate is given.

Early administration of some **beta-blockers** has been shown to be of benefit and should be given to patients without contra-indications.

ACE inhibitors, and angiotensin-II receptor antagonists if an ACE inhibitor cannot be used, are also of benefit to patients who have no contra-indications; in hypertensive and normotensive patients treatment with an ACE inhibitor, or an angiotensin-II receptor antagonist, can be started within 24 hours of the myocardial infarction and continued for at least 5–6 weeks (see below for long-term treatment).

All patients should be closely monitored for hyperglycaemia; those with diabetes or raised blood-glucose concentration should receive insulin.

Long-term management Long-term management following STEMI involves the use of several drugs which should ideally be started before the patient is discharged from hospital.

Aspirin should be given to all patients, unless contra-indicated, at a dose of 75mg daily. The addition of **clopidogrel** has been shown to reduce morbidity and mortality. Prasugrel or ticagrelor are alternatives to clopidogrel in certain patients. For those intolerant of clopidogrel, and who are at low risk of bleeding, the combination of **warfarin** and aspirin should be considered. In those intolerant of both aspirin and clopidogrel, warfarin alone can be used. Warfarin should be continued for those who are already being treated for another indication, such as atrial fibrillation, with the addition of aspirin if there is a low risk of bleeding. The combination of aspirin with clopidogrel or warfarin increases the risk of bleeding.

Beta-blockers should be given to all patients in whom they are not contra-indicated. Acebutolol, metoprolol, propranolol, and timolol are suitable; for patients with left ventricular dysfunction, carvedilol, bisoprolol, or long-acting metoprolol may be appropriate.

Diltiazem [unlicensed] or v**erapamil** can be considered if a beta-blocker cannot be used; however, they are contra-indicated in those with left ventricular dysfunction. Other calcium-channel blockers have no place in routine long-term management after a myocardial infarction

An **ACE inhibitor** should be considered for all patients, especially those with evidence of left ventricular dysfunction. If an ACE inhibitor cannot be used, an angiotensin-II receptor antagonist may be used for patients with heart failure. A relatively high dose of either the ACE inhibitor or angiotensin-II receptor antagonist may be required to produce benefit.

Nitrates are used for patients with angina.

Eplerenone is licensed for use following a myocardial infarction in those with left ventricular dysfunction and evidence of heart failure. **Statin**s should be used lifelong after myocardial infarction to prevent recurrent cardiovascular events.

Fibrinolytic drugs

Fibrinolytic drugs act as thrombolytics by activating plasminogen to form plasmin, which degrades fibrin and so breaks up thrombi.

The value of thrombolytic drugs for the treatment of myocardial infarction has been established. **Streptokinase** and **alteplase** have been shown to reduce mortality. **Reteplase** and t**enecteplase** are also use for acute myocardial infarction. Thrombolytic drugs are indicated for any patient with acute myocardial infarction for whom the benefit is likely to outweigh the risk of treatment. Patients should not be denied thrombolytic treatment on account of age alone because mortality in the elderly is high and the reduction in mortality is the same as in younger patients. **Alteplase** should be given within 6–12 hours of symptom onset, reteplase and streptokinase within 12 hours of symptom onset, but ideally all should be given within 1 hour; use after 12 hours requires specialist advice. **Tenecteplas**e should be given as early as possible and usually within 6 hours of symptom onset.

Alteplase, streptokinase, and **urokinase** can be used for other thromboembolic disorders such as deep-vein thrombosis and pulmonary embolism. Alteplase is also used for acute ischaemic stroke

Urokinase is also licensed to restore the patency of occluded intravenous catheters and cannulas blocked with fibrin clots.

Cautions Thrombolytic drugs should be used with caution if there is a risk of bleeding including that from venepuncture or invasive procedures. They should also be used with caution in external chest compression, elderly, hypertension, conditions in which thrombolysis might give rise to embolic complications such as

enlarged left atrium with atrial fibrillation (risk of dissolution of clot and

subsequent embolisation), and recent or concurrent use of drugs that increase the risk of bleeding.

Contra-indications Thrombolytic drugs are contraindicated in recent haemorrhage, trauma, or surgery (including dental extraction), coagulation defects, bleeding diatheses, aortic dissection, aneurysm, coma, history of cerebrovascular disease especially recent events or with any residual disability, recent symptoms of possible peptic ulceration, heavy vaginal bleeding, severe hypertension, active pulmonary disease with cavitation, acute pancreatitis, pericarditis, bacterial endocarditis, and oesophageal varices; also in the case of streptokinase, previous allergic reactions to either streptokinase or anistreplase (no longer available).

Prolonged persistence of antibodies to streptokinase and anistreplase (no longer available) can reduce the effectiveness of subsequent treatment; therefore, streptokinase should not be used again beyond 4 days of first administration of either streptokinase or anistreplase.

Hepatic impairment Thrombolytic drugs should be avoided in severe hepatic impairment as there is an increased risk of bleeding.

Pregnancy Thrombolytic drugs can possibly lead to premature separation of the placenta in the first 18 weeks of pregnancy. There is also a risk of maternal haemorrhage throughout pregnancy and post-partum, and also a theoretical risk of fetal haemorrhage throughout pregnancy.

Side-effects: Side-effects of thrombolytics are mainly nausea and vomiting and bleeding. When thrombolytics are used in myocardial infarction, reperfusion arrhythmias and recurrent ischaemia and angina may occur. Reperfusion may also cause cerebral and pulmonary oedema. Hypotension can also occur and can usually be controlled by elevating the patient's legs, or by reducing the rate of infusion or stopping it temporarily. Back pain, fever, and convulsions have been reported. Bleeding is usually limited to the site of injection, but intracerebral haemorrhage or bleeding from other sites can occur. Serious bleeding calls for discontinuation of the thrombolytic and may require administration of coagulation factors and antifibrinolytic drugs (e.g. tranexamic acid). Rarely further embolism may occur (either due to clots that break away from the original thrombus or to cholesterol crystal emboli). Thrombolytics can cause allergic reactions (including rash, flushing and uveitis) and anaphylaxis has been reported. Guillain-Barre´ syndrome has been reported rarely after streptokinase treatment.

STREPTOKINASE

Indications: acute myocardial infarction; deep-vein thrombosis, pulmonary embolism, acute arterial thromboembolism, and central retinal venous or arterial thrombosis

Cautions: *see notes above;* hepatic impairment,pregnancy

Contra-indications: *see notes above*

Interactions: *see Appendix-2*

Side-effects: *see notes above*

Dose: myocardial infarction (initiated within 12 hours of symptom onset), by intravenous infusion, 1.5 million units over 60 minutes. Deep-vein thrombosis, pulmonary embolism, acute arterial thromboembolism, central retinal venous or arterial thrombosis, by intravenous infusion, 250 000 units over 30 minutes, then 100 000 units every hour for up to 12–72 hours according to condition with monitoring of clotting parameters

Proprietary Preparations

Eptase *(Beacon),* Inj., Tk. 3,900.00/Vial
Streptase*(Sanofi,),* Inj., 1.5 MIU/Vial, Tk.5,250.00/Vial
S-Kinase *(Popular),* Inj., 1.5 MIU/Vial, Tk.3,900.00/Vial
STK *(Incepta),* Inj., 1.5 MIU/Vial, Tk.3,600.00/Vial
Streptase (I) *(CSL Behring),* Inj. 1.5 MIU, Tk. 5250.00/Vial

UROKINASE

Indications: acute myocardial infarction; thromboembolic occlusive vascular disease including deep-vein thrombosis, pulmonary embolism, and occlusive peripheral arterial disease; occluded arteriovenous haemodialysis shunts, and intravenous catheters and cannulas blocked by fibrin clots
Cautions: *see notes above*
Contra-indications: *see notes above*; hepatic impairment- dose reduction may be required; see also notes above; renal impairment- dose reduction may be required; pregnancy(see notes above); breast-feeding
Side-effects: *see notes above*
Dose: deep-vein thrombosis, *by intravenous infusion*, initially 4400 units/kg over 10–20 minutes, followed by 100 000 units/hour for 2–3 days.
Pulmonary embolism, by intravenous infusion, initially 4400 units/kg over 10–20 minutes, followed by 4400 units/kg/hour for 12 hours.
Occlusive peripheral arterial disease, consult product literature
Occluded central venous catheters, by injection directly into catheter, dissolve in sodium chloride 0.9% to a concentration of 5000 units/mL; use a volume sufficient to
fill the catheter lumen; leave for 20–60 minutes then aspirate the lysate; repeat if necessary Occluded arteriovenous haemodialysis shunts, consult product literature.

Proprietary Preparation
Uronase *(Beacon),* Inj., 500000 IU, Tk. 3,500.00/Vial

3.11 ANTIFIBRINOLYTIC DRUGS AND HAEMOSTATICS

Tranexamic acid, a synthetic amino acid, has strong antifibrinolytic activity. The anti-haaemorrhagic action of this acid is due to an inhibition of the plasminogen activation of both exogenous activator like streptokinase and endogenous activators like urokinase and the plasminogen tissue activators.

AMINOCAPROIC ACID (EACA-EPSILON AMINOCAPROIC ACID)

Indications: all haemorrhagic syndromes due to enhanced fibrinolysis

Contraindications: thromboembolic disease, arterial and venous thrombosis.

Interactions: *see Appendix-2*

Side-effcets: fatigue, conjunctival irritation, pruritus, skin reshes after oral administration, nausea, diarrhoea, dizziness, hypersensitization

Dose: the average dose is 8-16 g a day *orally* and is to be given as 2-4 grams (diluted in sugared water) 6 hourly

Proprietary Preparation
Caprolex *(Techno),* Inj, 1 gm/5 ml, Tk. 35.00/10 ml Vial; Tk. 14.50/5 ml Vial
Hemosin *(Chemist),* Inj., 1 gm/5 ml, Tk. 30.34/5 ml

TRANEXAMIC ACID

Indications: hereditary angiedema. In prophylaxis and therapy of digestive haemorrhages, haemorrhagic syndromes in leukemia, cirrhosis of liver, hemophilia, throm-bocytopenic purpura, accidents during thrombolytic therapy and transfusion

surgical prophylaxis: anti-haemorrhagic therapy during operations, particularly in pulmonary, cardiovascular and abdominal surgery

In urology: prophylaxis and anti haemorrhagic therapy of prostatic, vesical, renal surgery and haematurias.
In obstetrics: postpartum and puerperal haemorrhages; meno-rrhagias

Cautions: renal impairment, massive haematuria, disturbances in colour vision, pregnancy

Contraindications: known individual hypersensitivity to the product, thromboembolic disease, endocavity haemorr-hages, serious kidney failure

Interactions: *see Appendix-2*

Side-effects: sense of fatigue, conjunctival irritation, nasal blockade, itching, skin reddening, nausea, diarrhoea

Dose: *by mouth* in menorrhagias, 1-1.5 g 2-4 times daily for 3-4 days
By mouth in local fibrinolysis 15-25 mg/kg 2-3 times daily.

By slow intravenous injection in case of local fibrinolysis 0.5-1 g 3 times daily.

Proprietary Preparations

Anaxyl *(ACI),* Inj., 500 mg/5 ml, Tk. 50.19/Vial; Tab., 500mg, Tk. 20.00/Tab.
Enclot *(Opsonin),* Cap., 250 mg, Tk.6.04/Cap.; 500 mg, Tk. 11.32/Cap.; Inj., 500 mg/5 ml, Tk. 37.74/Vial
Fibrino *(Eskayef),* Cap, 500 mg, Tk.15.00/Cap. ;Inj., 500mg/Vial, Tk. 50.00/Vial
Fibrostat *(Globe),* Inj., 500 mg/5 ml, Tk. 225/5 ml Amp.; Cap., 500 mg, Tk. 15/Cap.
Frabex *(Square),* Cap., 500 mg, Tk.12.05/Cap.; Inj., 500 mg/5 ml, Tk. 40.15/Vial
Hemostat *(Aristo),* Cap., 500 mg, Tk.15.00/Cap. ; Inj., 250 mg/5ml, Tk. 30.00/Vial
Hemostop *(Apex),* Cap., 500 mg, Tk.15.00/Cap.
Intrax *(Incepta),* Cap., 500 mg, Tk.16.00/Cap.; Inj., 500 mg/5 ml, Tk. 50.00/Vial
Oranex *(Orion),* Cap., 500 mg, Tk. 15.00/Tab.
Tracid *(Acme),* Tab., 500 mg, Tk. 15.05/Tab.; Tab., 500 mg, Tk. 15.05/Tab.; Inj., 500mg/5ml, Tk. 15.05/Vial
Tramic *(Pacific),* Cap., 500 mg, Tk. 14.29/Cap.
Tranexil *(Beximco),* Inj., 500 mg/5 ml, Tk.50.00/Vial.
Trexam *(Healthcare),* Inj., 250 mg/5 ml, Tk.40.00/Vial; Tab., 500 mg, Tk. 15.00/Tab
Xamic *(Renata),* Inj., 250 mg/5 ml, Tk.80.00/Vial ; Cap., 500 mg, Tk. 15.05/Cap.

3.12 LIPID LOWERING DRUGS

Lipoprotein disorders or dyslipidaemias are among the commonest metabolic disorders seen in clinical practice. They may lead to a number of sequelae including coronary heart disease, dermatological manifestations like xanthelasmata and xanthomata, pancreastitis, and neurolgical and ocular anomalies.

Type 1 hyperlipoproteinaemia is the autosomal recessive abnormality manifesting itself in childhood as an intolerance of dietary fat. Management consists of limiting dietary fat intake to no more than 30 g/day.

In Type 2 hyperlipoproteinaemic patients present with elevated plasma LDL cholesterol levels. Treatment is aimed at maximizing the efficiency of functional LDL receptors using bile acid sequestrant resins like **cholestyramine** (up to 24 g/day) or HMGCoA Reductase inhibitors like **pravastatin** or **simvastatin** (10-40 g/day).

In Type 3 hyperlipoproteinaemic patients accumulate IDL in plasma. This Type responds well to diet and drug therapy, particularly with the new generation of **clofibrate**, **benzafibrate** and **gemfibrozil**. These agents are very effective in reducing the high circulating IDL levels.

Type 4 hyperlipoproteinaemia is associated with accumulation in the plasma of VLDL of normal composition, which appears to be oversynthesized in some individuals. Dietary modification is the first line of treatment of Type 4 hyperlipoproteinaemic subjects. Carbo-hydrate and alcohol restriction achieves satisfactory control of their plasma TG level. Where the response is inadequate, it may be necessary to add nicotinic acid (3-4 g/day).

There is evidence that lowering LDL-cholesterol by 25-30% is effective in both primary and secondary prevention of coronary heart disease. Treatment with **statins** (see Statins below) has been shown to reduce myocardial infarction,

coronary deaths and overall mortality. However, any drug therapy must be combined with strict diet control, maintenance of ideal body weight and cessation of smoking.

CAUTION: Severe hyperlipidaemia often requires combination of lipid lowering drugs such as anion exchange resin with a fibrate, a statin, or nicotinic acid. Combi-nations of a statin with nicotinic acid or a fibrate or carry an increased risk of side-effects including rhabdomyolysis and should be used with caution. Concomitant treatment of a statin with cyclosporin may also increase the risk of muscle toxicity

3.12.1 ANION EXCHANGE RESINS

Cholestyramine and **cholestipol** are anion exchange resins. These resins prevent the reabsorption of bile acids by binding it.

Cautions: interfere with the absorption of fat-soluble vitamins

Interactions: *see Appendix-2*

Side-effects: constipation is common but diarrhoea may occur; gastrointestinal discomfort and increased bleeding tendency have been reported

3.12.2 FIBRATES

Clofibrate, benzafibrate, cipro-fibrate, fenofibrate, and **gemfibrozil**. can decrease mainly serum triglycerides; they also tend to decrease LDL-cholesterol and increase HDL-cholesterol.

FENOFIBRATE

Indications: for types 2, 3, 4 and 5 hyperlipoproteinaemias in patient who do not respond adequaetly to diet and other appropriate measure
Cautions: renal impairment; liver function test recommended every 3 months for first year, discontinue treatment if significantly raised
Contraindications: sever hepatic and renal impairment; pregnancy and breast-feeding; existing gall bladder disease
Interactions: *see Appendix-2*
Side-effcets: nausea, anorexia, gastric pain; pruritus, urtecaria; impotence; also headache, dizziness, vertigo, hair-loss; mytoxicity; photosensivity, raised serum transaminase; renal impairment
Dose : initially 200 mg daily in divided dose with food, then adjusted according to response to between 200 mg and 400 mg daily (dose form not appropiate for children or in renal impairment)

Proprietary Preparations
Atorvast *(Medimet),* Tab., 10mg, Tk.8.00/Tab.
Fenatrol *(Drug Int.),* Tab., 200 mg , Tk.8.00/Tab.
Fenobate *(Renata),* Cap., 200 mg, Tk.7.00/Cap.
FenoCap *(Orion),* Cap, 200 mg, Tk. 7.03/Cap.
Fenolid *(General),* Cap., 200 mg, Tk.7.03/Cap.
Fenorat *(Pacific),* Cap., 200 mg, Tk. 5.26/Cap.
Fibre *(White Horse),* Cap. , 200 mg, Tk.7.00/Cap.
Lipicut *(Rangs),* Tab., 10mg, Tk. 10.00/Tab.; 20mg, Tk. 18.00/Tab.
Lipidof *(Acme),* Cap., 200 mg, Tk. 7.02/Cap.
Lipired *(Square),* Tab., 160 mg, Tk.5.00/Tab.; Cap. , 200 mg, Tk. 7.02/Cap.
Liplo *(Globe),* Tab., 20 mg, Tk. 15.00/Tab.; 10 mg, Tk. 10.00/Tab.
Lofat *(Beximco),* Cap. , 200 mg, Tk. 7.00/Cap.
Nofiate *(Incepta),* Cap. , 200 mg, Tk.7.00/Cap.
Noficon *(Eskayef),* Cap, 200 mg, Tk.7.00/Cap.
Tigicon *(Aristo),* Cap., 200 mg, Tk. 7.00/Cap.
Tigirate *(Opsonin),* Cap., 200 mg, Tk.5.29/Cap.
Tizabet *(ACI),* Cap. , 200 mg, Tk. 7.00/Cap.
Trigent *(Unimed),* Cap. , 200 mg, Tk.7.00/Cap.
Vastor *(Ad-din),* Tab., 10mg, Tk. 10.00/Tab.

GEMFIBROZIL

Indications: for the prevention of coronary heart disease in patients with hyperlipidaemias of types 2, 3 and 4 who do not respond well to dietary restrictions
Contraindications: biliary obstructions, chronic liver disease, pregnancy and breast-feeding
Interactions: *see Appendix-2*
Side-effcets: nausea, diarrhoea, pruritus, rashes, blurred vision, impotence, cholestatic jaundice, myopathy, laryngeal edema

Dose : 1-2 g daily in 2 divided doses

Proprietary Preparations
Delipid *(Square),* Cap. 300 mg, Tk. 6.98/Cap
Fibril *(Beximco),* Cap. 300 mg, Tk.7/Cap
Gelicon *(Eskayef),* Cap. 300 mg, Tk.7/Cap
Gemfil *(Aristo),* Cap. 300 mg, Tk. 7/Cap
Lipozil *(Rephco),* Cap. 300 mg, Tk. 6.50/Cap

3.12.3 STATINS

Statins include **atorovastatin, cerivastatin, fluvastatin, pravastatin simvastatin, rosuvastatin, and pitavastatin.** These drugs inhibit HMGCoA reductase an enzyme involved in choles-terol synthesis, especially in the liver. This enzyme is required for the synthesis of cholesterol in the liver. These drugs are very effective in lowering LDL-Cholesterol but less effective than the fibrates in reducing triglycerides and raising HDL-cholesterol.

Cautions: Statins should be used with caution in those with a history of liver disease or with a high alcohol intake (use should be avoided in active liver disease). Hyperthyroidism should be managed adequately before staring treatment. Liver function tests to be carried out before and within 1-3 months of starting treatment and such tests should be repeated at intervals of 6 months for about 1 year. Treatment should be discontinued if serum transaminase concentration rises to, and persists at, 3 times the upper limit of the reference range. Patient should be advised to report unexplained muscle pain.Statin should be avoided in porphyria.

Contra-indications: are contraindi-cated in active liver diseases (or persistently abnormal liver function test); in pregnancy; in breast feeding

Side effect: The most common side effect is gastrointestinal disturbance. Other side effects reported include headache, altered liver function tests and paraesthesia. Reversible myositis is a rare but significant side effect of the satins. Rash and hypersensitivity reaction (including angiedema and anaphylaxis) have been reported rarely.

Effects on muscle: Myalgia,myositis and myopathy have been reported with statin;if myopathy is suspected and certain kinase is markedly elevated (more than 5 times upper limit of normal),treatment should be discontinued; in patients at high risk of muscle effects a stain should not be started if creatine kinase is elevated. There is an increased incidence of mypathy if the stains are given at high doses or given with a fibrate, with liquid-lowering doses of nicotinic acid, or with immuno-suppressments such as ciclosporin; close monitering of liver function and if symptomatic, of creatine kinase is required in patients receiving these drugs. Rhabdomyolysis with acute renal impairment secondary to myoglobinuria has also been reported.

ATORVASTATIN

Indications: treatment of hypercholesterolaemias and mixed hyper-lipidaemia

Side-effects; Cautions; Contraindica-tions: as for simvastatin

Interactions: *see Appendix-2*

Dose: *by mouth* as calcium salt; initial dose is 10 mg daily which may be adjusted at intervals of 4 weeks up to a maximum of 80 mg daily

Proprietary Preparations
Anzitor *(Square),* Tab., 10 mg, Tk. 10.04/Tab.; 20 mg, Tk. 18.06/Tab.; 40 mg, Tk. 24.09/Tab.
Astin *(Jayson),* Tab., 10 mg, Tk.8.04/Tab.; 20mg, Tk.15.05/Tab.;
Astiva *(Supreme),* Tab., 10mg, Tk. 10.00/Tab.; 20mg, Tk. 18.00/Tab.
Atasin *(ACI),* Tab., 10mg, Tk. 10.04/Tab.; 20mg, Tk.18.07/Tab.; 40mg, Tk. 24.09/Tab.; 80mg, Tk. 40.00/Tab.
Atonor *(Asiatic),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.
Atorvast *(Medimet),* Tab., 10mg, Tk.8.00/Tab.
Atorvastatin *(Albion),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.
Atostin *(Somatec),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.
Atova *(Beximco),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.; 40 mg, Tk.24.00/Tab.
Atovex *(RAK),* Tab., 10 mg, Tk.10.00/Tab.; 20mg, Tk.18.00/Tab.
Atovin *(Alco),* Tab., 10 mg, Tk.10.00/Tab.; 20mg, Tk.15.00/Tab.; 40 mg, Tk.22.00/Tab.

Atv *(Delta),* Tab., 10 mg, Tk.5.00/Tab.; 20 mg, Tk. 10.00/Tab.; 40 mg, Tk. 15.00/Tab.
Avas *(Opsonin),* Tab., 10 mg , Tk. 7.55/Tab.; 20 mg, Tk.13.59/Tab.; 40 mg, Tk. 18.11/Tab.
Avator *(Nipro Jmi),* Tab., 10 mg, Tk. 10.00/Tab.; 20 mg, Tk. 18.00/Tab.
Avocard *(White Horse),* Tab., 10 mg, Tk. 10.00/Tab.; 20 mg, Tk. 13.00/Tab.
Aztor *(Sun),* Tab., 10 mg, Tk.10.05/Tab.; 20mg, Tk.18.10/Tab.; 40 mg, Tk.24.00/Tab.
Colostat *(Ibn Sina),* Tab., 10 mg, Tk.10.00/Tab.
Divastin *(Drug Intl),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.; 40 mg, Tk. 24.00/Tab.
G-Atorvast *(Gonoshasthaya),* Tab. 10 mg, Tk.7.00/Tab.; 20 mg, Tk. 12.50/Tab.;
Lipex *(Orion),* Tab., 10 mg, Tk.9.03/Tab.; 20 mg, Tk. 15.06/Tab.
Lipicon *(Eskayef),* Tab, 10 mg, Tk.10.00/Tab.; 20 mg, Tk. 18.00/Tab.
Lipicut *(Rangs),* Tab., 10mg, Tk. 10.00/Tab.; 20mg, Tk. 18.00/Tab.
Lipigent *(Pacific),* Tab., 10 mg, Tk. 7.52/Tab.; 20 mg, Tk. 13.53/Tab.
Lipiles *(Pharmasia),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.
Lipistat *(Veritas),* Tab., 10 mg, Tk.12.00/Tab.
Lipitin *(General),* Tab., 10 mg, Tk.10.04/Tab.; 20 mg, Tk.18.07/Tab.; 40 mg, Tk. 24.00/Tab.
Lipiva *(Leon),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.
Liplo *(Globe),* Tab., 20 mg, Tk. 15.00/Tab.; 10 mg, Tk. 10.00/Tab.
Lipostat *(Navana),* Tab.,10 mg, Tk.10.00/Tab.
Lipovast *(Sharif),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.15.00/Tab.
Liptor *(Acme),* Tab., 10 mg, Tk.10.04/Tab.; 20mg, Tk.18.06/Tab.; 40 mg, Tk.24.09/Tab.
Locol *(Popular),* Tab., 10 mg, Tk.10.04/Tab.; 20 mg, Tk.18.07/Tab.; 40 mg, Tk.24.09//Tab.
Optivas *(Concord),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.
Orva *(Sanofi),* Tab., 10 mg, Tk.12.00/Tab.; 20mg, Tk.18.07/Tab.; 40 mg, Tk.25.00/Tab.
Orvatin *(Kemiko),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.
Stacor *(Unimed),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.; 40 mg, Tk.24.00/Tab.
Taven *(Renata),* Tab., 10 mg, Tk.10.04/Tab.; 20 mg, Tk.18.06/Tab.; 40 mg, Tk.24.00/Tab.
Tcl-R *(Aristo),* Tab., 10mg, Tk. 10.00/Tab.; 20mg, Tk. 18.00/Tab.
Tiginor *(Incepta),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.; 40 mg, Tk.24.00/Tab.
Trova *(Biopharma),* Tab., 10 mg, Tk. 10.00/Tab.; 20 mg, Tk. 18.00/Tab.
Vass *(Novartis),* Tab., 10 mg, Tk.12.00/Tab.; 20 mg, Tk.20.00/Tab.; 40 mg, Tk.25.00/Tab.
Vastor *(Ad-din),* Tab., 10mg, Tk. 10.00/Tab.
Xelpid *(Healthcare),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk. 18.00/Tab.;
Xerova *(Beacon),* Tab., 10 mg, Tk.10.00/Tab.; 20 mg, Tk.18.00/Tab.

FLUVASTATIN

Indications: type 2 hyperlipidaemia; retardation of coronary atherosclerosis in patients not responding adequately to dietary control
Contraindications: primary biliary cirrhosis, chronic liver disease; pregnancy and breast-feeding; nephrotic syndrome
Cautions: liver function tests to be carried out before starting treatment and such tests should be repeated at intervals of 6 months for about 1 year
Interactions: *see Appendix-2*
Side-effcets: altered liver function tests, dyspepsia, nausea, abdominal pain, rash, urticaria, insomnia and headache
Dose: 20-40 mg daily in the evening

Proprietary Preparation
Lescol(i) *(Novartis),* Cap., 20 mg, Tk. 37.50/Cap.; Cap., 40 mg, Tk. 57.00/Cap.
Lescol XL(i) *(Novartis),* Tab., 80 mg, Tk. 58.50/Tab.

LOVASTATIN

Indications: hypercholesterolaemia (plasma cholesterol level > 5.5 mmol/l); to halt the progression of coronary heart disease

Contraindications: active liver disease, pregnancy and breast-feeding

Cautions: alcoholics, history of liver disease

Interactions: *see Appendix-2*

Side-effcets: chest pain, acid reflux, alopecia, pruritus and dry mouth

Dose: primary hypercholesterol-aemia, combined hyperlipidaemia, 20 mg daily to be taken with the evening meal

Proprietary Preparation
Lovatin *(Ambee),* Tab. 20mg,

PITAVASTATIN

Indications: it is indicated as an adjunct to diet in patients with primary hyperlipidemia or mixed dyslipidemia to reduce elevated total cholesterol, LDL-C, apo B, and TG levels and to increase HDL-C.
Cautions; Contraindications; Side-effects: as for simvastatin
Interactions: *see appendix-2*
Dose: usual starting dose is 2 mg/day taken at any time of day and a maximum of 4 mg/day. For patients with renal disease, the recommended starting dose is 1 mg/day up to a maximum of 2 mg/day.

Proprietary Preparations
Liploss *(Drug Intl),* Tab., 2 mg, Tk. 10.00/Tab.
Pavigard *(Acme),* Tab., 2 mg, Tk. 10.00/Tab.
Pitavas *(Aristo),* Tab., 2 mg, Tk. 10.00/Tab.
Pivalo *(Square),* Tab., 2 mg, Tk. 10.00/Tab.

ROSUVASTATIN CALCIUM

Indications: increase HDL-C in patient with primary hypercholesterolaemia (heterozygous familial and non familial) and mixed dyslipidemia (Type IIa and Iib).or homozygous familial hypercholes-terolaemia in patient who have not responded adequately to diet and other appropriate measure
Cautions: *see notes above.* Patient of Asian origin max 20mg dose daily
Contra-indications: *see notes above*
Interactions: *see Appendix-2*
Dose: *by mouth* as calcium salt; initial dose is 10 mg daily which may be adjusted at intervals of 4 weeks up to a maximum of 20 mg once daily; max 20mg daily
Note. 20mg daily with concomitant fibrate

Proprietary Preparations
Corestin *(Unimed),* Tab. 10 mg, Tk.25.00/Tab.; 5 mg, Tk. 12.50/Tab.
Creston *(Eskayef),* Tab., 10 mg, Tk.20.00/Tab.; 5 mg, Tk. 10.00/Tab.
Nestor *(Navana),* Tab., 10 mg, Tk.20.00/Tab.; 20 mg, Tk. 30.00/Tab.; 5 mg, Tk. 10.00/Tab.
Rocovas *(Incepta),* Tab., 10 mg, Tk.15.00/Tab.; 5 mg, Tk. 8.00/Tab.
Rolip *(Renata),* Tab., 10 mg, Tk. 20.00/Tab.
Ropitor *(Opsonin),* Tab., 10 mg, Tk.15.04/Tab.;Tab. , 5 mg, Tk. 7.52/Tab.
Rosetor *(ACI),* Tab., 10 mg, Tk.18.00/Tab.; 5mg , Tk. 10.00/Tab.
Rostab *(Acme),* Tab., 10 mg, Tk.20.00/Tab.; 20 mg, Tk. 25.00/Tab.; 5mg, Tk. 10.00/Tab.
Rostatin *(Drug Int.),* Tab., 20 mg, Tk.25.00/Tab.; 10 mg, Tk. 15.00/Tab.; 5mg, Tk. 8.00/Tab.
Rosu *(Popular),* Tab., 10 mg, Tk.18.00/Tab.; 20 mg, Tk.30.00/Tab.; 5mg, Tk.10.00/Tab.
Rosugen *(General),* Tab., 10 mg, Tk.20.00/Tab.; 5 mg, Tk.10.00/Tab.
Rosutin *(Beximco),* Tab. , 10 mg, Tk.20.00/Tab.; 5 mg, Tk.10.00/Tab.
Rosuva *(Square),* Tab., 10 mg, Tk.20.07/Tab.; Tab. , 20 mg, Tk.30.00/Tab.; 5mg, Tk.10.00/Tab.
Rovast *(Healthcare),* Tab., 5 mg, Tk.10.00/Tab.; 10 mg, Tk.20.00/Tab.
Rozavas *(Albion),* Tab., 10 mg, Tk.20.07/Tab.; 5 mg, Tk.8.00/Tab.
Rozavel *(Sun),* Tab., 10 mg, Tk.25.00/Tab.; 5mg, Tk.12.50/Tab.
Ruvastin *(Aristo),* Tab., 10 mg, Tk.20.00/Tab.; 5 mg, Tk.10.00/Tab.

SIMVASTATIN

Indications : in patients with type 2 hyperlipidaemia who does not respond to diet control adequately; patients having coronary heart disease with plasma cholesterol level 5.5 mmol/l or higher; concomitant therapy with immunosuppressives

Contraindications: active liver disease; pregnancy and breast-feeding

Cautions: *same as that of fluvastatin*

Interactions: *see Appendix-2*

Side-effcets: *same as that of fluvastatin*

Dose: primary hypercholesterol-aemia, combined hyperlipidaemia, 10 mg daily at night, to be adjusted at intervals of 4 weeks; coronary heart disease, 20 mg once daily at night, to be adjusted at intervals of 4 weeks; max. 80 mg once daily

Proprietary Preparations
Novastin *(Drug Int.)* Tab., 10 mg, Tk. 10/Tab.
Simacor *(Square),*Tab., 10 mg, Tk. 10.04/Tab.
Simvastatin *(Albion),* Tab., 10 mg,Tk. 15/Tab.
Simvatin *(Acme),* Tab., 10 mg, Tk.11.04/Tab.; 20 mg, Tk. 18.06/Tab.
Vastin *(Amico),* Tab., 10 mg, Tk. 15.00/Tab.
Vastocor *(Incepta),* Tab., 10 mg, Tk.12/Tab.

3.12.4 EZETIMIBE

Ezetimibe inhibits the intestinal absorption of cholesterol. It is used as an adjunct to dietary manipulation in patients with primary hypercholesterolaemia in combination with a statin or alone (if a statin is inappropriate), in patients with homozygous familial hypercholesterol-aemia in combination with a statin, and in patients with homozygous familial sitosterolaemia (phytosterolaemia). If ezetimibe is used in combination with a statin, there is an increased risk of rhabdomyolysis

EZETIMIBE

Indications: adjunct to dietary measures and statin treatment in primary hypercholesterolaemia and homozygous familial hypercholesterolaemia (ezetimibe alone in primary hypercholesterolaemia if statin inappropriate or not tolerated); adjunct to dietary measures in homozygous sitosterolaemia
Cautions: hepatic impairment- avoid in moderate and severe impairment—may accumulate; pregnancy manufacturer advises use only if potential benefit outweighs risk—no information available;breast-feeding -manufacturer advises avoid—present in milk in animal studies
Contraindications: the combination of ezetimibe with statin is contraindicated in patients with active liver disease or unexplained persistent elevations in serum transaminases.
Interactions: *see Appendix-2*
Side-effects: gastro-intestinal disturbances; headache, fatigue; myalgia; rarely arthralgia, hypersensitivity reactions (including rash, angioedema, and anaphylaxis), hepatitis; very rarely pancreatitis, cholelithiasis, cholecystitis, thrombocytopenia, raised creatine kinase, myopathy, and rhabdomyolysis
Dose ADULT and CHILD over 10 years, 10 mg once daily

Proprietary Preparations
Ezeta *(Beximco),* Tab. 10 mg, Tk. 10.04/Tab.
Ezetrol *(Unimed),* Tab. 10 mg, Tk. 10.00/Tab.
Ezetim *(Incepta),* Tab. 10 mg, Tk. 10.00/Tab.

3.12.5 OMEGA-3 FATTY ACID COMPOUNDS

The omega-3 fatty acid compounds comprise omega-3-acid ethyl esters and omega-3-marine triglycerides. Omega-3 fatty acid compounds may be used to reduce triglycerides, as an alternative to a fibrate and in addition to a statin, in patients with combined (mixed) hyperlipidaemia not adequately controlled with a statin alone. A triglyceride concentration exceeding 10 mmol/litre is associated with acute pancreatitis and lowering the concentration reduces this risk. The fat content of omega-3 fatty acid compounds (including excipients in the preparations) should be taken into consideration when treating hypertriglyceridaemia. There is little clinical trial evidence that the triglyceride lowering effect decreases the risk of cardiovascular disease.

OMEGA-3-ACID ETHYL ESTERS

Indications: adjunct to diet and statin in type IIb or III hypertriglyceridaemia; adjunct to diet in type IV hypertriglyceridaemia; adjunct in secondary prevention in those who have had a myocardial infarction in the preceding 3 months
Cautions: haemorrhagic disorders, anticoagulant treatment (bleeding time increased); hepatic impairment and breast-feeding
Side-effects: gastrointestinal disturbances; less commonly taste disturbances, dizziness, and hypersensitivity reactions; rarely hepatic disorders, headache, hyperglycaemia, acne, and rash; very rarely hypotension, nasal dryness, urticaria, and increased white cell count

Dose: hypertriglyceridaemia, initially 2 capsules daily with food, increased if necessary to 4 capsules daily.Secondary prevention after myocardial infarction, 1 capsule daily with food.

Proprietary Preparations
Neomega *(Opsonin),*Cap. 1 gm, Tk. 4.53/Cap.
OMG-3 *(Drug Int),* Cap. 1 gm, Tk. 6.00/Cap.
Omesoft SG*(Pacific),*Cap. 1 gm, Tk. 7.52/Cap.

3.12.6 NICOTINIC ACID AND DERIVATIVES

Indications: for prevention and treatment of pellagra, hypercholesterolaemia, hypertriglyceridaemia
Contraindications: pregnancy, breast-feeding, active peptic ulcer disease
Cautions: diabetes mellitus, gout, peptic ulcer and liver disease, acute myocardial infarction
Interactions: *see Appendix-2*
Side-effcets: flushing, dizziness, palpitation, pruritus, nausea, vomiting.
Dose: 100-200 mg 3 times daily; it is better to take the drug with meals

Proprietary Preparation
Niapid *(Drug Int),* Tab., 500 mg, Tk.6.00/Tab

INOSITOL NICOTINATE

see section 3.3.4.

3.13 DRUGS FOR THE MANAGEMENT OF PULMONARY HYPERTENSION

Pulmonary arterial hypertension (PAH) is a rare and incurable progressive disease, including idiopathic PAH, heritable PAH, and PAH secondary to other diseases. PAH can occur in isolation (primary pulmonary hypertension), or be related to other diseases such as human immunodeficiency virus infection, congenital heart disease, connective tissue disorders like scleroderma and systemic lupus erythematosus, or idiopathic pulmonary fibrosis. PAH can also be induced by substance abuse with appetite suppressants, cocaine, or other drugs.

Idiopathic PAH is panvasculopathy in which clones of endothelial cells proliferate and give rise to plexiform lesions, the pathological hallmark of this condition, thereby promoting complex vascular lesions with near-total or total lumen obliteration acting by multiple mechanisms including increased serotonin release. Thus there is increasing vascular smooth muscle damage. The functional consequences include decreased endothelial NO production and increased PDE-5 expression and activity in both PA and in the RV muscle cells. The overall result is an increase in PVR in a disease that affects both the PA and the right ventricle. These obstructive proliferative changes in the lung microcirculation promote RV hypertrophy, eventually leading to right heart failure and premature death. Optimal therapy remains undecided.

There is no cure for PAH, but treatment options include prostanoids, PDE-5 inhibitors, and ET-receptor antagonists.
Ambrisentan, bosentan, iloprost, sildenafil, sitaxentan, and **tadalafil** are indicated for the treatment of pulmonary arterial hypertension and should be used under specialist supervision.
Epoprostenol (prostacyclines) can be used in patients with primary pulmonary hypertension resistant to other treatments. Phosphordiesterase-5inhibitors (**sildenafil, tadalafil**) vasodilate by acting on PDE-5 in the pulmonary and systemic vasculature. Furthermore, vascular remodeling can be promoted by decreased proliferation and increased apoptosis of pulmonary artery smooth muscle cells. RV inotropy also increases. There is also a direct action on the lungs, in which expression of PDE-5 is suppressed. Thus sildenafil also preferentially improves blood flow to well-ventilated regions of the lung in patients with lung disease such as idiopathic pulmonary fibrosis
The first oral therapy approved for therapy of PAH was **bosentan** (endothelin receptor antagonists). Bosentan gives combined ET_A/ET_B receptor antagonism. Selective ET_A

antagonists (**sitaxsentan**; **ambrisentan**) theoretically preserve the vasodilatory action of the ET_B receptor. However, no trial data show whether selective ET_A antagonism is better than combined ET_A and ET_B antagonism. Bosentan is also licensed to reduce the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer disease.

AMBRISENTAN

Indication: pulmonary arterial hypertension
Cautions: not to be initiated in significant anaemia, monitor haemoglobin concentration or haematocrit after 1 month and 3 months of starting treatment, and periodically thereafter , hepatic and renal impairment ,pregnancy and breast-feeding, renal impairment use with caution if eGFR less than 30 mL/minute/ 1.73m^2;
Side-effects: abdominal pain, constipation; palpitation, flushing, peripheral oedema, headache; anaemia; less commonly hypersensitivity reactions
Dose: ADULT over 18 years, 5 mg once daily, increased if necessary to 10 mg once daily.

Generic Preparation
Tablet, 10mg, 5mg

BOSENTAN

Indications: pulmonary arterial hypertension; systemic sclerosis with ongoing digital ulcer disease (to reduce number of new digital ulcers)
Cautions: not to be initiated if systemic systolic blood pressure is below 85 mmHg; monitor haemoglobin before and during treatment (monthly for first 4 months, then 3-monthly), avoid abrupt withdrawal, monitor 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, hepatic impairment-avoid in moderate and severe impairment; pregnancy avoid (teratogenic in animal studies); effective contraception required during and for at least 3 months after administration (hormonal contraception not considered effective),monthly pregnancy tests advised; breast-feeding
Contra-indication: acute porphyria
Interactions: *see Appendix -2*
Side-effects: GI disturbances, dry mouth, rectal haemorrhage, flushing, hypotension, palpitation, oedema, dyspnea, dizziness, fatigue, back pain and pain in extremitie anaemia, hypersensitivity reactions
Dose: pulmonary arterial hypertension, initially 62.5 mg twice daily increased after 4 weeks to 125 mg twice daily; max. 250 mg twice daily. Systemic sclerosis with ongoing digital ulcer disease, initially 62.5 mg twice daily increased after 4 weeks to125 mg twice daily

Proprietary Preparation
Pulmoten*(Unimed),*Tab., 62.5mg,Tk.150/Tab.

SILDENAFIL

Indications,**Cautions**
Side-effects: *See section 6.4.4*
Dose: *by mouth,* 20 mg 3 times daily; CHILD under 18 years not recommended.
By intravenous injection, when oral route not appropriate, 10 mg three times daily

Proprietary Preparations
see section 6.4.4