PHC Chapter 4: Cardiovascular conditions

4.1 PREVENTION OF ISCHAEMIC HEART DISEASE AND ATHEROSCLEROSIS

I20.0-1/I20.8-9/I21.0-4/I21.9/I22.0-1/I22.8-9/I24.0-1/I24.8-9/I25.0-6/I25.8-9/I63.0-6/I63.8-9/I64/I65.0-3/I65.8-9/I73.8-9/G45.0-2/G45.8-9

Patients at risk for cardiovascular events (such as stroke or myocardial infarction) may benefit from lifestyle modification and lipid-lowering medicine therapy. Patients should be managed according to their level of risk, and lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.

Indications for lipid lowering medicine therapy

Patients with any of the following factors are at a relatively high risk for a cardiovascular event and should receive lipid lowering therapy:

- Established atherosclerotic disease:
  - ischaemic heart disease.
  - peripheral vascular disease.
  - atherothrombotic stroke.
- Type 2 diabetes with age >40 years.
- Diabetes for >10 years. *LoE:IIa*[1]
- Diabetes with chronic kidney disease (eGFR <60 mL/min).

Patients with any of the following factors are also potentially at risk for cardiovascular disease (other than the categories above)

- Diabetes mellitus.
- Hypertension.
- Central obesity: waist circumference ≥ 94 cm (men) and ≥ 80 cm (women).
- Smoking.
- Age: men >55 years of age, women >65 years of age. *LoE:IIIb*[2]
- Psychological stress.

These patients should be managed according to their 10-year risk of a cardiovascular event (See Appendix III: Cardiovascular risk assessment), as calculated using either:

A. BMI - based risk assessment, or
B. Framingham risk score (cholesterol-based assessment).

Management is based on the patient's 10-year risk of a cardiovascular event as follows:

- <10% risk: lifestyle modification and risk assess patient every 5 years.
- 10–20% risk: lifestyle modification and risk assess patient annually.
- ≥ 20% risk: lifestyle modification and start statin treatment.

Screening for familial hypercholesteroleamia:

In addition to the above cardiovascular risk assessment, measure random total cholesterol in patients with the following features (suggestive of familial hypercholesterolaemia or other heritable dyslipidaemias), regardless of their cardiovascular risk:

- Cardiovascular event <55 years in men or <65 years in women.
- Family history of early onset cardiovascular disease in male relatives <55 years of age and in female relatives <65 years of age.

» Skin or tendon xanthomata in patient or first degree relative.
» Family history of familial hyperlipidaemia.

Refer patients with random total cholesterol >7.5 mmol/L for further investigation.

GENERAL MEASURES

All patients with any risk factors for cardiovascular disease should be encouraged to make the following lifestyle changes as appropriate:

LoE:IIIb[3]

» Maintain ideal weight, i.e. BMI 18 to 25 kg/m^2. Weight reduction in the overweight patient.
» Reduce alcohol intake to no more than 2 standard drinks per day for males and 1 for females. (1 standard drink = a can of beer = a glass of wine = a shot of spirits.)
» Follow a prudent eating plan i.e. low fat, high fibre and unrefined carbohydrates, with fresh fruit and vegetables.
» Regular moderate aerobic exercise, e.g. 30 minutes brisk walking 5 to 7 times/week (150 minutes/week).
» Stop smoking.

MEDICINE TREATMENT

» Lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.
» When lipid-lowering medicines are used, this is ALWAYS in conjunction with ongoing lifestyle modification.

▪ HMGCoA reductase inhibitors (statins), according to table below:

INDICATION	HMGCoA REDUCTASE INHIBITOR (STATIN)
A: Primary prevention - no existing CVD	
» Type 2 diabetes with age >40 years. » Diabetes for >10 years. » Diabetes with chronic kidney disease. » ≥20% 10-year risk of cardiovascular event.	▪ HMGCoA reductase inhibitors (low intensity statin), e.g.: • Simvastatin, oral, 10 mg at night.
» Patients on protease inhibitors. (Risks as above, after switching to atazanavir – see section below).	• Atorvastatin, oral, 10 mg once daily.
» Pregnant and breastfeeding women	• Do not prescribe statins unless on the advice of a specialist
B: Secondary prevention – existing CVD	
» Ischaemic heart disease. » Atherothrombotic stroke. » Peripheral vascular disease.	▪ HMGCoA reductase inhibitors (moderate intensity statin), e.g.:Rosuvastatin, oral, 10 mg once daily. *LoE:Ia*[4]
» Patients on protease inhibitors (see section below).	• Rosuvastatin 10mg, oral once daily, *LoE:Ia*[5]
» If patient complains of muscle pain.	Reduce dose:

	▪ HMGCoA reductase inhibitors (statin), e.g.: • Rosuvastatin, oral, 5 mg once daily. If not tolerated switch to low intensity statin e.g.: Simvastatin 10mg at night. **OR** Consult specialist for further management. *LoE:IIIb*[6]
» Pregnant and breastfeeding women	Do not prescribe statins unless on the advice of a specialist. *LoE:IVb*[7]

Table 4.1: Management with HMGCoA reductase inhibitors

Protease inhibitor-induced dyslipidaemia:

» Certain antiretroviral medication, particularly protease inhibitors (e.g. lopinavir/ritonavir, atazanavir/ritonavir and darunavir/ritonavir), can cause dyslipidaemia.
» Patients taking protease inhibitor-containing ART, should be assessed for eligibility to be switched to a dolutegravir-containing regimen.
» Patients with persistent dyslipidaemia despite switching to dolutegravir-containing ART regimen, qualify for lipid lowering therapy. Criteria for initiating lipid lowering therapy are the same as for HIV-negative patients (refer to table 4.1 above).
» Lopinavir/ritonavir is associated with a higher risk of dyslipidaemia (specifically hypertriglyceridaemia) than atazanavir/ritonavir. Patients at high risk (>20% risk of developing a CV event in 10 years or existing CVD) should switch to atazanavir/ritonavir if not eligible for a dolutegravir-containing ART regimen.
» If ART with a protease inhibitor is essential, fasting lipid levels should be monitored 3 months after initiating protease inhibitor therapy.
» Protease inhibitors inhibit the metabolism of most statins, resulting in higher statin levels in the blood. Simvastatin is contraindicated for this reason. Other statins may be co-prescribed with protease inhibitors at a reduced dose, see Appendix V: Comparative dose tables, for more information.
» Patients with persistent dyslipidaemia despite switching to atazanavir/ritonavir and employing lifestyle modification, qualify for a statin. Criteria for initiating lipid lowering therapy are the same as for HIV-negative patients (refer to table 4.1 above).
» Recommended statins for patients on protease inhibitor containing ART are as follows:
  ▪ HMGCoA reductase inhibitors:
    • Primary prevention: e.g. Atorvastatin, oral, 10 mg once daily.
    • Secondary prevention: e.g. Rosuvastatin 10mg once daily

REFERRAL

» Random cholesterol >7.5 mmol/L (to be evaluated for genetic disorders), after excluding secondary causes such as uncontrolled diabetes, hypothyroidism, or protease inhibitor use.
» Tendon or skin xanthomata (except xanthelasma around the eyes).
» Statins not tolerated by patients, despite lower dose (for consideration of alternative treatment).

4.2 ANGINA PECTORIS, STABLE

I20.20

DESCRIPTION

Characteristic chest pain (burning or heavy discomfort behind the sternum), of duration <15 minutes, due to myocardial ischaemia, usually with exercise and relieved by rest.

GENERAL MEASURES

Lifestyle modification. See Section 4.1: Prevention of ischaemic heart disease and atherosclerosis.

MEDICINE TREATMENT (doctor initiated)

Long-term prophylaxis for thrombosis:

- Aspirin, oral, 150 mg daily. *LoE:Ia*[8]

AND

Relief of angina:

- Nitrates, short acting e.g.:
- Isosorbide dinitrate, sublingual, 5 mg.
  - May be repeated if required at 5-minute intervals for 3 or 4 doses.
  - Instruct patients to keep the tablets in the airtight and lightproof container in which they are supplied.
  - Instruct patients that nitrates are not addictive.
  - Instruct patients to use prophylactically, before activities which may provoke angina. *LoE:IVb*[9]

AND

Step 1

- Beta-blocker
- Atenolol, oral, 50 to 100 mg daily.
  - Titrate to resting heart rate of approximately 60 beats/minute.

If beta-blocker cannot be tolerated or is contraindicated, consider long-acting calcium channel blocker.

Step 2

ADD

- Long-acting calcium channel blocker e.g.:
- Amlodipine, oral, 5 mg daily.

Step 3
ADD
- Isosorbide mononitrate, oral, 10–20 mg twice daily. *LoE:IIIb*[10]

OR
- Isosorbide dinitrate, oral, 20–30 mg twice daily.
  - Take either medicine at 8:00 and 14:00 in order to provide a nitrate-free period to prevent tolerance. *LoE:IIIb*[11]
  - Modify for night shift workers.

Angina is a high-risk condition for cardiovascular disease and an indication for a statin.
- HMGCoA reductase inhibitors (moderate intensity statin), e.g.:
- Rosuvastatin, oral, 10 mg once daily. *LoE:Ia*[12]

Patients on protease inhibitor:
- Rosuvastatin, oral 10mg once daily. *LoE:Ia*[13]

If patient complains of muscle pain:
Reduce dose e.g.:
- Rosuvastatin, oral, 5mg once daily.

OR
Low intensity statin e.g.
- Simvastatin, oral, 10mg at night.

OR
Refer for further management. *LoE:IIIb*[14]

REFERRAL
» When diagnosis is in doubt.
» Failed medical therapy.

4.3 ANGINA PECTORIS, UNSTABLE / NON-ST ELEVATION MYOCARDIAL INFARCTION (NSTEMI)

I21.4/ I21.9/I22.0-1/I22.8-9/I24.8-9/I25.6/I25.8-9

DESCRIPTION
Unstable angina is a medical emergency and if untreated can progress to NSTEMI.
Presents as chest pain or discomfort similar to stable angina but with the following additional characteristics:
» angina at rest or minimal effort,
» angina occurring for the first time, particularly if it occurs at rest,
» prolonged angina >10 minutes, not relieved by sublingual nitrates,
» the pattern of angina accelerates and gets worse.

DIAGNOSIS

» Made from good history.
» ECG may show ST segment depression, transient ST segment elevation or T wave inversion.
» Normal ECG does not exclude the diagnosis. For this reason, history is of paramount importance.

MEDICINE TREATMENT

- Oxygen 40% via facemask, if saturation <94% or if in distress.

CAUTION
Do not administer oxygen to acutely ill patients who are not hypoxic (SPO_2 ≥96%).

ADD

- Aspirin, oral, 150 mg as a single dose (chewed or dissolved) as soon as possible.

ADD

- Nitrates, short acting, e.g.: *LoE:Ia*[15]
- Isosorbide dinitrate, sublingual, 5 mg immediately as a single dose. *LoE:IIb*[16]
  - May be repeated at 5-minute intervals for 3 or 4 doses. *LoE:IVb*[17]

ADD

- Morphine 10 mg diluted with 10 mL of water for injection or sodium chloride 0.9%, slow IV. (Doctor prescribed.)
  - Start with 5 mg; thereafter slowly increase by 1 mg/minute up to 10 mg.
  - Can be repeated after 4 to 6 hours, if necessary, for pain relief.
  - Beware of hypotension.

Continuation of aftercare treatment initiated at higher level of care:
Continue therapy with appropriate lifestyle modification and adherence support.

- Aspirin, oral, 150 mg daily (continued indefinitely in absence of contraindications). *LoE:Ia*[18]

<u>When clinically stable without signs of heart failure, hypotension, bradydysrhythmias or asthma:</u>

- Cardio-selective beta-blocker, e.g.: (doctor initiated)
- Atenolol, oral, 50 mg daily.

AND

- HMGCoA reductase inhibitors (moderate intensity statin), e.g.:
- Rosuvastatin, oral, 10 mg, oral, once daily. *LoE:Ia*[19]

<u>Patients on protease inhibitor:</u>

- Rosuvastain, oral, 10 mg once daily. *LoE:Ia*[20]

<u>If patient complains of muscle pain:</u>
Reduce dose e.g.: *LoE:IIIb*[21]

- Rosuvastatin, oral, 5mg once daily.

OR
Low intensity statin

- Simvastatin, oral, 10 mg at night.

OR
Refer for further management.
AND

If there is cardiac failure or LV dysfunction (doctor initiated):
- ACE-inhibitor, e.g.:
- Enalapril, oral, target dose 10 mg 12 hourly (usually titrated from 2.5 mg 12 hourly).

LoE:IVb[22]

Angioedema is a potentially serious complication of ACE-inhibitor treatment and if it occurs it is a contraindication to continue therapy or to re-challenge.

REFERRAL
Urgent
All suspected or diagnosed cases.

4.4 MYOCARDIAL INFARCTION, ACUTE (AMI)/ ST ELEVATION MYOCARDIAL INFARCTION (STEMI)
I21.0-3/I21.9/I22.0-1/I22.8-9/I24.8-9/I25.6/I25.8-9

DESCRIPTION
AMI/STEMI is caused by the complete or partial occlusion of a coronary artery and requires prompt hospitalisation and intensive care management.
The major clinical feature is severe chest pain with the following characteristics:
- site: retrosternal or epigastric,
- quality: crushing, constricting, or burning pain or discomfort,
- radiation: to the neck and/or down the inner part of the left arm,
- duration: at least 20 minutes and often not responding to sublingual nitrates,
- occurrence: at rest.

May be associated with:
- pallor
- sweating
- arrhythmias
- pulmonary oedema
- a decrease in blood pressure

Note: Not all features have to be present.

EMERGENCY TREATMENT
Before transfer
Cardio-pulmonary resuscitation if necessary (see Section 21.1: Cardiac arrest – cardiopulmonary resuscitation).
- Oxygen 40% via facemask, if saturation <90% or if in distress.

CAUTION
Do not administer oxygen to acutely ill patients who are not hypoxic ($SPO_2 \geq 96\%$)

LoE:IIb[23]

AND

- Aspirin, oral, 150 mg as a single dose (chewed or dissolved) as soon as possible.

AND LoE:Ia[24]

- Nitrates, short acting, e.g.:
- Isosorbide dinitrate, sublingual, 5 mg immediately as a single dose.
  - May be repeated at 5-minute intervals for 3 or 4 doses. LoE:IVb[25]

AND

- Morphine 10 mg diluted with 10 mL of water for injection or sodium chloride 0.9%, slow IV (doctor prescribed).
  - Start with 5 mg; thereafter slowly increase by 1 mg/minute up to 10 mg.
  - Can be repeated after 4 to 6 hours, if necessary, for pain relief.
  - Beware of hypotension.

AND LoE:IIb[26]

- Thrombolytic (see table for time window below) (Doctor initiated), e.g.:
- Streptokinase, IV 1.5 million units diluted in 100 mL sodium chloride 0.9%, infused over 30 to 60 minutes. **Do not use heparin if streptokinase is given.** LoE:IIb[27]
  - Hypotension may occur. If it does, reduce the rate of infusion but strive to complete it in <60 minutes.
  - Streptokinase is antigenic and should not be re-administered in the period of 5 days to 2 years after 1st administration.
  - Severe allergic reactions are uncommon but antibodies which may render it ineffective may persist for years.

Considerations for initiating thrombolytics	Contra-indications
» <u>For acute myocardial infarction with ST elevation or left bundle branch block:</u> » maximal chest pain is ≤ 6 hours doctor to initiate treatment. – If beyond 6 hours and chest pain, consult a specialist. » >6 hours and no chest pain, thrombolytic not indicated. Manage as above and refer patient. LoE:Ia[28]	» <u>Absolute:</u> – streptokinase used within the last year, » previous allergy, – CVA within the last 3 months, – history of recent major trauma, – bleeding within the last month, – aneurysms, – brain or spinal surgery or head injury within the preceding month, or recent (<3 weeks) major surgery, – active bleeding or known bleeding disorder, – aortic dissection. » <u>Relative (consult specialist):</u> – refractory hypertension, – warfarin therapy, – recent retinal laser treatment, – subclavian central venous catheter, – pregnancy, – TIA in the preceding 6 months, – traumatic resuscitation.

Table 4.2: Streptokinase therapy

Note: Refer all suspected or diagnosed cases urgently.

Continuation of aftercare treatment initiated at higher level of care:
Continue therapy with appropriate lifestyle modification and adherence support.

- Aspirin, oral, 150 mg daily (continued indefinitely in absence of contraindications).

LoE:Ia[29]

When clinically stable without signs of heart failure, hypotension, bradydysrhythmias or asthma:

- Cardio-selective beta-blocker, e.g.: (doctor prescribed)
- Atenolol, oral, 50 mg daily.

AND

- HMGCoA reductase inhibitors (moderate intensity statins), e.g.:
- Rosuvastatin, oral, 10 mg once daily.

LoE:Ia[30]

Patients on protease inhibitor:

- Rosuvastatin, oral, 5 mg once daily.

LoE:Ia31

If patient complains of muscle pain:
Reduce dose e.g.:

- Rosuvastatin, oral, 5mg once daily

If not tolerated switch to low intensity statin e.g.:

- Simvastatin 10mg at night.

OR

LoE:IIIa[32]

Refer for further management.

AND

If there is cardiac failure or LV dysfunction (Doctor initiated):

- ACE-inhibitor, e.g.:
- Enalapril, oral, target dose 10 mg 12 hourly (usually titrated from 2.5 mg 12 hourly).

Angioedema is a potentially serious complication of ACE-inhibitor treatment and if it occurs it is a contraindication to continued therapy or to re-challenge.

REFERRAL

Urgent
All suspected or diagnosed cases.

4.5 CARDIAC ARREST, CARDIO-PULMONARY RESUSCITATION

See Chapter 21: Emergencies and injuries.

4.6 CARDIAC FAILURE, CONGESTIVE (CCF)

4.6.1 CARDIAC FAILURE, CONGESTIVE (CCF), ADULTS

I50.0-1/I50.9

DESCRIPTION

CCF is a clinical syndrome and has several causes. The cause and immediate precipitating factor(s) must be identified and treated to prevent further damage to the heart.

Symptoms of CCF include:

- » Progressive effort intolerance (worsening breathlessness, or fatigue with physical activity such as walking uphill, climbing stairs, sweeping or carrying a heavy load). If severe, breathlessness, or fatigue, may occur when doing activities of daily living such as dressing and washing and may even occur at rest.
- » Orthopnoea (breathless when lying down flat).
- » Paroxysmal nocturnal dyspnoea (PND) (sudden awakening with breathlessness).
- » Ankle (or body) swelling.
- » Fatigue.

Signs of CCF include:

- » dyspnoea (breathlessness)
- » ankle swelling with pitting oedema
- » tachycardia
- » raised jugular venous pressure
- » inspiratory basal crackles or wheezing on auscultation of the lungs
- » tachypnoea
  - men: breathing rate >18 breaths/ minute
  - women: breathing rate >20 breaths/ minute
- » enlarged liver, often tender

GENERAL MEASURES

- » Monitor body weight to assess changes in fluid balance.
- » Salt (sodium chloride) restriction to less than 2 to 3 g/day.
- » Regular exercise within limits of symptoms.

MEDICINE TREATMENT

All patients should be assessed by a doctor for initiation or change of treatment.

- » Many of the medicines used can affect renal function and electrolytes.
- » Monitor sodium, potassium and serum creatinine.

STEP 1: Diuretic plus ACE-inhibitor

Mild volume overload (mild CCF) and normal renal function – thiazide/thiazide-like diuretic e.g.:

- Hydrochlorothiazide, oral 25 to 50 mg daily. *LoE:IIb*[33]

- Caution in patients with gout.
- Less effective in impaired renal function.
- Higher doses can cause hyponatremia.
- Caution in patients with a history or family history of skin cancer; and counsel all patients on sun avoidance and sun protection.

Significant volume overload or abnormal renal function – loop diuretic

- Furosemide, oral, daily (doctor initiated).
  - Initial dose: 40 mg daily.
  - If dose >80 mg/day is required, change dose interval to 12 hourly.
  - Higher doses may be needed if co-morbid kidney impairment is present.
  - Once CCF has improved, consider switching to hydrochlorothiazide.
  - Monitor electrolytes and creatinine.

Acute pulmonary oedema

- Furosemide, IV. See Section 21.2.8: Pulmonary oedema, acute.

Note:

» Use a lower diuretic dose when given in combination with an ACE-inhibitor.

» Routine use of potassium supplements with diuretics is not recommended. They should only be used short-term to correct documented low serum potassium level.

All patients with CCF, unless contraindicated or poorly tolerated *LoE:IVb*[34]

- ACE-inhibitor, e.g.:
- Enalapril, oral, 2.5 mg 12 hourly, up to maximum of 10 mg twice daily.
  - Titrate dosages gradually upwards until an optimal dose is achieved.
  - Absolute contraindications include: (refer to package insert for a complete list)
    - cardiogenic shock,
    - bilateral renal artery stenosis, or stenosis of an artery to a dominant/single kidney,
    - aortic valve stenosis and hypertrophic obstructive cardiomyopathy,
    - pregnancy,
  - history of angioedema associated with previous ACE-inhibitor or angiotensin II receptor blocker (ARB) therapy.

STEP 2: After titration of ACE-inhibitor add carvedilol (alpha 1 and non-selective beta blocker) unless contra-indicated (Refer to package insert for full prescribing information).

Note: Do not use atenolol for cardiac failure. *LoE:IIIb*[35]

- Carvedilol, oral (doctor initiated).
  - Starting dose: 3.125 mg twice daily.
  - Increase dose at two-weekly intervals by doubling the daily dose until a maximum of 25 mg twice daily, if tolerated.
  - If >85 kg, titrate to a maximum of 50 mg twice daily, if tolerated. If patient remains symptomatic on maximum tolerated dose, do an ECG and refer if there is indication of heart block or bradyarrthymias that may be of concern. *LoE:IIIb*[36] Alternatively, refer if access to ECG monitoring is not available.
  - If not tolerated, i.e., worsening of cardiac failure manifestations, reduce the dose to the previously tolerated dose.

- Up-titration may take several months.
- Should treatment be discontinued for >14 days, reinstate therapy as above.
- Absolute contraindications include: (refer to package insert)
  - cardiogenic shock, bradycardia, various forms of heart block,
  - severe fluid overload,
  - hypotension,
  - asthma.

OR

- Spironolactone, oral, 25 mg daily (doctor initiated).

CAUTION

Spironolactone can cause severe hyperkalaemia and should only be used when serum potassium and renal function can be monitored. Check potassium levels within one month of starting therapy and thereafter, as per clinical need. Routine monitoring of potassium levels is essential if spironolactone is used with an ACE-inhibitor, other potassium sparing agents or in the elderly. Avoid concomitant potassium supplements and use of NSAIDs. **Do not use in kidney failure (Do not use if eGFR <30 mL/min).**

STEP 3:

- Spironolactone, oral, 25 mg daily (doctor initiated). *LoE:IVb*[37]

OR

- Carvedilol, oral (doctor initiated).
  - Starting dose: 3.125 mg twice daily.
  - Increase dose at two-weekly intervals by doubling the daily dose until a maximum of 25 mg twice daily, if tolerated.
  - If >85 kg and target heart rate has not been achieved, titrate to a maximum of 50 mg twice daily, if tolerated. If patient remains symptomatic on maximum tolerated dose, do an ECG and refer if there is indication of heart block or bradyarrthymias that may be of concern.
  - If not tolerated, i.e. worsening of cardiac failure manifestations, reduce the dose to the previously tolerated dose.
  - Up-titration can take several months.
  - Should treatment be discontinued for >14 days, reinstate therapy as above.
  - Absolute contraindications include: (refer to professional information leaflet)
  - cardiogenic shock, bradycardia, various forms of heart block,
  - severe fluid overload,
  - hypotension,
  - asthma.

STEP 4:

Symptomatic CCF despite above-mentioned therapy:

- Refer to hospital for step up therapy with digoxin.

CAUTION
Patients with CCF on diuretics may become hypokalaemic.
Digoxin therapy should not be initiated if the patient is hypokalaemic.

REFERRAL

Urgent

» Patients with prosthetic heart valve.
» Suspected infective endocarditis.
» Fainting spells.

Non urgent

» Initial assessment and initiation of treatment.
» Poor response to treatment.

4.6.2 CARDIAC FAILURE, CONGESTIVE (CCF), CHILDREN

I50.0/I50.1-9

DESCRIPTION

The congestion of the systemic or pulmonary venous systems due to cardiac dysfunction of various different causes; including congenital heart disease and acquired cardiac and lung conditions (e.g. cor-pulmonale due to bronchiectasis in children living with HIV). Often mistaken for respiratory infection.

Signs and symptoms

Infants

» rapid breathing
» rapid heart rate
» cardiomegaly
» enlarged tender liver
» chest indrawing
» crackles or wheezing in lungs
» active cardiac impulse

Often presents primarily with shortness of breath, difficulty in feeding and sweating during feeds. Oedema is usually not an obvious feature.

Children

» rapid breathing
» rapid heart rate
» cardiomegaly
» enlarged tender liver
» chest indrawing
» crackles or wheezing in lungs
» active and displaced cardiac impulse
» oedema of the lower limbs or lower back

GENERAL MEASURES

While arranging transfer:

- Oxygen, using nasal cannula at 2 to 3 L per minute.

OR

- Oxygen 40%, using face mask at 2 to 3 L per minute.
  - Semi-Fowlers position.

Note: If hypertensive, consider glomerulonephritis in children.

MEDICINE TREATMENT

While arranging transfer:

If CCF is strongly suspected

- Furosemide, IV, 1 mg/kg, over 5 minutes. See dosing table: Chapter 23.
  - Do not put up a drip or run in any IV fluids.

REFERRAL

All children with suspected congestive cardiac failure.

4.7 HYPERTENSION

4.7.1 HYPERTENSION IN ADULTS

I10

DESCRIPTION

A condition characterised by an elevated blood pressure (BP) measured on 3 separate occasions, a minimum of 2 days apart:

» Systolic BP ≥ 140 mmHg.

and/or

» Diastolic BP ≥ 90 mmHg.

However, when BP is severely elevated (refer to the table below), a minimum of 3 BP readings must be taken at the 1st visit to confirm hypertension. Ensure that the correct cuff size is used in obese patients.

LEVELS OF HYPERTENSION IN ADULTS

Level of hypertension	Systolic mmHg	Diastolic mmHg
Mild	140–159	90–99
Moderate	160–179	100–109
Severe	≥ 180	≥ 110

Table 4.3: Classification of hypertension

LoE:IIb[38]

The aim of hypertension management is to achieve and maintain target BP: Systolic <140 mmHg and diastolic <90 mmHg (applicable to patients of all ages with uncomplicated hypertension).

MONITORING

At every visit:

» Weight.

» Blood pressure.

Baseline:

» Serum creatinine concentration (and eGFR) – see Section 8.1: Chronic Kidney Disease (CKD).

» Urine protein by dipstix to screen for secondary causes of hypertension.
  - In patients with diabetes see Section 9.2: Type 2 diabetes mellitus.
» BMI for cardiovascular risk assessment (see Section 4.1: Prevention of ischaemic heart disease and atherosclerosis).
» Abdominal circumference.
» Serum potassium concentration, if on ACE-inhibitor or eGFR <30 mL/min. (See Section 9.2.2: Type 2 Diabetes Mellitus, Adults.)

Six monthly:

» Serum potassium concentration in patients on spironolactone or eGFR <30 mL/min.

Annually:

» Finger prick blood glucose (see Section 9.2.2: Type 2 Diabetes Mellitus, Adults).
» Urine protein by dipstix (see Section 8.1: Chronic Kidney Disease (CKD)).
» Serum creatinine concentration (and eGFR) in patients who have:
  - proteinuria 1+ or more,
  - existing cardiovascular disease,
  - hypertension present for 10 years or more,
  - if uncontrolled hypertension,
  - chronic kidney disease (eGFR <60 mL/min).

GENERAL MEASURES

Screen all patients for cardiovascular disease risk factors (see Section 4.1: Prevention of ischaemic heart disease and atherosclerosis) and prescribe a statin if required.
Screen for presence of compelling indications (see table below) and manage patients accordingly.

Lifestyle modification

All people with hypertension should be encouraged to make the following lifestyle changes as appropriate.

» Smoking cessation.
» Maintain ideal weight, i.e. BMI 18 to 25 kg/m^2. Weight reduction in the overweight patient. *LoE:IIIb*[39]
» Salt restriction with increased potassium intake from fresh fruits and vegetables (e.g. remove salt from the table, gradually reduce added salt in food preparation and avoid processed foods). Dietician's advice recommended.
» Reduce alcohol intake to no more than 2 standard drinks per day for males and 1 for females.
» Follow a healthy eating plan i.e. low fat, high fibre and unrefined carbohydrates, with adequate fresh fruit and vegetables. Dietician's advice recommended.
» Regular moderate aerobic exercise, e.g. 30 minutes brisk walking at least 5 to 7 times a week. *LoE:IIIb*[40]

MEDICINE TREATMENT

Initial medicine choices are dependent on the presence or absence of compelling indications for specific medicines. See Table 4.5: Treatment of hypertension with

compelling indications, for a list of compelling indications and recommendations for specific medicines.

In the absence of compelling indications, see Table 4.4: Stepwise approach of treating hypertension without compelling indications.

Advise patient to take medication regularly, including on the day of the clinic visit, but a single missed dose does not account for severe elevations in BP.

Note:

- » Check adherence to antihypertensive therapy by doing pill counts and questioning family members.
- » The use of fixed dose combination medication for control of hypertension results in greater adherence and such agents should be used when they are available. *LoE:IIIb*[41]
- » The prescribing of antihypertensive medication should be guided by the time of day that is most convenient for patients and that would optimize adherence and minimize side effects for individual patients
- » Monitor patients monthly and adjust therapy, if necessary, until the BP is stable.
- » Check adherence to medication before escalating therapy.
- » After target BP is achieved, patients may be seen at 3 to 6 monthly intervals.

Mild hypertension

When there are no cardiovascular risk factors, initiate lifestyle modification measures (Step 1). If there is poor response to lifestyle modification measures after 3 months, initiate medicine therapy (Step 2).

If mild hypertension with the presence of risk factors (see Section 4.1: Prevention of ischaemic heart disease and atherosclerosis), initiate medicine therapy as well as lifestyle modification (Step 2).

Moderate hypertension

Confirm diagnosis within 2 weeks. Initiate treatment after confirmation of diagnosis (medicine and lifestyle modification) at Step 2.

Severe hypertension

Confirm diagnosis within 1 hour.

In patients who are not symptomatic, initiate treatment (medicine and lifestyle modification) at Step 3.

Patients with symptoms of progressive target organ damage or associated clinical conditions: See hypertensive urgency, below and Section 4.7.2: Hypertensive emergency.

Special cases

Pregnancy-induced hypertension

See Section 6.4.2: Hypertensive disorders of pregnancy.

Asymptomatic severe hypertension

- » These patients have severe hypertension, are asymptomatic and have no evidence of progressive target organ damage.

- » Observe the patient in the health care setting and repeat BP measurement after the patient has rested for 1 hour.
- » If the second measurement is still elevated at the same level, start oral treatment with 2 agents (Step 3), one of which should be low dose hydrochlorothiazide and the second medicine is usually a calcium channel blocker, e.g. amlodipine.
- » Patient should be followed up within a week.
- » Refer to doctor if BP >160/100 mmHg after 4 weeks.

Hypertensive urgency

- » Most have a systolic BP >180 mmHg and/or diastolic BP >110 mmHg.
- » Patients are symptomatic, usually with severe headache, shortness of breath and oedema, but there are no immediate life threatening neurological or cardiac complications such as are seen in hypertensive emergencies (see Section 4.7.2: Hypertensive emergency).
- » Start treatment with 2 oral agents (Step 3) with the aim to lower diastolic BP to 100 mmHg slowly, over 48–72 hours.
- » Amlodipine and furosemide or hydrochlorothiazide should be used, if there is renal insufficiency or evidence of pulmonary congestion (see Section 4.6.1: Cardiac failure, congestive (CCF), adults).
- » All patients with hypertensive urgency should be referred to a hospital.

Stroke

BP is often elevated in acute stroke. Do not treat elevated BP at PHC but refer patient urgently.

Elderly

In patients without co-existing disease, initiate medicine treatment only when the BP >160/90 mmHg.

CAUTION

Lower BP over a few days.
A sudden decrease in BP can be dangerous, especially in the elderly.

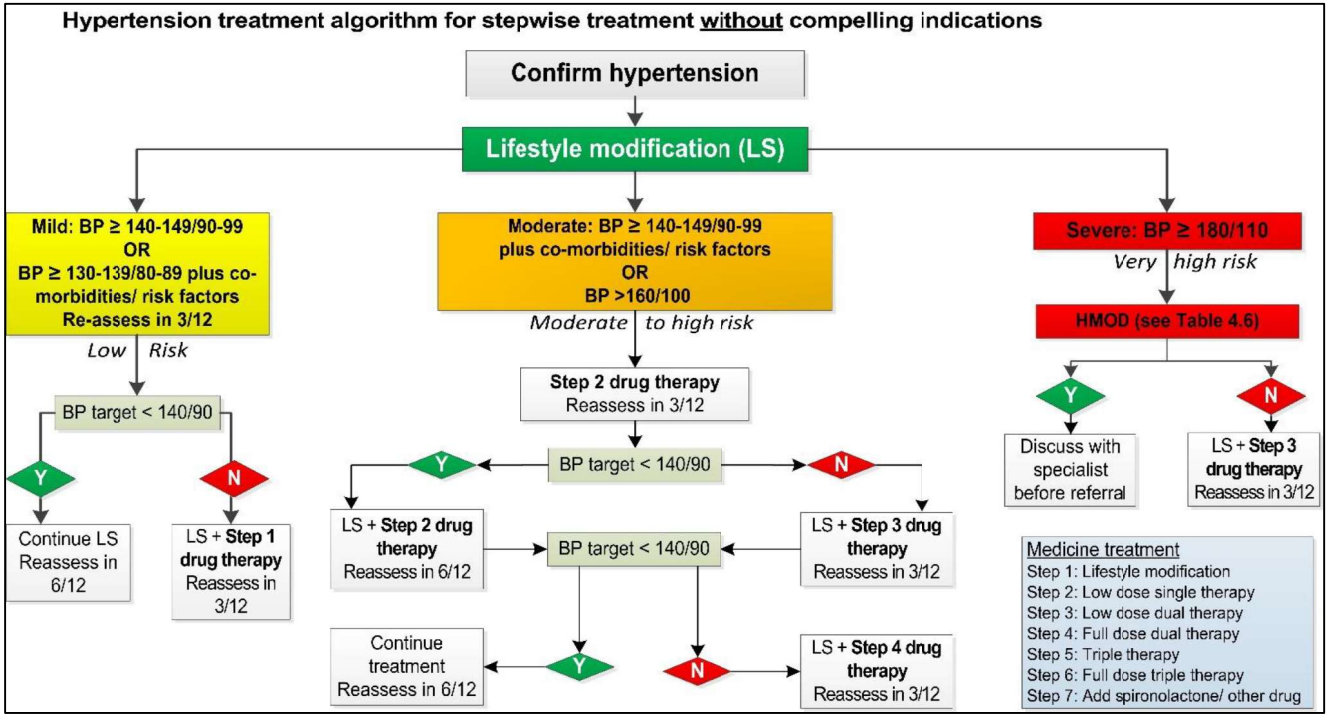
RISK ASSESSMENT OF HYPERTENSIVE PATIENTS

- » Cardiovascular risk should be assessed in all hypertensive patients based on BP levels, additional risk factors, hypertension-mediated organ damage (HMOD), and previous disease, before starting treatment. Refer to the simplified classification of hypertension risk, below.
- » **Other risk factors** include: Age (>65 years), sex (male>female), heart rate (>80 beats/min), increased body weight, diabetes, high LDL-C/triglyceride, family history of CVD, family history of hypertension, early-onset menopause, smoking habits, psychosocial or socioeconomic factors.
- » **HMOD** includes: LVH (LVH on ECG), moderate-severe CKD (eGFR <60 mL/min/1.73m^2), any other available measure of organ damage. *LoE:IIIb*[42]
- » **Previous disease includes:** previous coronary heart disease (CHD), CCF, stroke, peripheral vascular disease, atrial fibrillation, CKD stage 3+.

Other risk factors, HMOD, or disease	BP (mmHg) grading			
	High normal SBP 130-139 DBP 85-89	Mild SCP 140-159 DBP 90-99	Moderate SBP 160-179 DBP 100-109	Severe SBP≥180 Or DBP ≥110
No other risk factors	Low risk	Low risk	Moderate risk	High risk
1 or 2 risk factors	Low risk	Moderate risk	Moderate to High risk	High risk
≥ 3 risk factors	Low to Moderate risk	Moderate to High risk	High risk	High risk
HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to High risk	High risk	High risk	High to very high risk
Established CVD, CKD grade ≥4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk

Figure 4.1: Simplified classification of hypertension risk

Source: Williams B, et al. Authors/Task Force Members. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension.. J Hypertens. 2018 Oct;36(10):1953-2041.



***Caution**: Consider monotherapy in low-risk grade 1 hypertension and patients >80 years or the frail (monitor for postural hypotension).*

LoE:IIIb[43]

Figure 4.2: Algorithm for the stepwise approach of treating hypertension without compelling indications

STEPWISE TREATMENT WITHOUT COMPELLING INDICATION

STEP 1: Lifestyle modification.

Entry to Step 1	Treatment	Target
» Diastolic BP 90–99 mmHg and/or systolic BP 140–159 mmHg without any existing disease. **AND** » No major risk factors.	» Lifestyle modification.	» BP control within 3 months to <140/90 mmHg.

STEP 2: Add thiazide/thiazide-like diuretic e.g.:hydrochlorothiazide.

Entry to Step 2	Treatment	Target
» Diastolic BP 90–99 mmHg and systolic BP 140–159 mmHg without any existing disease. **AND** » No major risk factors. **AND** » Failure of lifestyle modification alone to reduce BP after 3 months. **OR** » Mild hypertension with major risk factors or existing disease. **OR** » Moderate hypertension at diagnosis.	» Lifestyle modification. **AND** ▪ **Thiazide/thiazide-like diuretic e.g.:** • Hydrochlorothiazide, oral, 12.5 mg daily. ***LoE:IIIb***[44]	» BP control within 1 month to <140/90 mmHg.

STEP 3: Add a second antihypertensive medicine.

Entry to Step 3	Treatment	Target
» Failure to achieve targets in Step 2 after 1 month despite adherence to therapy. **OR** » Severe hypertension (see table).	» Lifestyle modification. **AND** ▪ **Thiazide/thiazide-like diuretic e.g.:** • Hydrochlorothiazide, oral, 12.5 mg daily. **ADD** ▪ Long-acting calcium channel blocker, e.g.: • Amlodipine, oral, 5 mg once daily. **OR** ▪ ACE-inhibitor. e.g.: • Enalapril, oral, 10 mg once daily. *LoE:IVb*[45]	» BP control within 1 month to <140/90 mmHg.

STEP 4: Increase the dose of the second antihypertensive medicine.

Entry to Step 4	Treatment	Target
» Failure of step 3 after 1 month of adherence.	» Lifestyle modification. **AND** ▪ **Thiazide/thiazide-like diuretic e.g.:** • Hydrochlorothiazide, oral, 12.5 mg. daily. **AND** Increase dose of antihypertensive started in Step 3: ▪ Long-acting calcium channel blocker, e.g.: • Amlodipine, oral, increase to 10 mg once daily. **OR** ▪ ACE-inhibitor, e.g.: • Enalapril, oral, increase to 20 mg once daily.	» BP control within 1month to <140/90 mmHg with no adverse reactions.

STEP 5: Add a third antihypertensive medicine

Entry to Step 5	Treatment	Target
» Failure of step 4 after 1 month of adherence.	» Lifestyle modification. **AND** ▪ **Thiazide/thiazide-like diuretic e.g.:** • Hydrochlorothiazide, oral, 12.5 mg daily. **AND** ▪ ACE-inhibitor, e.g.: Enalapril, oral: continue Step 4 dose, or if not started previously start at 10 mg once daily. **AND** ▪ Long-acting calcium channel blocker, e.g.: • Amlodipine, oral: continue Step 4 dose, or if not started previously start at 5 mg once daily.	» BP control within 1 month to <140/90 mmHg with no adverse medicine reactions.

STEP 6: Increase the dose of the third antihypertensive medicine

Entry to Step 6	Treatment	Target
» Failure of step 5 after 1 month of adherence.	» Lifestyle modification **AND** ▪ **Thiazide/thiazide-like diuretic e.g.:** • Hydrochlorothiazide, oral, 12.5 mg daily **AND** ▪ ACE-inhibitor, e.g.:	» BP control within 1 month to <140/90 mmHg with no adverse medicine reactions.

	• Enalapril, oral, 20 mg once daily. **AND** ▪ Long-acting calcium channel blocker, e.g.: • Amlodipine, oral, 10 mg once daily.	

STEP 7: Increase the dose of HCTZ and add a fourth antihypertensive medicine

Entry to Step 7	Treatment	Target
» Failure of step 7 after 1 month of adherence.	» Lifestyle modification. **AND** ▪ **Thiazide/thiazide-like diuretic e.g.:** • Hydrochlorothiazide, oral, 25 mg daily. **AND** ▪ ACE-inhibitor, e.g.: • Enalapril, 20 mg once daily **AND** ▪ Long-acting calcium channel blocker, e.g.: • Amlodipine, oral 10 mg once daily. *LoE:Ia*[46] **AND ADD** • Spironolactone, oral, 25 mg daily (doctor initiated).	» BP control within 1 month to <140/90 mmHg, with no adverse medicine reactions.

Table 4.4: Stepwise approach of treating hypertension without compelling indications

CAUTION

Spironolactone can cause severe hyperkalaemia and should only be used when serum potassium and renal function can be monitored. Check potassium levels within one month of starting therapy and thereafter, as per clinical need. Routine monitoring of potassium levels is essential if spironolactone is used with an ACE-inhibitor, other potassium sparing agents or in the elderly.
Do not use together with potassium supplements.
Avoid NSAIDs with spironolactone use.
Do not use in kidney failure (Do not use if eGFR <30 mL/min).

LoE:IVb[47]

If not controlled on step 7**–** refer.

Note:

» If lifestyle modification failed to achieve BP control: Counsel patient on the risk of major cardiovascular events associated with elevated BP; and initiate monotherapy. *LoE:IIIb*[48]

» If BP control is suboptimal: Up titrate treatment (maximise dose of current antihypertensive and/or add additional medicine). Evidence suggests that treatment inertia contributes to suboptimal BP control with patients remaining on monotherapy and/or suboptimal doses.

» Initiate combination medicine therapy in cases of severe hypertension and hypertension urgency (see Section 4.7.2: Hypertensive emergency).

TREATMENT OF HYPERTENSION WITH COMPELLING INDICATIONS

Compelling indications for specific medicines	Medicine therapeutic class
Angina	• Beta-blocker **OR** • Long-acting calcium channel blocker
Prior myocardial infarction	• Beta-blocker **AND** • ACE-inhibitor
Heart failure	• ACE-inhibitor **AND** • Carvedilol, oral **OR** • Spironolactone, oral For significant volume overload: • Loop diuretic
Left ventricular hypertrophy (confirmed by ECG)	• ACE-inhibitor
Stroke: secondary prevention	• Hydrochlorothiazide, oral **AND** • ACE-inhibitor
Diabetes type 1 and 2 with/without evidence of microalbuminuria/proteinuria	• ACE-inhibitor, usually in combination with diuretic
Chronic kidney disease	• ACE-inhibitor, usually in combination with diuretic
Isolated systolic hypertension	• Hydrochlorothiazide, oral **OR** • Long-acting calcium channel blocker
Pregnancy	• Methyldopa, oral

Table 4.5: Treatment of hypertension with compelling indications

Contraindications to individual medicines

Hydrochlorothiazide *LoE:IIIb*[49]

» gout,
» pregnancy,
» severe liver impairment,
» kidney impairment (eGFR <30 mL/min),
» use with caution in patients with a history or family history of skin cancer, and counsel all patients on sun avoidance and sun protection.

Calcium channel blockers

» untreated heart failure.

Spironolactone

» kidney impairment (eGFR <30 mL/min), *LoE:IVb*[50]
» pregnancy.

ACE-inhibitors

» pregnancy,

» bilateral renal artery stenosis or stenosis of an artery to a dominant/single kidney,
» aortic valve stenosis,
» history of angioedema,
» hyperkalaemia, *LoE:IVb*[51]
» severe renal impairment (eGFR <30 mL/min), unless dose-adjusted usage is recommended by a specialist – See Section 8.1: Chronic kidney disease (CKD).

CAUTION
Advise all patients receiving ACE-inhibitors about the symptoms of ACE-induced angioedema.

REFERRAL
» Young adults (<30 years of age).
» BP not controlled by 4 medicines and where there is no doctor available.
» Pregnancy.
» Signs of hypertension-mediated organ damage e.g. oedema, dyspnoea, proteinuria, angina, etc.
» If severe adverse drug reactions develop.
» Hypertensive urgency and hypertensive emergency.
» Severe renal impairment (eGFR <30 mL/min).

4.7.2 HYPERTENSIVE EMERGENCY
I10

DESCRIPTION
A markedly elevated BP: systolic BP >180 mmHg and/or a diastolic BP >130 mmHg **associated with** one or more of the following:
» unstable angina/chest pain,
» neurological signs, e.g. severe headache, visual disturbances, confusion, coma or seizures,
» pulmonary oedema,
» renal failure.

MEDICINE TREATMENT
- Amlodipine, oral, 10 mg immediately as a single dose.

<u>If pulmonary oedema:</u>
- Furosemide, IV, 40 mg as a single dose (see Section 21.2.8: Pulmonary oedema, acute).

CAUTION
A hypertensive emergency is life threatening and needs immediate referral to hospital.

REFERRAL
Urgent
All patients.

4.7.3 HYPERTENSION IN CHILDREN

I10

DESCRIPTION

Hypertension is defined as systolic and/or diastolic blood pressure ≥ the 95th percentile for gender, age, and height percentile on at least 3 consecutive occasions. Refer to table below.

The use of appropriate cuff size is important. Too small a cuff for the arm leads to false high BP. The cuff bladder must encircle at least 80% of the upper arm and should cover at least 75% of the distance between the acromion and the olecranon. It is better to use a cuff that is slightly too large than one that is too small. Large cuffs, if covered with linen-like material, can be folded to the appropriate size in smaller infants as long as the bladder encompasses the arm.

Infants and preschool-aged children are almost never diagnosed with essential hypertension and are most likely to have secondary forms of hypertension.

With age, the prevalence of essential hypertension increases, and after 10 years of age, it becomes the leading cause of elevated BP. Obesity currently is emerging as a common comorbidity of essential hypertension in paediatric patients, often manifesting during early childhood.

DIAGNOSIS

Age years	**95th BP percentiles for boys mmHg**	**95th BP percentiles for girls** mmHg
1	103/56	104/58
3	109/65	107/67
5	112/72	110/72
6	114/74	111/74
8	116/78	115/76
9	118/79	117/77
10	119/80	119/78
11	121/80	121/79
12	123/81	123/80

Table 4.6: Diagnosis of high blood pressure in children and adolescents

Adapted from U.S Department of Health and Human Services National Institutes of Health (National Heart, Lung, and Blood Institute): The 4th report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents, May 2005 (using the 50th height percentile).

REFERRAL

All cases with BP above the 95th percentile.

4.8 PULMONARY OEDEMA, ACUTE

See Section 21.2.8: Pulmonary oedema, acute.

4.9 RHEUMATIC FEVER, ACUTE

I00/I01.0-2/I01.8-9

Note: notifiable condition.

DESCRIPTION

A condition in which the body develops antibodies against its own tissues, following a streptococcal throat infection. Effective treatment and prevention of recurrent of streptococcal pharyngitis can markedly reduce the occurrence and repeat episodes of rheumatic carditis.

Commonly occurs in children, 3 to 15 years of age.

Recurrences are frequent.

Clinical signs and symptoms include:

- » arthralgia or arthritis that may shift from one joint to another,
- » carditis, including cardiac failure,
- » heart murmurs,
- » subcutaneous nodules,
- » erythema marginatum,
- » chorea (involuntary movements of limbs or face),
- » other complaints indicating a systemic illness e.g. fever.

MEDICINE TREATMENT

Eradication of streptococci in throat:

Children: 18 months–11 years of age

- Phenoxymethylpenicillin, oral, 250 mg 12 hourly for 10 days. A

Children >11 years of age and adults

- Phenoxymethylpenicillin, oral, 500 mg 12 hourly for 10 days. A

OR

Children

- Amoxicillin, oral, 50 mg/kg daily for 10 days. A

Weight kg	Dose mg	Use one of the following				Age Months/years
		Susp		Capsule		
		125 mg/5mL	250 mg/5mL	250 mg	500 mg	
>2–2.5 kg	100 mg	4 mL	2 mL	–	–	>34–36 weeks
>2.5–3.5 kg	150 mg	6 mL	3 mL	–	–	>36 weeks–1 month
>3.5–5 kg	200 mg	8 mL	4 mL	–	–	>1–3 months
>5–7 kg	275 mg	11 mL	5.5 mL	–	–	>3–6 months
>7–11 kg	400 mg	–	8 mL	–	–	>6–18 months
>11–17.5 kg	575 mg	–	11.5 mL	–	–	>18 months–5 years
>17.5–25 kg	750 mg	–	15 mL	3	–	>5–7 years
>25–35 kg	1000 mg	–	20 mL	4	2	>7–11 years
>35 kg	2000 mg	–	–		4	>11years

LoE:IIb[52]

Adults

- Benzathine benzylpenicillin, IM, single dose. A
  - Children <30 kg: 600 000 IU.
  - Children ≥ 30 kg and adults: 1.2 MU.
  - Dissolve benzathine benzylpenicillin 1.2 MU in 3.2 mL lidocaine 1% without adrenaline (epinephrine) or 3 mL water for injection.

LoE:IIIb[53]

OR

- Amoxicillin, oral, 1 000 mg 12 hourly for 10 days. A

LoE:IIb[54]

Severe penicillin allergy:
Z88.0

Children

- Macrolide, e.g.:
- Azithromycin, oral, 10 mg/kg daily for 3 days. W See dosing table: Chapter 23.

Children >35 kg and adults

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days. W

Prophylaxis for rheumatic fever: (Z29.2)

All patients with confirmed rheumatic fever and no persistent rheumatic valvular disease

» Treat for 10 years or until the age of 21 years, whichever is longer.

All patients with confirmed rheumatic fever and persistent rheumatic valvular disease

» Treat lifelong.

- Phenoxymethylpenicillin, oral, 12 hourly. A
  - Children: 125 mg
  - Adults: 250 mg

OR

- Amoxicillin, oral, daily. A
  - Children <30 kg: 125 mg
  - Children ≥30 kg and adults: 250 mg

LoE:IVb

OR

- Benzathine benzylpenicillin, IM, every 21 to 28 days (i.e., 3 to 4 weeks). A
  - Children <30 kg: 600 000 IU
  - Children ≥ 30 kg and adults: 1.2 MU
  - For benzathine benzylpenicillin, IM injection, dissolve benzathine benzylpenicillin 1.2 MU in 3.2 mL lidocaine 1% without adrenaline (epinephrine) or 3 mL water for injection.

Note: For guidance on warfarin management, see Adult Hospital Level STGs and EML, Appendix II: Prescribing information for specific medicines.

CAUTION
Avoid IM injections if patients are on warfarin.

Severe penicillin allergy:
Z88.0

Children <11 years
- Macrolide, e.g.:
- Azithromycin, oral, 10mg/kg/day, 3 times weekly. W See dosing table: Chapter 23.

LoE:IVb[55]

Children ≥ 11 years and adults
- Macrolide, e.g.:
- Azithromycin, oral, 250 mg daily. W

LoE:IVb[56]

REFERRAL
All patients for diagnosis and management.

4.10 VALVULAR HEART DISEASE AND CONGENITAL STRUCTURAL HEART DISEASE
I05.0-2/I05.8-9/I06.0-2/I06.8-9/I07.0-2/I07.8-9/I08.0-3/I08.8-9/I34.0-2/I34.8-9/I35.0-2/I35.8-9/I36.0-2/I36.8-9/I37.0-2/I37.8-9/Q22.0-6/Q22.8-9/Q23.0-4/Q23.8-9

DESCRIPTION
Damage to heart valves or chamber, or vessel wall anomalies caused by rheumatic fever or other causes, e.g. congenital heart defects, degenerative disease and ischaemic heart disease.
May be complicated by:
- » heart failure
- » infective endocarditis
- » pulmonary hypertension
- » atrial fibrillation
- » systemic embolism

GENERAL MEASURES
- » Advise all patients with a heart murmur regarding the need for prophylactic treatment prior to undergoing certain medical and dental procedures.
- » Advise patients to inform health care providers of the presence of the heart murmur when reporting for medical or dental treatment.

MEDICINE TREATMENT
Prophylactic antibiotic treatment for infective endocarditis:
- » Should be given prior to certain invasive diagnostic and therapeutic procedures e.g. tooth extraction, to prevent infective endocarditis.
- » Is essential for all children with congenital or rheumatic heart lesions needing dental extraction.

Dental extraction, if no anaesthetic is required:
Z29.2

- Amoxicillin, oral, 50 mg/kg (maximum dose: 2 g), 1 hour before the procedure. A
  - Repeat dose 6 hours later.

Age	Dose
<5 years	750 mg
5 to 10 years	1 500 mg
≥ 10 years	2 g

Severe penicillin allergy:
Z88.0
Refer.

If anaesthetic is required:
Refer.

Prophylaxis for rheumatic fever:
See Section 4.9: Rheumatic fever, acute.

REFERRAL

» All patients with pathological heart murmurs for assessment.
» All patients with heart murmurs not on a chronic management plan.
» Development of cardiac signs and symptoms.
» Worsening of clinical signs and symptoms of heart disease.
» Any newly developing medical condition, e.g. persistent fever.
» All patients with valvular heart disease for advice on prophylactic antibiotic treatment prior to any invasive diagnostic or therapeutic procedure.

References

[1] Risk factors for prevention of ischaemic heart disease and atherosclerosis (diabetes): de Vries FM, Kolthof J, Postma MJ, Denig P, Hak E. Efficacy of standard and intensive statin treatment for the secondary prevention of cardiovascular and cerebrovascular events in diabetes patients: a meta-analysis. PLoS One. 2014 Nov 5;9(11):e111247. http://www.ncbi.nlm.nih.gov/pubmed/25372483

[2] Risk factors for prevention of ischaemic heart disease and atherosclerosis (psychological stress):Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004 Sep 11-17;364(9438):937-52. http://www.ncbi.nlm.nih.gov/pubmed/15364185

[3] Ideal BMI: McGee DL. McGee DL; Diverse Populations Collaboration. Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. Ann Epidemiol. 2005 Feb;15(2):87-97. https://pubmed.ncbi.nlm.nih.gov/15652713/

Ideal BMI: National Heart, Lung, and Blood Institute in cooperation with The National Institute of Diabetes and Digestive and Kidney Diseases. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, September 1998. Report No.: 98-4083. https://www.ncbi.nlm.nih.gov/books/NBK2003/

[4] Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

[5] Statins (secondary prevention of ischaemic events – patients on protease inhibitors):

Ansari R, Khalili H, Mohammadi K. Optimizing statin therapy in HIV-infected patients: a review of pharmacotherapy considerations. BMC Cardiovasc Disord. 2025 May 31;25(1):421. doi: 10.1186/s12872-025-04887-2. PMID: 40450213; PMCID: PMC12125728.

Chastain DB, Stover KR, Riche DM. Evidence-based review of statin use in patients with HIV on antiretroviral therapy. J Clin Transl Endocrinol. 2017 Feb 22;8:6-14. https://www.ncbi.nlm.nih.gov/pubmed/29067253

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Atorvastatin, oral (drug-drug interaction with protease inhibitors): University of Liverpool. HIV drug interaction database. https://www.hiv-druginteractions.org/

[6] High dose statins (management of adverse drug reactions): NICE: Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline, 18 July 2014. www.nice.org.uk/guidance/cg181

[7] Statins (pregnancy and lactation) Kay HY, Jang HY, Kim IW, Oh JM. Pregnancy and neonatal outcomes after fetal exposure to statins among women with dyslipidemia: a nationwide cohort. Eur J Pediatr. 2025 May 14;184(6):340. doi: 10.1007/s00431-025-06119-3. PMID: 40366447; PMCID: PMC12078441.

Christensen JJ, Holven KB, Bogsrud MP, Retterstøl K, Roeters van Lennep JE, Michelsen TM, Veierød MB, Nordeng H. Statin use in pregnancy and risk of congenital malformations: a Norwegian nationwide study. Eur Heart J. 2026 Jan 16;47(3):318-327. doi: 10.1093/eurheartj/ehaf592. PMID: 40838827; PMCID: PMC12807567.

Holven KB, Raal FJ, Watts GF, Christensen JJ, Roeters van Lennep J. Challenges in the care of women with familial hypercholesterolaemia during the reproductive period - current evidence and practical guidance. Atherosclerosis. 2026 Apr;415:120679. doi: 10.1016/j.atherosclerosis.2026.120679. Epub 2026 Feb 11. PMID: 41713387.

[8] Aspirin, oral (stable angina): Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients.BMJ. 2002 Jan 12;324(7329):71-86. Erratum in: BMJ 2002 Jan 19;324(7330):141. https://www.ncbi.nlm.nih.gov/pubmed/11786451

[9] Nitrates, short acting: National Department of Health: Essential Drugs Programme. Adult Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Isosorbide dinitrate, sublingual (dosing): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[10] Isosorbide mononitrate, oral: National Department of Health: Essential Drugs Programme. Adult Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Isosorbide mononitrate, oral: Thadani U, Lipicky RJ. Short and long-acting oral nitrates for stable angina pectoris. Cardiovasc Drugs Ther. 1994 Aug;8(4):611-23. https://www.ncbi.nlm.nih.gov/pubmed/7848896

Isosorbide mononitrate, oral: Parker JO. Eccentric dosing with isosorbide-5-mononitrate in angina pectoris. Am J Cardiol. 1993 Oct 15;72(12):871-6. https://www.ncbi.nlm.nih.gov/pubmed/8213541

Isosorbide mononitrate, oral: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[11] Organic nitrates (Isosorbide mononitrate and dinitrate, oral): Thadani U, Lipicky RJ. Short and long-acting oral nitrates for stable angina pectoris.Cardiovasc Drugs Ther. 1994 Aug;8(4):611-23. https://www.ncbi.nlm.nih.gov/pubmed/7848896

Organic nitrates (Isosorbide mononitrate and dinitrate, oral): Parker JO. Eccentric dosing with isosorbide-5-mononitrate in angina pectoris.Am J Cardiol. 1993 Oct 15;72(12):871-6. https://www.ncbi.nlm.nih.gov/pubmed/8213541

[12] Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

[13] Statins, oral (secondary prevention of ischaemic events – patients on protease inhibitors):

Ansari R, Khalili H, Mohammadi K. Optimizing statin therapy in HIV-infected patients: a review of pharmacotherapy considerations. BMC Cardiovasc Disord. 2025 May 31;25(1):421. doi: 10.1186/s12872-025-04887-2. PMID: 40450213; PMCID: PMC12125728.

Chastain DB, Stover KR, Riche DM. Evidence-based review of statin use in patients with HIV on antiretroviral therapy. J Clin Transl Endocrinol. 2017 Feb 22;8:6-14. https://www.ncbi.nlm.nih.gov/pubmed/29067253

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

Atorvastatin, oral (drug-drug interaction with protease inhibitors): University of Liverpool. HIV drug interaction database. https://www.hiv-druginteractions.org/

[14] High dose statins (management of adverse drug reactions): NICE: Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline, 18 July 2014. www.nice.org.uk/guidance/cg181

[15] Aspirin, oral (NSTEMI): Peters RJ, Mehta SR, Fox KA, Zhao F, Lewis BS, Kopecky SL, Diaz R, Commerford PJ, Valentin V, Yusuf S; Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Trial Investigators. Effects of aspirin dose when used alone or in combination with clopidogrel in patients with acute coronary syndromes: observations from the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) study. Circulation. 2003 Oct 7;108(14):1682-7. https://www.ncbi.nlm.nih.gov/pubmed/14504182

[16] Oxygen (medically ill patients): National Department of Health. Affordable Medicines, EDP-Primary Healthcare and Adult Hospital Level. Evidence summary – oxygen therapy in acutely ill patients, 9 September 2021. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Oxygen (medically ill patients): Chu DK, Kim LH, Young PJ, Zamiri N, Almenawer SA, Jaeschke R, Szczeklik W, Schünemann HJ, Neary JD, Alhazzani W. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. Lancet. 2018 Apr 28;391(10131):1693-1705. https://www.ncbi.nlm.nih.gov/pubmed/29726345

Oxygen (medically ill patients): Siemieniuk RAC, Chu DK, Kim LH, Güell-Rous MR, Alhazzani W, Soccal PM, et al. Oxygen therapy for acutely ill medical patients: a clinical practice guideline. BMJ. 2018 Oct 24;363:k4169. https://pubmed.ncbi.nlm.nih.gov/30355567/

Oxygen (medically ill patients): Alves M, Prada L, Costa J, Ferreira JJ, Pinto FJ, Caldeira D. Effect of oxygen supply on mortality in acute ST-elevation myocardial infarction: systematic review and meta-analysis. Eur J Emerg Med. 2021 Jan 1;28(1):11-18. https://pubmed.ncbi.nlm.nih.gov/33079738/

[17] Nitrates, short acting: National Department of Health: Essential Drugs Programme. Adult Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Isosorbide dinitrate, sublingual (dosing): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[18] Aspirin, oral (NSTEMI): Peters RJ, Mehta SR, Fox KA, Zhao F, Lewis BS, Kopecky SL, Diaz R, Commerford PJ, Valentin V, Yusuf S; Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Trial Investigators. Effects of aspirin dose when used alone or in combination with clopidogrel in patients with acute coronary syndromes: observations from the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) study. Circulation. 2003 Oct 7;108(14):1682-7. https://www.ncbi.nlm.nih.gov/pubmed/14504182

[19] Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

[20] Statins, oral (secondary prevention of ischaemic events – patients on protease inhibitors):

Ansari R, Khalili H, Mohammadi K. Optimizing statin therapy in HIV-infected patients: a review of pharmacotherapy considerations. BMC Cardiovasc Disord. 2025 May 31;25(1):421. doi: 10.1186/s12872-025-04887-2. PMID: 40450213; PMCID: PMC12125728.

Chastain DB, Stover KR, Riche DM. Evidence-based review of statin use in patients with HIV on antiretroviral therapy. J Clin Transl Endocrinol. 2017 Feb 22;8:6-14. https://www.ncbi.nlm.nih.gov/pubmed/29067253

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Atorvastatin, oral (drug-drug interaction with protease inhibitors): University of Liverpool. HIV drug interaction database. https://www.hiv-druginteractions.org/

[21] High dose statins (management of adverse drug reactions): NICE: Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline, 18 July 2014. www.nice.org.uk/guidance/cg181

[22] Enalapril (cardiac failure/ LV dysfunction): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[23] Oxygen (medically ill patients): National Department of Health. Affordable Medicines, EDP-Primary Healthcare and Adult Hospital Level. Evidence summary – oxygen therapy in acutely ill patients, 9 September 2021. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Oxygen (medically ill patients): Chu DK, Kim LH, Young PJ, Zamiri N, Almenawer SA, Jaeschke R, Szczeklik W, Schünemann HJ, Neary JD, Alhazzani W. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. Lancet. 2018 Apr 28;391(10131):1693-1705. https://www.ncbi.nlm.nih.gov/pubmed/29726345

Oxygen (medically ill patients): Siemieniuk RAC, Chu DK, Kim LH, Güell-Rous MR, Alhazzani W, Soccal PM, et al. Oxygen therapy for acutely ill medical patients: a clinical practice guideline. BMJ. 2018 Oct 24;363:k4169. https://pubmed.ncbi.nlm.nih.gov/30355567/

Oxygen (medically ill patients): Alves M, Prada L, Costa J, Ferreira JJ, Pinto FJ, Caldeira D. Effect of oxygen supply on mortality in acute ST-elevation myocardial infarction: systematic review and meta-analysis. Eur J Emerg Med. 2021 Jan 1;28(1):11-18. https://pubmed.ncbi.nlm.nih.gov/33079738/

[24] Aspirin, oral (STEMI): Berger JS, Stebbins A, Granger CB, Ohman EM, Armstrong PW, Van de Werf F, White HD, Simes RJ, Harrington RA, Califf RM, Peterson ED. Initial aspirin dose and outcome among ST-elevation myocardial infarction patients treated with fibrinolytic therapy. Circulation. 2008 Jan 15;117(2):192-9. https://www.ncbi.nlm.nih.gov/pubmed/18086929

Aspirin, oral (STEMI): CURRENT-OASIS 7 Investigators, Mehta SR, Bassand JP, Chrolavicius S, Diaz R, Eikelboom JW, Fox KA, Granger CB, Jolly S, Joyner CD, Rupprecht HJ, Widimsky P, Afzal R, Pogue J, Yusuf S. Dose comparisons of clopidogrel and aspirin in acute coronary syndromes. N Engl J Med. 2010 Sep 2;363(10):930-42. https://www.ncbi.nlm.nih.gov/pubmed/20818903

[25] Nitrates, short acting: National Department of Health: Essential Drugs Programme. Adult Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Isosorbide dinitrate, sublingual (dosing): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[26] Thrombolytics (Therapeutic class): Dundar Y, Hill R, Dickson R, Walley T. Comparative efficacy of thrombolytics in acute myocardial infarction: A systematic review. QJM - Monthly Journal of the Association of Physicians. 2003;96(2):103-13. http://www.ncbi.nlm.nih.gov/pubmed/12589008

Thrombolytics (Therapeutic class): National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Thrombolytics, therapeutic class for STEMI, July 2015. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[27] Do not use heparin if streptokinase is given: Jinatongthai P, Kongwatcharapong J, Foo CY, Phrommintikul A, Nathisuwan S, Thakkinstian A, Reid CM, Chaiyakunapruk N. Comparative efficacy and safety of reperfusion therapy with fibrinolytic agents in patients with ST-segment elevation myocardial infarction: a systematic review and network meta-analysis. Lancet. 2017 Aug 19;390(10096):747-759. https://www.ncbi.nlm.nih.gov/pubmed/28831992

Do not use heparin if streptokinase is given: Eikelboom JW, Quinlan DJ, Mehta SR, Turpie AG, Menown IB, Yusuf S. Unfractionated and low-molecular-weight heparin as adjuncts to thrombolysis in aspirin-treated patients with ST-elevation acute myocardial infarction: a meta-analysis of the randomized trials. Circulation. 2005 Dec 20;112(25):3855-67. https://www.ncbi.nlm.nih.gov/pubmed/16344381

[28] Streptokinase: Squire IB, Lawley W, Fletcher S, Holme E, Hillis WS, Hewitt C, Woods KL. Humoral and cellular immune responses up to 7.5 years after administration of streptokinase for acute myocardial infarction.Eur Heart J. 1999 Sep;20(17):1245-52. http://www.ncbi.nlm.nih.gov/pubmed/10454976

Streptokinase: Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet. 1996 Sep 21;348(9030):771-5. http://www.ncbi.nlm.nih.gov/pubmed/8813982

[29] Aspirin, oral (stable angina): Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients.BMJ. 2002 Jan 12;324(7329):71-86. Erratum in: BMJ 2002 Jan 19;324(7330):141. https://www.ncbi.nlm.nih.gov/pubmed/11786451

[30] Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Rosuvastatin 10mg, oral (secondary prevention of ischaemic events): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

[31] Statins, oral (secondary prevention of ischaemic events – patients on protease inhibitors):

Ansari R, Khalili H, Mohammadi K. Optimizing statin therapy in HIV-infected patients: a review of pharmacotherapy considerations. BMC Cardiovasc Disord. 2025 May 31;25(1):421. doi: 10.1186/s12872-025-04887-2. PMID: 40450213; PMCID: PMC12125728.

Chastain DB, Stover KR, Riche DM. Evidence-based review of statin use in patients with HIV on antiretroviral therapy. J Clin Transl Endocrinol. 2017 Feb 22;8:6-14. https://www.ncbi.nlm.nih.gov/pubmed/29067253

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Atorvastatin, oral (drug-drug interaction with protease inhibitors): University of Liverpool. HIV drug interaction database. https://www.hiv-druginteractions.org/

[32] High dose statins (management of adverse drug reactions): NICE: Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline, 18 July 2014. www.nice.org.uk/guidance/cg181

[33] Hydrochlorothiazide, oral (mild CCF): Faris R, Flather M, Purcell H, Henein M, Poole-Wilson P, Coats A. Current evidence supporting the role of diuretics in heart failure: a meta analysis of randomised controlled trials. Int J Cardiol. 2002 Feb;82(2):149-58. https://pubmed.ncbi.nlm.nih.gov/11853901/

Hydrochlorothiazide, oral (mild CCF): McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726. https://pubmed.ncbi.nlm.nih.gov/34447992/

Hydrochlorothiazide, oral (mild CCF): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

Hydrochlorothiazide, oral (skin cancer risk): Pedersen SA, Gaist D, Schmidt SAJ, Hölmich LR, Friis S, Pottegård A. Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark. J Am Acad Dermatol. 2018 Apr;78(4):673-681.e9. https://www.ncbi.nlm.nih.gov/pubmed/29217346

Hydrochlorothiazide, oral (skin cancer risk): Pottegård A, Hallas J, Olesen M, Svendsen MT, Habel LA, Friedman GD, Friis S. Hydrochlorothiazide use is strongly associated with risk of lip cancer. J Intern Med. 2017 Oct;282(4):322-331. https://www.ncbi.nlm.nih.gov/pubmed/28480532

Hydrochlorothiazide, oral (skin cancer risk): National Department of Health, Essential Drugs Programme: Updated Notice: Risk of skin cancer associated with hydrochlorothiazide, 6 March 2019. https://www.knowledgehub.org.za/

[34] Enalapril (cardiac failure/ LV dysfunction): South African Medicines Formulary. 14th Edition. Division of Clinical Pharmacology. University of Cape Town. 2022.

[35] Step 2 of CCF protocol: McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726. https://pubmed.ncbi.nlm.nih.gov/34447992/

[36] Carvedilol (dosing if >85 kg): McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726. https://pubmed.ncbi.nlm.nih.gov/34447992/

[37] Spironolactone: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[38] Target BP for primary hypertension: Black A, Parrish AG, Rayner B, Leong TD, Mpongoshe V. Target blood pressure: a South African perspective. Cardiovasc J Afr. 2019 Mar/Apr;30(2):71-73. https://pubmed.ncbi.nlm.nih.gov/31155633/

Target BP for primary hypertension: Brunström M, Carlberg B. Association of Blood Pressure Lowering With Mortality and Cardiovascular Disease Across Blood Pressure Levels: A Systematic Review and Meta-analysis. JAMA Intern Med. 2018 Jan 1;178(1):28-36. https://pubmed.ncbi.nlm.nih.gov/29131895/

[39] Ideal BMI: McGee DL. McGee DL; Diverse Populations Collaboration. Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. Ann Epidemiol. 2005 Feb;15(2):87-97. https://pubmed.ncbi.nlm.nih.gov/15652713/

Ideal BMI: National Heart, Lung, and Blood Institute in cooperation with The National Institute of Diabetes and Digestive and Kidney Diseases. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, September 1998. Report No.: 98-4083. https://www.ncbi.nlm.nih.gov/books/NBK2003/

[40] Lifestyle modification - hypertension: National Department of Health: Essential Drugs Programme. Adult Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

Lifestyle modification – hypertension (exercise): Costa EC, Hay JL, Kehler DS, Boreskie KF, Arora RC, Umpierre D, Szwajcer A, Duhamel TA. Effects of High-Intensity Interval Training Versus Moderate-Intensity Continuous Training On Blood Pressure in Adults with Pre- to Established Hypertension: A Systematic Review and Meta-Analysis of Randomized Trials. Sports Med. 2018 Sep;48(9):2127-2142. https://pubmed.ncbi.nlm.nih.gov/29949110/

Lifestyle modification – hypertension (exercise): Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. J Hypertens. 2020 Jun;38(6):982-1004. https://pubmed.ncbi.nlm.nih.gov/32371787/

[41] Antihypertensives – fixed dose combinations: Gupta P, Patel P, Štrauch B, Lai FY, Akbarov A, Marešová V, White CMJ, Petrák O, Gulsin GS, Patel V, Rosa J, Cole R, Zelinka T, Holaj R, Kinnell A, Smith PR, Thompson JR, Squire I, Widimský J Jr, Samani NJ, Williams B, Tomaszewski M. Risk Factors for Nonadherence to Antihypertensive Treatment. Hypertension. 2017 Jun;69(6):1113-1120. https://www.ncbi.nlm.nih.gov/pubmed/28461599

[42] Risk assessment for hypertension: Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. J Hypertens. 2020 Jun;38(6):982-1004. https://pubmed.ncbi.nlm.nih.gov/32371787/

[43] Algorithm for the stepwise treatment of hypertension without compelling indications: Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. J Hypertens. 2020 Jun;38(6):982-1004. https://pubmed.ncbi.nlm.nih.gov/32371787/

[44] Hydrochlorothiazide, oral (1st line treatment - hypertension without compelling indications): National Department of Health: Affordable Medicines, EDP- PHC/Adult Hospital level. Medicine Review: Indapamide, oral as 1st line treatment - hypertension without compelling indications, July 2021. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[45] Enalapril, oral (daily dosing): Girvin B, McDermott BJ, Johnston GD. A comparison of enalapril 20 mg once daily versus 10 mg twice daily in terms of blood pressure lowering and patient compliance. J Hypertens. 1999 Nov;17(11):1627-31. https://www.ncbi.nlm.nih.gov/pubmed/10608477

Enalapril, oral (daily dosing): Davies RO, Gomez HJ, Irvin JD, Walker JF. An overview of the clinical pharmacology of enalapril. Br J Clin Pharmacol. 1984;18 Suppl 2:215S-229S. https://www.ncbi.nlm.nih.gov/pubmed/6099737

[46] Spironolactone (hypertension):Williams B, MacDonald TM, Morant S, Webb DJ, Sever P, McInnes G, Ford I, Cruickshank JK, Caulfield MJ, Salsbury J, Mackenzie I, Padmanabhan S, Brown MJ; British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet. 2015 Nov 21;386(10008):2059-68. http://www.ncbi.nlm.nih.gov/pubmed/26414968

[47] Spironolactone: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[48] Suboptimal BP control – treatment inertia: Tiffe T, Wagner M, Rucker V, Morbach C, Gelbrich G, Stork S, Heuschmann PU. Control of cardiovascular risk factors and its determinants in the general population- findings from the STAAB cohort study. BMC Cardiovasc Disord 2017;17:276. https://www.ncbi.nlm.nih.gov/pubmed/29096615

Suboptimal BP control – treatment inertia: Berry KM, Parker WA, Mchiza ZJ, Sewpaul R, Labadarios D, Rosen S, Stokes A. Quantifying unmet need for hypertension care in South Africa through a care cascade: evidence from the SANHANES, 2011-2012. BMJ Glob Health. 2017 Aug 16;2(3):e000348. https://www.ncbi.nlm.nih.gov/pubmed/29082013

[49] Hydrochlorothiazide, oral (skin cancer risk): Pedersen SA, Gaist D, Schmidt SAJ, Hölmich LR, Friis S, Pottegård A. Hydrochlorothiazide use and risk of nonmelanoma skin cancer: A nationwide case-control study from Denmark. J Am Acad Dermatol. 2018 Apr;78(4):673-681.e9. https://www.ncbi.nlm.nih.gov/pubmed/29217346

Hydrochlorothiazide, oral (skin cancer risk): Pottegård A, Hallas J, Olesen M, Svendsen MT, Habel LA, Friedman GD, Friis S. Hydrochlorothiazide use is strongly associated with risk of lip cancer. J Intern Med. 2017 Oct;282(4):322-331. https://www.ncbi.nlm.nih.gov/pubmed/28480532

Hydrochlorothiazide, oral (skin cancer risk): National Department of Health, Essential Drugs Programme: Updated Notice: Risk of skin cancer associated with hydrochlorothiazide, 6 March 2019. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[50] Spironolactone, oral (contra-indications): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[51] ACE-inhibitor (contra-indications – severe renal impairment): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

ACE-inhibitor (contra-indications – severe renal impairment): National Department of Health: Essential Drugs Programme. Adult Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[52] Amoxicillin, oral (children): Clegg HW, Ryan AG, Dallas SD, Kaplan EL, Johnson DR, Norton HJ, Roddey OF, Martin ES, Swetenburg RL, Koonce EW, Felkner MM, Giftos PM. Treatment of streptococcal pharyngitis with once-daily compared with twice-daily amoxicillin: a noninferiority trial. Pediatr Infect Dis J. 2006 Sep;25(9):761-7. https://www.ncbi.nlm.nih.gov/pubmed/16940830

Amoxicillin, oral (children): Lennon DR, Farrell E, Martin DR, Stewart JM. Once-daily amoxicillin versus twice-daily penicillin V in group A beta-haemolytic streptococcal pharyngitis. Arch Dis Child. 2008 Jun;93(6):474-8. https://www.ncbi.nlm.nih.gov/pubmed/18337284

[53]Lidocaine 1%: Amir J, Ginat S, Cohen YH, Marcus TE, Keller N, Varsano I. Lidocaine as a diluent for administration of benzathine penicillin G. Pediatr Infect Dis J. 1998 Oct;17(10):890-3. http://www.ncbi.nlm.nih.gov/pubmed/9802630

[54] Amoxicillin, oral (adults): Brink AJ, Cotton M, Feldman C, Finlayson H, Friedman R, Green R, Hendson W, Hockman M, Maartens G, Madhi S, Reubenson G, Silverbauer E, Zietsman I. Updated recommendations for the management of upper respiratory tract infections in South Africa. S Afr Med J. 2015 Apr 6;105(5):344-52. http://www.ncbi.nlm.nih.gov/pubmed/26242659

Amoxicillin, oral (adults): National Department of Health: Affordable Medicines, EDP-Primary Health Care level. Medicine Review: Phenoxymethylpenicillin vs amoxicillin for tonsilitis_pharyngitis, October 2016. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[55] Azithromycin: National Department of Health: Essential Drugs Programme. Paediatric Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

[56] Azithromycin, oral: National Department of Health: Essential Drugs Programme. Adult Hospital level STGs and EML, draft. https://www.knowledgehub.org.za/content/standard-treatment-guidelines-and-essential-medicines-list

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

SOUTH AFRICAN NATIONAL DEPARTMENT OF HEALTH
NEMLC SUMMARY REPORT ON UPDATES MADE TO THE
THE STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINE LIST GUIDANCE PRODUCTS
PHC Chp 4 Cardiovascular System (CVS)

Document Version Control

Report Version	Date	Detail
V1.0	*14/08/2026*	• *Updates to statins based on latest HP09 tender circular.* • *Editorial updates*

Summary Tables

Medicine Amendments

Medicine amendment recommendations, with supporting evidence and rationale are listed below. If appropriate can include non-medicine amendments if appropriate (for example if item has a large impact on how medicine is accessed). Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG).

STG/SECTION	GUIDANCE PRODUCTS (Tick relevant)				MEDICINE / MANAGEMENT	ADDED / DELETED / AMENDED	TI* CONSIDERATIONS (if applicable)
	PHC STGs & EML	AH STG & EML	PaedH STG & EML	TQ EML			
Section 4.1 Prevention of Ischaemic heart disease and atherosclerosis,	√	√			Simvastatin 10mg, oral – primary prevention	Retained	Yes
	√	√			Atorvastatin 10mg, oral – primary prevention for patients on PI-based ART	Retained	Yes
	√	√			Rosuvastatin 10mg, oral – secondary prevention	Added	Yes
	√	√			Atorvastatin 10mg, oral – secondary prevention for patients on PI-based ART	Deleted	Yes
	√	√			Rosuvastatin 10mg, oral – secondary prevention for patients on PI-based ART	Added	Yes
	√	√			Rosuvastatin 5mg, oral – secondary prevention for	Added	Yes

					statin-related muscle pain		
	√	√			Simvastatin 10mg, oral – secondary prevention for statin-related muscle pain	Retained	Yes
Section 4.4 Myocardial infarction, acute (AMI)/ ST Elevation myocardial infarction (STEMI)	√	√			Oxygen supplementation	Guidance amended	No
Section 4.6.1 Cardiac failure, congestive (CCF), Adults	√				Carvedilol	Editorial update	

*Therapeutic Interchange

Report V1.0
PHC Cardiovascular System Chapter 2

Section 4.1 PREVENTION OF ISCHAEMIC HEART DISEASE AND ATHEROSCLEROSIS

HMGCoA reductase inhibitors/statins

Simvastatin 10mg, oral - primary prevention: Retained as example within therapeutic class
Atorvastatin 10mg, oral – primary prevention for patients on protease inhibitor-based ART: Retained as example within therapeutic class
Rosuvastatin 10mg, oral – secondary prevention: Added as example within therapeutic class
Atorvastatin 10mg, oral – secondary prevention for patients on protease inhibitor-based ART: Deleted as example within therapeutic class
Rosuvastatin 10mg, oral – secondary prevention for patients on protease inhibitor-based ART: Added as example within therapeutic class
Rosuvastatin 5mg, oral – secondary prevention for statin-related muscle pain: Added as example within therapeutic class
Simvastatin 10mg, oral - secondary prevention for statin-related muscle pain: Retained as example within therapeutic class

STG recommendations on the use of statins for primary and secondary prevention have been amended to align with the most recently published HP09 contract circular[1] and in accordance with NEMLC's previous recommendations on therapeutic interchangeability. NEMLC's previous recommendation in support of the 'fire and forget' approach is retained. Additional guidance to avoid the use of statins during pregnancy and lactation[2] has been included in the STG. External comments for NEMLC to consider switching from the 'fire and forget' to 'treat to target' therapeutic strategy has been added to the list of topics for prioritisation for future consideration by NEMLC.

STG updates are as tabulated below:

AMENDED FROM:

MEDICINE TREATMENT

- » Lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.
- » When lipid-lowering medicines are used, this is ALWAYS in conjunction with ongoing lifestyle modification.

▪ HMGCoA reductase inhibitors (statins), according to table below:

INDICATION	HMGCOA REDUCTASE INHIBITOR (STATIN) DOSE
A: Primary prevention - no existing CVD	

AMENDED TO:

MEDICINE TREATMENT

- » Lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.
- » When lipid-lowering medicines are used, this is ALWAYS in conjunction with ongoing lifestyle modification.

▪ HMGCoA reductase inhibitors (statins), according to table below:

INDICATION	HMGCOA REDUCTASE INHIBITOR (STATIN) DOSE
A: Primary prevention - no existing CVD	
» Type 2 diabetes with age >40 years. » Diabetes for >10 years. » Diabetes with chronic kidney disease.	▪ HMGCoA reductase inhibitors (low intensity statin), e.g.: • Simvastatin, oral, 10 mg at night.

[1] HP09-2026SD: supply and delivery of solid dosage forms to the Department of health for the period 1 May 2026 to 30 April 2029.
[2] Kay HY, Jang HY, Kim IW, Oh JM. Pregnancy and neonatal outcomes after fetal exposure to statins among women with dyslipidemia: a nationwide cohort. Eur J Pediatr. 2025 May 14;184(6):340. doi: 10.1007/s00431-025-06119-3. PMID: 40366447; PMCID: PMC12078441.
Christensen JJ, Holven KB, Bogsrud MP, Retterstøl K, Roeters van Lennep JE, Michelsen TM, Veierød MB, Nordeng H. Statin use in pregnancy and risk of congenital malformations: a Norwegian nationwide study. Eur Heart J. 2026 Jan 16;47(3):318-327. doi: 10.1093/eurheartj/ehaf592. PMID: 40838827; PMCID: PMC12807567.
Holven KB, Raal FJ, Watts GF, Christensen JJ, Roeters van Lennep J. Challenges in the care of women with familial hypercholesterolaemia during the reproductive period - current evidence and practical guidance. Atherosclerosis. 2026 Apr;415:120679. doi: 10.1016/j.atherosclerosis.2026.120679. Epub 2026 Feb 11. PMID: 41713387.

» Type 2 diabetes with age >40 years. » Diabetes for >10 years. » Diabetes with chronic kidney disease. » ≥ 20% 10-year risk of cardiovascular event.	▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 10 mg at night.
» Patients on protease inhibitors. (Risks as above, after switching to atazanavir – see section below).	• Atorvastatin, oral, 10 mg daily.
B: Secondary prevention - existing CVD	
» Ischaemic heart disease. » Atherothrombotic stroke. » Peripheral vascular disease.	▪ HMGCoA reductase inhibitors (statins), e.g.: • Rosuvastatin, oral, 10 mg at night.
» Patients on protease inhibitors.	• Atorvastatin, oral, 10 mg daily.
» Patients on amlodipine (and not on protease inhibitor).	• Simvastatin, oral, 10–20 mg at night.
» If patient complains of muscle pain.	Reduce dose: ▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 10 mg at night. **OR** Consult specialist for further management.
» ≥ 20% 10-year risk of cardiovascular event.	
» Patients on protease inhibitors. (Risks as above, after switching to atazanavir – see section below).	• Atorvastatin, oral, 10 mg once daily.
» Pregnant and breastfeeding women	• Do not prescribe statins unless on the advice of a specialist
B: Secondary prevention - existing CVD	
» Ischaemic heart disease. » Atherothrombotic stroke. » Peripheral vascular disease.	▪ HMGCoA reductase inhibitors (moderate intensity statin), e.g.: • Rosuvastatin, oral, 10 mg once daily.
» Patients on protease inhibitors (see section below).	• Rosuvastatin, oral, 10 mg daily.
» If patient complains of muscle pain.	Reduce dose: ▪ HMGCoA reductase inhibitors (statin), e.g.: • Rosuvastatin, oral, 5 mg once daily. If not tolerated, switch to low intensity statin e.g.: • Simvastatin, oral, 10 mg at night. **OR** Consult specialist for further management.
» Pregnant and breastfeeding women	Do not prescribe statins unless on the advice of a specialist.

Table 4.1: Management with HMGCoA reductase inhibitors

Protease inhibitor-induced dyslipidaemia:

» Certain antiretroviral medication, particularly protease inhibitors, can cause dyslipidaemia. Fasting lipid levels should be done 3 months after starting lopinavir/ritonavir. Lopinavir/ritonavir is associated with a higher risk of dyslipidaemia (specifically hypertriglyceridaemia) than atazanavir/ritonavir.

» Patients at high risk (>20% risk of developing a CVD event in 10 years) should switch to atazanavir/ritonavir and repeat the fasting lipid profile in 3 months.

» Patients with persistent dyslipidaemia despite switching, qualify for lipid lowering therapy. Criteria for initiating lipid lowering therapy are the same as for HIV-negative patients. Many statins (including simvastatin) cannot be used with protease inhibitors, as protease inhibitors inhibit the metabolism of the statin resulting in extremely high blood levels.

Table 4.1: Management with HMGCoA reductase inhibitors

Protease inhibitor-induced dyslipidaemia:

» Certain antiretroviral medication, particularly protease inhibitors (e.g. lopinavir/ritonavir, atazanavir/ritonavir and darunavir/ritonavir), can cause dyslipidaemia.

» Patients taking protease inhibitor-containing ART, should be assessed for eligibility to be switched to a dolutegravir-containing regimen.

» Patients with persistent dyslipidaemia despite switching to dolutegravir-containing ART regimen, qualify for lipid lowering therapy. Criteria for initiating lipid lowering therapy are the same as for HIV-negative patients (refer to table 4.1 above).

» Lopinavir/ritonavir is associated with a higher risk of dyslipidaemia (specifically hypertriglyceridaemia) than atazanavir/ritonavir. Patients at high risk (>20% risk of developing a CV event in 10 years or existing CVD) should switch to atazanavir/ritonavir if not eligible for a dolutegravir-containing ART regimen.

» If ART with a protease inhibitor is essential, fasting lipid levels should be monitored 3 months after initiating protease inhibitor therapy.

» Protease inhibitors inhibit the metabolism of most statins, resulting in higher statin levels in the blood. Simvastatin is contraindicated for this reason. Other statins may be co-prescribed with protease inhibitors at a reduced dose, see Appendix IV: Comparative dose tables, for more information.

» Patients with persistent dyslipidaemia despite switching to atazanavir/ritonavir and employing lifestyle modification, qualify

» Patients at high risk for CVD who fail to respond to lifestyle modification and have dyslipidaemia on atazanavir/ritonavir treat with: • Atorvastatin, oral, 10 mg at night.	for a statin. Criteria for initiating lipid lowering therapy are the same as for HIV-negative patients (refer to table 4.1 above). » Recommended statins for patients on protease inhibitor containing ART are as follows: ▪ HMGCoA reductase inhibitors: • Primary prevention: e.g. Atorvastatin, oral, 10 mg once daily. • Secondary prevention: e.g. Rosuvastatin 10mg once daily.

The above guidance on statin selection for primary and secondary prevention has been incorporated in all relevant STGs in the PHC chapter. Additionally, the table below detailing NEMLC approved comparative dosing of statins has been included in the newly developed Appendix V: Comparative dose tables:

HMG-CoA REDUCTASE INHIBITORS (STATINS)

NEMLC approval for STG indications as follows:

- Low intensity statins approved for primary prevention.
- Moderate intensity statins approved for secondary prevention.
- High intensity statin approved for familial hypercholesteraemia.

Comparative Doses for STG Indications				Drug-drug Interactions
Statin Intensity	**LOW**	**MODERATE**	**HIGH**	*Co-administration with protease inhibitor (PI) ARVs or Amlodipine*
STG Indication	**PRIMARY PREVENTION**	***SECONDARY PREVENTION**	**FAMILIAL HYPERCHOLESTERAEMIA**	
Statin	**Recommended dose**			
Atorvastatin	[redacted]	20mg	80mg	PI: Max dose 10mg/day**
Pravastatin	20mg	80mg	[redacted]	PI: Avoid Potential interaction with LPV/r – no data available for recommended dosing.
Simvastatin	10mg	40mg		PI: Contraindicated Amlodipine: Use max 10-20 mg.
Rosuvastatin	[redacted]	10mg	40mg	PI: Max dose 10mg/day**
Notes: *Reduce dose if myalgia suspected. **Recommended maximum doses may vary for different protease inhibitors (PIs). NEMLC recommends the lowest recommended statin dose for ease of implementation.				

Section 4.4 Myocardial infarction, acute (AMI)/ ST Elevation myocardial infarction (STEMI)

Oxygen - supplementation during STEMI**:** Amended

Guidance on the use of oxygen supplementation has been amended. Supplementation is recommended if oxygen saturation is < 90% (amended from < 94%) and has been aligned to the European Society of Cardiology's clinical guideline, which states: *"Oxygen supplementation is recommended in ACS patients with hypoxaemia (oxygen saturation <90%) oxygen supplementation in patients who are not hypoxic (oxygen saturation >90%) is not associated with clinical benefits and is therefore not recommended."*[3]

[3] 2023 ESC guidelines for the management of acute coronary syndromes. 25 Aug 2023.

STG guidance has been amended as tabulated below:

AMENDED FROM	AMENDED TO:
4.4 Myocardial infarction, acute (AMI)/ ST elevation myocardial infarction (STEMI) **I21.0-I21.3/I21.9/I22.0-1/I22.8-9** **EMERGENCY TREATMENT** **Before transfer** Cardio-pulmonary resuscitation if necessary (see Section 21.1: Cardiac arrest – cardiopulmonary resuscitation). • Oxygen 40% via facemask, if saturation <94% or if in distress.	**4.4 Myocardial infarction, acute (AMI)/ ST elevation myocardial infarction (STEMI)** **I21.0-I21.3/I21.9/I22.0-1/I22.8-9** **EMERGENCY TREATMENT** **Before transfer** Cardio-pulmonary resuscitation if necessary (see Section 21.1: Cardiac arrest – cardiopulmonary resuscitation). • Oxygen 40% via facemask, if saturation <90% or if in distress.

Section 4.6.1 Cardiac failure, congestive (CCF), Adults

Carvedilol: step 2 – addition of non-selective beta blocker: Editorial update
STG guidance on the dose titration of carvedilol in patients weighing >85kg has been clarified in line with the European Society of Cardiology guidelines for the diagnosis and treatment of acute and chronic heart failure[4]. If a target heart rate of 50-70 beats per min is not achieved on the maximum tolerated dose, patients should be referred for further assessment.

Amended from

- If >85 kg and target heart rate has not been achieved, titrate to a maximum of 50 mg twice daily, if tolerated

Amended to.

If >85 kg, titrate to a maximum of 50 mg twice daily, if tolerated. If patient remains symptomatic on maximum tolerated dose, do an ECG and refer if there is indication of heart block or bradyarrthymias that may be of concern. Alternatively, refer if access to ECG monitoring is not available.

Appendix III: Cardiovascular Risk Assessment

Amended

A typographical error in the table: calculation of risk of developing cardiovascular events over 10 years, has been corrected as detailed below:

Calculation of risk of developing cardiovascular events over 10 years
(in the absence of cardiovascular disease or genetic disorders such as familial hypercholesterolaemia)

AMENDED FROM

HDL cholesterol (mmol/L)	MEN	WOMEN
>1.5	–2	–2
1.3–1.49	–1	–1
1.2–1.29	0	0
0.9–1.119	1	1
<0.9	2	2

AMENDED TO

HDL cholesterol (mmol/L)	MEN	WOMEN
>1.5	–2	–2
1.3–1.49	–1	–1
1.2–1.29	0	0
0.9–1.19	1	1
<0.9	2	2

[4] McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726. https://pubmed.ncbi.nlm.nih.gov/34447992/ **supplementary data accessed online : https://academic.oup.com/eurheartj/article/42/36/3599/6358045#supplementary-data**