CHAPTER 3
CARDIOVASCULAR SYSTEM

3.1 ISCHAEMIC HEART DISEASE AND ATHEROSCLEROSIS, PREVENTION

Major risk factors for ischaemic cardio- and cerebrovascular disease:
» Diabetes mellitus.
» Hypertension.
» Central obesity (waist circumference): men ≥102 cm, women ≥88 cm.
» Smoking.
» Dyslipidaemia:
  - Total cholesterol >5.0 mmol/L, or
  - LDL >3 mmol/L, or
  - HDL <1 mmol/L in men and <1.2 mmol/L in women.
» Family history of premature cardiovascular disease in first degree male relatives <55 years and in first degree female relatives <65 years.
» Age: men >55 years, women >65 years.
» Psychological stress. *LoE:IIIb*[i]

GENERAL MEASURES

Lifestyle modification, especially smoking cessation, is essential and often has greater beneficial impact on prognosis than vascular interventions and medications.

All persons should be encouraged to make the following lifestyle changes as appropriate (consult dietitian, if available): *LoE:IIIb*[ii]
» Smoking cessation.
» Weight reduction in overweight patients, i.e. maintain BMI 18.5 to 25 kg/m^2.
» Reduce alcohol intake to no more than 2 standard drinks/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 saturated fat, high fibre and unrefined carbohydrates, with adequate fresh fruit and vegetables.
» Moderate aerobic exercise, e.g. 30 minutes brisk walking 5-7 times/week (150 minutes/week).

MEDICINE TREATMENT

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. *LoE:IIa[iii]*

» Type 2 diabetes with age >40 years.
» Diabetes for >10 years.
» Diabetes with chronic kidney disease (eGFR <60 mL/minute).

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[iv]*
» psychological stress.

These patients should be managed according to their 10–year risk of a cardiovascular event as calculated using either:

A. BMI–based risk assessment, or
B. Framingham risk score (cholesterol-based assessment). See Appendix VII Cardiovascular risk assessment.

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

– <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.

Note:

» Lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.
▪ 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. » ≥ 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[v]
» Patients on protease inhibitors (see section below).	• Rosuvastatin, oral, 10 mg daily. LoE:Ia[vi]
» 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. LoE:IIIb[vii]
» Pregnant and breastfeeding women	Do not prescribe statins unless on the advice of a specialist. LoE:IVb[viii]

Table 3.1: Management with HMGCoA reductase inhibitors
Note: Lipid-lowering medicines must always be used in conjunction with ongoing lifestyle modification.

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 3.1 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 VIII: 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.
» Fasting (14 hours) triglycerides >10 mmol/L.

3.2 ACUTE CORONARY SYNDROMES

These conditions should be managed in a high care setting with continuous ECG and frequent BP monitoring.

Reference guide for ECG analysis: "ECG APPtitude" smartphone app can be downloaded from the relevant app stores - available for iOS and Android.

3.2.1 ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

I21.0-I21.3/I21.9/I22.0-1/I22.8-9

DESCRIPTION

Ischaemic chest pain that is prolonged, ongoing or associated with nausea, sweating and syncope or associated with persistent ST elevation or new / presumed new left bundle branch block (LBBB). Repeat ECG at 20 to 30-minute intervals if the initial ECG is not diagnostic. Treatment should not be delayed while waiting for troponin results.

MEDICINE TREATMENT

Note: The following guidance is not for primary percutaneous coronary intervention (PCI).

- Oxygen if saturation <90%, or shock. *LoE:IIb[x]*

CAUTION

Do not administer oxygen if the patient is not hypoxic as evidence indicates that liberal oxygen therapy does not improve patient-important outcomes and may actually increase mortality.

- Clopidogrel, oral, 75 mg daily for one month. *LoE:Ia[x]*

AND

- Aspirin, oral, 150 mg immediately as a single dose (chewed or dissolved). LoE:Ia[xi]
  - Followed with 150 mg daily (continued indefinitely in absence of contraindications). LoE:Ia[xii]

AND

Thrombolytic therapy

- Streptokinase, IV 1.5 million units diluted in 100 mL sodium chloride 0.9%, infused over 30–60 minutes. **Do not use heparin if streptokinase is given**.
  - 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 12 months after 1st administration.
  - Severe allergic reactions are uncommon but antibodies which may render it ineffective may persist for years. LoE:IIIb[xiii]

Considerations for initiating thrombolytics	Contra-indications
» For acute myocardial infarction with ST elevation or left bundle branch block: - maximal chest pain is ≤6 hours - if beyond 6 hours and ongoing chest pain - >6 hours and no chest pain, thrombolytic not indicated (see Section 3.2.2: NSTEMI) LoE:Ia[xiv]	» Absolute: - streptokinase used within the last year, - previous allergy, - Confirmed 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. » Relative (consult specialist): - refractory hypertension, - warfarin therapy, - recent retinal laser treatment, - subclavian central venous catheter, - pregnancy, - TIA in the preceding 6 months, - traumatic resuscitation.

Table 3.2: Indications and contraindications for streptokinase

OR

If streptokinase is unavailable: LoE:Ia[xv]

- Thrombolytic e.g.:
- Alteplase, IV infusion:
  - Do not exceed 100 mg.

- If history of onset is less than 6 hours (beyond 6 hours consult a specialist or treat as NSTEMI (see below):

	Bolus	Next 30 minutes	Next 60 minutes
>65 kg	15 mg	50 mg	35 mg
≤65 kg	15 mg	0.75 mg/kg	0.5 mg/kg

LoE:IVb[xvi]

- Indications and contraindications are similar to those for streptokinase as above (except that prior use of streptokinase is not a contraindication).

Monitor the following, continuously and also during transfer:
» pulse
» BP
» respiration depth and rate (count for a full minute)
» ECG
Note: Defibrillator should be readily available at all times including during transport.

Adjunctive treatment
- Enoxaparin (after alteplase, do not use heparins after streptokinase).
  - Loading dose: IV, 30 mg as a bolus, followed by SC, 1 mg/kg as a single dose (total cumulative dose not to exceed 100 mg).
  - Maintenance dose: SC, 1.5 mg/kg daily or 1 mg/kg 12 hourly.
  - Continue enoxaparin therapy until coronary angiography, or for the duration of hospitalisation to a maximum of 8 days. LoE:IIb[xvii]
  - In the elderly (>75 years of age), omit IV loading dose and reduce SC dose:
    - Loading dose: SC, 0.75 mg/kg as a single dose.
    - Maintenance dose: SC, 1.5 mg/kg daily or 1 mg/kg 12 hourly. LoE:Ia[xviii]

<u>Pain not responsive to thrombolytics may suggest ongoing unresolved ischaemia.</u>
Discuss with specialist and consider the following treatments:
- Nitrates, e.g.:
- Isosorbide dinitrate, SL, 5 mg immediately as a single dose.
  - May be repeated at 5-minute intervals for 3 or 4 doses. LoE:IIIb[xix]

<u>For ongoing chest pain, to control hypertension or treat pulmonary oedema:</u>
- Glyceryl trinitrate (GTN), IV, 5–200 mcg/minute, titrated to response.
  - Guidance on preparation and administration included below.

CAUTION
Glyceryl trinitrate IV formulation must be diluted before infusion.

STEP 1: Select the concentration as required for the individual patient

- For patients who are fluid congested or require higher doses for a clinical response, consider using a more concentrated solution e.g. 200 or 400 mcg/mL.

STEP 2: Select the volume of the diluent

- Patients who are likely to require treatment for a longer duration e.g. unstable angina prepare a larger volume e.g. 500mL.
- Compatible diluents include sodium chloride 0.9% or dextrose 5%.

STEP 3: Confirm the formulation of glyceryl trinitrate (GTN) available and mix with diluent

- Confirm the strength of the GTN solution i.e. whether a 1mg/mL or 5mg/mL formulation is available.
- Depending on the formulation available, select the number of ampoules to be used based on the concentration and volume of the diluent as decided in Step 1 and 2 above.
- Ensure that the equivalent volume of diluent is removed from the bag before adding the total GTN volume e.g. if 100mLs of GTN is to be added, first remove 100mL of diluent from the bag before adding the GTN.

STEP 4: Set the flow rate for infusion

- Flush the PVC tube before administering to patient.
- Start with the lowest flow rate possible based on the concentration of the solution prepared.
- Increase by 5 mcg/minute every 5 minutes until response achieved or until the rate is 20 mcg/minute.
- If no response after 20 mcg/minute increase by 20 mcg/minute until response.
- Monitor blood pressure carefully.

E.g. To prepare a 200mcg/mL solution for a patient likely to require several hours of the GTN infusion:
Use 10 ampoules (100mL) of the 1mg/mL GTN formulation mixed with 400mL of diluent (100mL to be removed from a 500mL bag). Initiate the infusion at a flow rate 3mL/hr and titrate the infusion rate based on the patient's response.

STEP 1	STEP 2	STEP 3			
Concentration of dilution	**Volume of diluent**	**Glyceryl trinitrate 1 mg/mL**		**Glyceryl trinitrate 5 mg/mL**	
		Volume (Dose)	Number of 10mL ampoules	Volume (Dose)	Number of 10mL ampoules
100 mcg/mL	250 mL	25 mL (25 mg)	2.5	5 mL (25 mg)	0.5
200 mcg/mL		50 mL (50 mg)	5	10 mL (50 mg)	1
400 mcg/mL		100 mL (100 mg)	10	20 mL (100 mg)	2
100 mcg/mL	500 mL	50 mL (50 mg)	5	10 mL (50 mg)	1
200 mcg/mL		100 mL (100 mg)	10	20 mL (100 mg)	2
400 mcg/mL		200 mL (200 mg)	20	40 mL (200 mg)	4

STEP 4	Solution concentration (mcg/mL)	100 mcg/mL solution	200 mcg/mL solution	400 mcg/mL solution
	Dose (mcg/min)	Flow rate (microdrops/min = mL/hr)		
	5	3	–	–
	10	6	3	–
	15	9	–	–
	20	12	6	3
	30	18	9	–
	40	24	12	6
	60	36	18	9
	80	48	24	12
	100	60	30	15
	120	72	36	18
	160	96	48	24
	200	–	60	30

Table 3.3: Dilution of glyceryl trinitrate

<u>For severe pain unresponsive to nitrates:</u>
Discuss with a specialist for possible transfer for rescue PCI, and then consider morphine:

- Morphine, IV, to a total maximum dose of 10 mg. (See Appendix II, for individual dosing and monitoring for response and toxicity.)
  - Ongoing severe pain despite all appropriate treatment above is an indication for urgent referral.

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

- Cardio-selective β-blocker, e.g.:
- Atenolol, oral, 50 mg daily.

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

Patients on protease inhibitor:

- Rosuvastatin, oral, 10 mg once daily. *LoEIa*[xxi]

If patient complains of muscle pain:

Reduce dose:

- Rosuvastatin, oral, 5mg once daily.

OR

Low intensity statin e.g.

- Simvastatin, oral, 10mg at night.

OR

Consult specialist for further management. *LoE:IIIb*[xxii]

For left ventricular (LV) dysfunction following myocardial infarction, heart failure or ejection fraction <40%:

- ACE-inhibitor, e.g.:
- Enalapril, oral, target dose, 10 mg 12 hourly.

If ACE-inhibitor intolerant, i.e. intractable cough or angio-oedema:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated.

» Angioedema is a potentially serious complication of ACE-inhibitor/ angiotensin receptor blocker treatment and if it occurs stop the medication and do not re-challenge.

» Concomitant use of fluoroquinolones with ACE-inhibitor/angiotensin receptor blocker is contraindicated in moderate to severe renal impairment (CrCl ≤30 mL/minute) and in the elderly. Assess renal function before initiating treatment and monitor during treatment. *LoE:IIIb*[xxiii]

Institute other therapy for heart failure and LV dysfunction as described in Section 3.4: Congestive cardiac failure.

REFERRAL

» Refractory cardiogenic shock.
» Refractory pulmonary oedema.
» Haemodynamically compromising ventricular dysrhythmia.

» Patients with the combination of new right bundle and posterior fascicular block post MI should be referred for permanent pacemaker consideration as they are at high risk for progression to complete heart block.
» Myocardial infarction-related mitral regurgitation or ventricular septal defect (VSD).
» Contraindication to thrombolytic therapy provided a PCI facility available (confirm with cardiologist).
» Ongoing ischaemic chest pain.
» Failed reperfusion (<50% reduction in ST elevation at 90 minutes after initiation of streptokinase and 60 minutes after initiation of thrombolytics (e.g., alteplase) in leads showing greatest ST elevation, especially in anterior infarct or inferior infarct with right ventricular involvement).

3.2.2 NON-ST ELEVATION MYOCARDIAL INFARCTION (NSTEMI) AND UNSTABLE ANGINA (UA)

I21.4/I21.9/I20.0

DESCRIPTION

Non-ST elevation MI: Chest pain that is increasing in frequency and/or severity or occurring at rest. The chest pain is associated with elevated cardiac biomarkers and ST segment depression or T wave inversion on ECG, or a normal ECG. Biomarker elevation in the absence of diagnostic ECG changes or symptoms compatible with myocardial ischemia should prompt consideration of alternative diagnoses (e.g. heart failure, pulmonary embolism, chronic kidney disease, sepsis, myopericarditis). LoE:IVb[xxiv]

Unstable angina pectoris: Chest pain that is increasing in frequency and or severity or occurring at rest. It also encompasses post-infarct angina. The chest pain may be associated with ST segment depression or T wave inversion on ECG. There is no rise in cardiac biomarkers.

MEDICINE TREATMENT

Note: The following guidance is not for primary percutaneous coronary intervention.

LoE:IIb[xxv]

- Oxygen, if saturation <94%.

LoE:Ia[xxvi]

- Clopidogrel, oral, 300 mg.
  Followed by 75 mg daily for 3 months.

LoE:Ia[xxvii]

AND

- Aspirin, oral, 150 mg immediately as a single dose (chewed or dissolved).
  - Followed with 150 mg daily (continued indefinitely in absence of contraindications).

AND

Anticoagulation:

For NSTEMI and UA (also for STEMI not given thrombolytic therapy):

- Enoxaparin, SC, 1 mg/kg 12 hourly for minimum of 2 days.

OR

LoE:Ia[xxviii]

- Unfractionated heparin, IV bolus, 5 000 units.
  - Follow with 1 000–1 200 units hourly monitored by aPTT.
  - Continue infusion for minimum of 2 days.

To relieve possible coronary spasm and pain and to reduce preload:

» Nitrates, e.g.:

- Isosorbide dinitrate SL, 5 mg immediately as a single dose.
  - May be repeated at 5-minute intervals for 3 or 4 doses.

For persistent pain and if oral therapy is insufficient:

- Glyceryl trinitrate, IV, 5–200 mcg/minute, titrated to response.
  - Start with 5 mcg/minute and increase by 5 mcg/minute every 5 minutes until response or until the rate is 20 mcg/minute.
  - If no response after 20 mcg/minute, increase by 20 mcg/minute every 5 minutes until pain reduction or medicine no longer tolerated.
  - Flush the PVC tube before administering the medicine to patient.
  - Monitor BP carefully.

For dilution of glyceryl trinitrate refer to Section 3.2.1: ST elevation myocardial infarction (STEMI).

For severe pain unresponsive to nitrates:

Discuss with a specialist for possible transfer for rescue PCI, and then consider morphine:

- Morphine, IV, to a total maximum dose of 10 mg (see Appendix II, for individual dosing and monitoring for response and toxicity).
  - Ongoing severe pain despite all appropriate treatment above is an indication for urgent referral.

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

▪ Cardio-selective β-blocker, e.g.:

- Atenolol, oral, 50 mg daily.

▪ HMGCoA reductase inhibitors (moderate intensity statin), e.g.:

- Rosuvastatin, oral, 10 mgonce daily.

LoE:Ia[xxix]

Patients on protease inhibitor:

- Rosuvastatin, oral, 10 mg once daily.

LoE:Ia[xxx]

If patient complains of muscle pain:

Reduce dose:

▪ Rosuvastatin, oral, 5mg once daily.

OR
Low intensity statin e.g.
- Simvastatin, oral, 10 mg at night. *LoE:IIIb*[xxxi]

OR

Consult specialist for further management.

If there is cardiac failure or LV dysfunction (see Section 3.4: Congestive cardiac failure):
(I50.0)
- ACE-inhibitor, e.g.:
- Enalapril, oral, target dose 10 mg 12 hourly. *LoE:IVb*[xxxii]

If ACE-inhibitor intolerant, i.e. intractable cough or angio-oedema:
- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated.

Institute other therapy for heart failure and LV dysfunction as described in Section 3.4: Congestive cardiac failure.

REFERRAL

» Patients with a diagnosis of acute coronary syndrome should be risk stratified at presentation to estimate their likelihood of developing a major adverse cardiac event (acute MI, heart failure, death or readmission for UA) over the subsequent 4-6 weeks. High risk patients (including those with positive troponins) should be discussed with a cardiology service for consideration for angiography and revascularization therapy. Two widely used and well validated risk stratification scores are TIMI (http://www.mdcalc.com/timi-risk-score-for-uanstemi/) and Grace Risk Scores (http://www.mdcalc.com/grace-acs-risk-and-mortality-calculator). The patient's co-morbidities and willingness to undergo revascularization, which may involve coronary surgery, should be taken into account when advising such referral.

» Other important indications for referral include:
- ongoing chest pain (non-responsive to nitrates, provided PCI facility is available – confirm with cardiologist at referral centre),
- post-infarct angina,
- sustained dysrhythmias,
- refractory heart failure,
- refractory cardiogenic shock. *LoE:IVb*[xxxiii]

3.2.3 CHRONIC MANAGEMENT OF STEMI / NSTEMI / UA

I25.2/I20.0

GENERAL MEASURES

Lifestyle modification. See Section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

MEDICINE TREATMENT

Continue oral therapy (see Sections 3.2.1: ST elevation myocardial infarction (STEMI) and 3.2.2: Non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA)).

If heart failure develops, replace atenolol with carvedilol. See Section 3.4: Congestive cardiac failure.

3.2.4 ANGINA PECTORIS, STABLE

I20.I/I20.8-9

DESCRIPTION

Characteristic chest pain due to myocardial ischaemia usually occurring on exercise and relieved by rest. Discomfort may occasionally be experienced in a site of referral (shoulder, jaw) but the characteristic provocation by exercise and relief by rest is a valuable clue.

GENERAL MEASURES

Lifestyle modification. See Section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

MEDICINE TREATMENT

Long-term prophylaxis for thrombosis:

- Aspirin, oral, 150 mg immediately as a single dose (chewed or dissolved).
  - Followed with 150 mg daily (continued indefinitely in absence of contraindications). *LoE:Ia*[xxxiv]

AND

Relief of angina:

- Nitrates, short acting e.g.:
- Isosorbide dinitrate, SL, 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.

AND
Step 1
- Cardio-selective β-blocker, e.g.:
- Atenolol, oral, 50–100 mg daily.
  - Titrate to resting heart rate of approximately 60 bpm.

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

Step 2
ADD
- Long-acting calcium channel blocker, e.g.:
- Amlodipine, oral, 5mg daily.
  - Increase to 10 mg daily if required.

Step 3
ADD
- Organic nitrates, e.g.:
- Isosorbide mononitrate, oral 10–20 mg twice daily.

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

Long-term secondary prophylaxis for coronary artery disease
- HMGCoA reductase inhibitors (moderate intensity statin), e.g.:
- Rosuvastatin, oral, 10 mg once daily. *LoE:Ia*[xxxvi]

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

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

OR
Low intensity statin e.g.
- Simvastatin, oral, 10 mg at night. *LoE:IIIb*[xxxviii]

OR
Consult specialist for further management.

REFERRAL
» When diagnosis is in doubt, despite exercise stress testing.
» Failed medical therapy. A common reason for “failed” therapy is that the patient has an alternative diagnosis. Therefore, this conclusion should be reached after reasonable effort for non-invasive diagnosis including exercise stress test.

3.2.5 ATHEROSCLEROTIC PERIPHERAL ARTERIAL DISEASE

I70.2, I70.20, I70.21

DESCRIPTION

History and palpation of pulses confirms diagnosis.

GENERAL MEASURES

Smoking cessation is essential and is the single most important intervention to prevent progression.
Exercise within exercise tolerance and other lifestyle modifications.
See Section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

MEDICINE TREATMENT

Long-term prophylaxis for thrombosis:

- Aspirin, oral, 150 mg daily.

AND

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

Patients on protease inhibitor:

- Rosuvastatin, oral, 10 mg once daily. LoE:Iaxl

If patient complains of muscle pain:
Reduce dose:

- Rosuvastatin, oral, 5mg once daily.

OR
Low intensity statin e.g. LoE:IIIb[xli]

- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management.

Therapy should be initiated together with appropriate lifestyle modification.
See Section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

REFERRAL

Ongoing vascular insufficiency, which may be surgically reversible.

3.3 CARDIAC DYSRHYTHMIAS

Exclude underlying structural cardiac disease in all patients with cardiac dysrhythmias (assess patients with an echocardiogram, where available).

3.3.1 NARROW QRS COMPLEX (SUPRAVENTRICULAR) TACHYDYSRHYTHMIAS

I47.1

DESCRIPTION

Sustained (>30 seconds) or non-sustained narrow QRS (≤0.12 seconds) tachycardias.

REFERRAL

» Poor rate control.
» Frequent or severe symptoms for curative radiofrequency catheter ablation.
» All symptomatic Wolf-Parkinson-White (WPW) syndrome patients (sinus rhythm ECG shows delta waves) for radiofrequency catheter ablation.
» Asymptomatic patients in whom the WPW pattern is detected on ECG do not need referral.

3.3.1.1 ATRIAL FIBRILLATION

I48.0-I48.2/I48.9

DEFINITION

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial electrical activation and chaotic, ineffective atrial contraction. On ECG, it is defined by the absence of distinct P waves and replacement with irregular fibrillatory waves alongside an irregularly irregular ventricular response.

Risk factors

– Hypertension
– Cardiac failure
– Diabetes Mellitus
– Obesity
– Obstructive sleep apnoea
– Physical inactivity
– Hyperthyroidism
– Advancing age
– Male sex
– Genetics

MEDICINE TREATMENT

Acute onset (<48 hours)

» Assess clinically, e.g., heart failure, mitral stenosis, thyrotoxicosis, hypertension, age and other medical conditions.
» Consider anticoagulation with warfarin (see table below on CHA_2DS_2-VASc Score).
» Synchronised direct current (DC) cardioversion is occasionally necessary in haemodynamic instability.

Non-acute/chronic (> 48 hours)
As above, but not immediate DC cardioversion, unless there is haemodynamic instability.

The main aims of therapy for patients with atrial fibrillation should be:
1. Reduction of stroke and systemic embolic risk.
2. Rate or rhythm control.
3. Relief of symptoms attributed to the atrial fibrillation.

A simple scoring system allows calculation of risk of stroke in patients with non-valvular atrial fibrillation.

Table 3.4: CHA_2DS_2-VASc Score:

Risk Factor	Score
Congestive heart failure/ Left ventricular dysfunction	1
Hypertension	1
Age ≥ 75 years of age	2
Diabetes mellitus	1
Stroke/TIA/Thromboembolism	2
Vascular disease	1
Age 65–74 years of age	1
Sex **C**ategory (female gender)	1

Source: Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest. 2010 Feb;137(2):263-72. http://www.ncbi.nlm.nih.gov/pubmed/19762550

» When the score is ≥ 2, use DOAC, warfarin, or equivalent. The higher the score, the greater the risk of stroke and therefore the more compelling the use of effective anticoagulation.
» **Note:** The CHA_2DS_2-VASc risk stratification tool applies specifically to non-valvular atrial fibrillation. Due to the high baseline risk of thromboembolism in patients with atrial fibrillation and rheumatic mitral valve disease, long-term anticoagulation (preferably warfarin) is advisable, irrespective of risk score.

Table 3.5: HAS-BLED Score:
The potential risk for bleeding needs to be assessed using the HAS-BLED score when initiating oral anticoagulation therapy.

Risk factor and definitions		Score
H	Uncontrolled hypertension » SBP > 160 mmHg	1
A	**Abnormal renal function** » Dialysis, transplant, serum creatinine > 200 mmol/L	1 point for renal, 1 for hepatic
	Abnormal hepatic function » Cirrhosis, bilirubin >2xULN, AST/ALT/ALP >3xULN	
S	**Stroke**[a] » Previous ischaemic or haemorrhagic stroke	1
B	**Bleeding history or predisposition**[a]	1

	» Previous major haemorrhagic, anaemia, severe thrombocytopenia	
L	**Labile INR**[b] » TTR ≤ 60% in patient receiving warfarin	1
E	**Elderly** » Aged > 65 years or extreme frailty	1
D	**Drugs predisposing to bleeding** » Concomitant use of antiplatelet or NSAID	1 point for drugs, 1 for alcohol
	Alcohol use[c] » Excessive alcohol per week	
Maximum score		**9**

a: Haemorrhagic stroke would score 1 additional point under the "B" criterion for bleeding history or predisposition.
b: Only relevant if patient receiving warfarin or other vitamin K antagonists
c: Alcohol excess/abuse refers to a high intake (e.g. >14 units per week) where the clinician assesses there would be an impact on health or bleeding risk
Source: Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C et al; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021 Feb 1;42(5):373-498. doi: 10.1093/eurheartj/ehaa612. PMID: 32860505.

» The HAS-BLED assessment identifies modifiable bleeding risk that can be managed. Patients should therefore be assessed at every visit.
» The higher the score, the greater the risk of bleeding. However, a high HAS-BLED score **is not a contraindication** for oral anticoagulation.
» Instead, use the HAS-BLED score to identify and correct modifiable bleeding risks (e.g., control blood pressure, stop unnecessary NSAIDs/aspirin, advise reduced alcohol use), and to schedule more frequent clinical reviews.

LoE:IIIa[xlii]

Initial therapy aimed at stroke reduction

1. Anticoagulation

a) Non-valvular atrial fibrillation:

- Direct-acting oral anticoagulant (DOAC), e.g.:
- Rivaroxaban, oral, 20 mg daily with food.
  - Reduce dose in moderate renal impairment (eGFR 30–50mL/min) to 15 mg daily.

Drug-drug interactions with rivaroxaban

Some common drug interactions with rivaroxaban are listed below. Evidence on potential drug-drug interactions is still evolving, so consult the latest literature if uncertain of potential drug interactions. The risk of some drug interactions may be increased in patients with renal impairment and require careful anticoagulation risk assessment.

Medicine groups	Interaction information	Recommendation
Strong inhibitors of both CYP3A4 & P-glycoprotein • Ketoconazole, • Protease Inhibitors e.g. Ritonavir	Increased rivaroxaban concentrations with risk of bleeding	Contraindicated Use warfarin with INR monitoring instead
Moderate inhibitors of CYP3A4 • Fluconazole	Interaction not significant	May be co-administered with rivaroxaban
Strong inducers of CYP3A4 Medicines intended for long term use • Phenytoin, • Carbamazepine:	Decreased rivaroxaban concentrations with risk of clotting	Refer to doctor to switch to safer alternative anti-seizure medicines, e.g., lamotrigine (see PHC STG & EML, Section 15.7.2: Epilepsy in Adolescents and Adults). *Consider warfarin with INR monitoring if a switch to alternative anti-seizure medicine is not possible.*
Strong inducers of CYP3A4 Medicines intended for limited duration • Rifampicin	Decreased rivaroxaban concentrations with risk of clotting	Use warfarin with INR monitoring for the duration of TB treatment instead.

b) Valvular heart disease (e.g., rheumatic heart disease), prosthetic heart valves (e.g. transcatheter aortic valve replacement), renal impairment (eGFR < 15mL/min) or hypersensitivity to DOAC,

Anticoagulation with warfarin is required:

- Warfarin, oral, 5 mg daily.
  - INR should be done after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to initiation dosing tables in Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to maintenance dosing tables in Appendix II).
  - Every effort should be made to keep the time in therapeutic range (TTR) > 65%. TTR ≤ 65% is associated with decreased benefit of warfarin therapy and a greater risk of stroke and haemorrhage.

LoE:IIb[xliii]

See Appendix II for guidance on calculating TTR for management with warfarin.

2. Rate control

- Atenolol, oral, 50–100 mg daily.

- Contraindicated in asthmatics, heart failure.

OR

If in CCF:(I50.0)

- Carvedilol, oral. See Section 3.4: Congestive cardiac failure.

If control is not adequate, **ADD**:

- Digoxin, oral, 0.125 mg daily, adjust according to rate response and trough plasma level
  - Measure digoxin trough plasma levels (before the morning dose) – Maintain levels between 0.6–1 nmol/L.
  - Patients at high risk of digoxin toxicity: the elderly, patients with renal dysfunction, hypokalaemia, and patients with low lean body mass.

LoE:IVb[xliv]

If beta-blockers are contraindicated, e.g., asthma or severe peripheral vascular disease:

LoE:IVb[xliv]

- Verapamil, oral, 40–120 mg 8 hourly.
  - Titrate against ventricular rate (verapamil is negatively inotropic, therefore avoid in heart failure due to LV dysfunction).

If not controlled on these agents, refer to specialist for consideration of alternative therapy, e.g., amiodarone or atrioventricular node ablation and pacemaker insertion.

DC cardioversion may be needed in selected cases, after 4 weeks of effective warfarin anticoagulation.

3. Long-term therapy

» Continue with anticoagulation long-term, unless contraindicated.

a) Non-valvular atrial fibrillation:

- Direct acting oral anticoagulant (DOAC), e.g.:
- Rivaroxaban, oral, 20 mg once daily with food.
  - Reduce dose in moderate renal impairment (eGFR 30-50mL/min) to 15 mg daily.

If on warfarin, consider converting to DOAC:

» Ensure no contraindications to DOACs:
  - Active bleeding
  - Severe risk of bleeding: Recent GI ulcer, malignant neoplasms, recent brain/spinal/ophthalmic surgery, recent intracranial haemorrhage, oesophageal varices, vascular aneurysm
  - Severe hepatic disease
  - Severe renal impairment (eGFR < 15 ml/min)

» Stop warfarin treatment and monitor INR until INR is ≤ 3 mmol/L, then initiate treatment with:

- Direct acting oral anticoagulant (DOAC), e.g.:
- Rivaroxaban, oral, 20 mg once daily with food.
  - INR values may be falsely elevated following the initiation of rivaroxaban.
  - Reduce dose in moderate renal impairment (eGFR 30–50mL/min) to 15 mg daily.

b) Valvular heart disease (e.g. rheumatic heart disease), prosthetic heart valves (e.g. transcatheter aortic valve replacement), renal impairment (eGFR < 15mL/min):

- Warfarin, oral, 5 mg daily.
  - Monitor dose to ensure therapeutic INR:
    - INR between 2–3 and patient stable: monitor every 2 months.
    - INR <1.5 or >3.5: monitor monthly. *LoE:IIIb*[xlvi]

CAUTION
Warfarin use requires regular INR monitoring and dose adjustment according to measured INR.

For rate control:

- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

OR

If in CCF: (I50.0)

- Carvedilol, oral. See Section 3.4: Congestive cardiac failure.

If control not adequate **ADD**:

- Digoxin, oral, start at 0.125 mg daily and adjust according to rate response and trough plasma level.
  - In patients with impaired renal function (eGFR <60 mL/min), consider 0.125 mg daily and adjust according to trough level monitoring.
  - In all patients, digoxin trough level monitoring is required at all doses.

LoE:IIIb[xlvii]

If beta-blockers are contra-indicated, e.g., asthma or severe peripheral vascular disease:

- Verapamil, oral, 40–120 mg 8 hourly. *LoE:IVb*[xlviii]
  - Titrate against ventricular rate (verapamil is negatively inotropic, avoid in heart failure due to left ventricular dysfunction).

If not controlled on these agents, refer to specialist for consideration of alternative therapy.

CAUTION
The risk of thromboembolic complications and stroke in those with paroxysmal AF is similar to that of patients with persistent AF and similar recommendations as to anticoagulation apply.

Only in patients with severe symptoms despite the above measures:
- Amiodarone, oral, 200 mg 8 hourly for 1 week. (Specialist initiated).
  - Follow with 200 mg, 12 hourly for one week.
  - Thereafter, 200 mg, daily. *LoE:Ia[xlix]*

Precautions:
» If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.
» Monitor heart rate closely when patient is on concomitant digoxin.
» Monitor thyroid function every 6 months as thyroid abnormalities may develop.
» Ophthalmological examination every 6 months.

For management of pregnant women with valvular disease and atrial fibrillation, see Section 6.3: Heart disease in pregnancy.

3.3.1.2 ATRIAL FLUTTER
I48.3-4/I48.9

DESCRIPTION
Atrial rate >250 bpm with no flat baseline.
Can be difficult to recognise if 2:1 atrioventricular (AV) block, as the first of the two p waves preceding each QRS complex might be confused with the T-wave of the preceding beat. Vagal stimulation might slow the ventricular rate (usually approximately 150 bpm) and make the dysrhythmia more obvious.
Synchronised direct current (DC) cardioversion may be necessary in haemodynamic instability.

MEDICINE TREATMENT
DC cardioversion
DC cardioversion is the most effective therapy and administer midazolam as adjunct therapy:
- Midazolam IV, 1–2.5 mg, administered over 2-3 minutes.

For rate control therapies as for atrial fibrillation: see Section 3.3.1.1 Atrial fibrillation.

CAUTION
Do not use verapamil as it will not convert flutter to sinus rhythm and may cause serious hypotension.

For anticoagulation as per the CHA2DS2-VASc score above: see Section 3.3.1.1 Atrial fibrillation.

If flutter has been present longer than 48 hours, defer cardioversion until after 4 weeks' anticoagulation with warfarin, unless severe symptoms or heart failure require urgent cardioversion.

Long-term therapy
Anticoagulants (See Section 3.3.1.1 Atrial fibrillation). Most consider that the thromboembolic risks in atrial flutter and atrial fibrillation are similar.
Rate control agents as for atrial fibrillation (See Section 3.3.1.1 Atrial fibrillation).
Recurrent atrial flutter is an indication for referral as many may be relatively simply cured by radio-frequency catheter ablation.

3.3.1.3 AV JUNCTIONAL RE-ENTRY TACHYCARDIAS
I47.0

Usually paroxysmal.
Often young patients with normal hearts.
AV nodal re-entry or atrioventricular re-entry (WPW syndrome).
P waves usually not visible (hidden by QRS complexes).

GENERAL MEASURES
Vagal manoeuvres: The modified Valsalva manoeuvre is the most effective – it should be done semi-recumbent with 15 seconds of strain, followed immediately by supine positioning and passive leg raising.
Carotid sinus massage: Should be done with the patient supine and as relaxed as possible.

MEDICINE TREATMENT
Initial therapy
<u>If vagal manoeuvres fail:</u>
- Adenosine, rapid IV bolus, 6 mg.
  - Followed by a bolus of 10 mL sodium chloride 0.9% to ensure that it reaches the heart before it is broken down.
  - Half-life: ± 10 seconds.
  - Run the ECG for 1 minute after the injection as a recording of method of cessation may be helpful diagnostically.
  - If 6 mg fails, repeat with 12 mg.
  - If this fails, repeat with another 12 mg.

» If the medicine reaches the central circulation before it is broken down the patient will experience flushing, sometimes chest pain, wheezing and anxiety.
» If the tachycardia fails to terminate without the patient experiencing those symptoms, the medicine did not reach the heart.

If none of the above is effective or if the patient is hypotensive, consider synchronised cardioversion. LoE:IVb

Note: Adenosine is contraindicated when atrial flutter is the obvious diagnosis, administration of adenosine can precipitate 1:1 conduction at ventricular rates 250–360 bpm and should be avoided.

Long term therapy
Teach the patient to perform vagal manoeuvres. Valsalva is the most effective.
For infrequent, non-incapacitating symptoms:
- Cardio-selective beta–blocker, e.g.:
- Atenolol, oral, 50–100 mg daily.

If asthmatic, without heart failure: LoE:IVb[I]

- Verapamil, oral, 40–120 mg 8 hourly.

Verapamil and digoxin are contraindicated in WPW syndrome

REFERRAL
If the patient continues to experience debilitating symptoms refer for radiofrequency ablation.

3.3.2 WIDE QRS (VENTRICULAR) TACHYARRHYTHMIAS

DESCRIPTION
Sustained (>30 seconds) or non-sustained wide QRS (>0.12 seconds) tachycardias.

3.3.2.1 REGULAR WIDE QRS TACHYCARDIAS
I47.2/I47.9

Regular wide QRS tachycardias are **ventricular** until proved otherwise.
Regular wide QRS supraventricular tachycardias are uncommon.
Refer all cases after resuscitation and stabilisation.
Emergency DC cardioversion is mandatory with a full protocol of cardiopulmonary resuscitation (CPR) if there is haemodynamic compromise.

GENERAL MEASURES

CPR if necessary.

If no cardiac arrest:

DC cardioversion, 200 J, after sedation with:

- Midazolam, IV, 1–2.5 mg, administered over 2-3 minutes.
  - Monitor and repeat dose after 2-3 minutes, as necessary.
  - If 200 J fails, use 360 J.

LoE:IVb

If cardiac arrest:

Defibrillate (not synchronised).

MEDICINE TREATMENT

LoE:IVb[ii]

CAUTION

Never give verapamil or adenosine IV to patients with wide QRS tachycardia as this may precipitate ventricular fibrillation.

DC cardioversion **is the preferred and safest first line therapy** for regular wide QRS tachycardias. Medicines are needed if ventricular tachycardia (VT) recurs after cardioversion or spontaneous termination.

LoE:IVb

If in doubt as to the nature of a tachycardia, and in all patients with haemodynamic compromise, DC cardioversion under IV sedation is the safest option.

DC cardioversion, 200 J, after sedation with:

- Midazolam, IV, 1–2.5 mg, administered over 2-3 minutes.
  - Monitor and repeat dose after 2-3 minutes, as necessary.

LoE:IVb

  - If 200 J fails, use 360 J.

- Amiodarone, IV, 5 mg/kg infused over 30 minutes.

Follow with:

- Amiodarone, oral, 200 mg 8 hourly for 7 days.
  - Then, 200 mg 12 hourly for 7 days.
  - Maintenance dose: 200 mg daily for the minimum time required to control the arrhythmia
  - Consult specialist before instituting long-term (>1 week) therapy.

LoE:IVb[iii]

Precautions:

- If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.

- Monitor heart rate closely when patient is on concomitant digoxin. Monitor thyroid function every 6 months as thyroid abnormalities may develop.
- Ophthalmological examination every 6 months.

REFERRAL

- If no response to DC cardioversion, consult a specialist.

3.3.2.2 SUSTAINED (>30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

I47.0-2/I47.9

These tachycardias are usually due to atrial fibrillation with bundle branch block, or pre-excitation (WPW syndrome).

If the QRS complexes have a pattern of typical right or left bundle branch block, with a rate <170 bpm, treat as for atrial fibrillation. See Section 3.3.1: Narrow QRS complex (supraventricular) tachycardias.

If the rate is >170 bpm, and/or the complexes are atypical or variable, the likely diagnosis is WPW syndrome with atrial fibrillation, conducting via the bypass tract. Treat with DC cardioversion.

Do not treat with medication.
Verapamil and digoxin may precipitate ventricular fibrillation by increasing the ventricular rate.

If in doubt as to the nature of a tachycardia, and in all patients with haemodynamic compromise, DC cardioversion under IV sedation is the safest option.
DC cardioversion, 200 J, after sedation with:

- Midazolam, IV, 1–2.5 mg, administered over 2-3 minutes.
  - Monitor and repeat dose after 2-3 minutes, as necessary. *LoE:IVb*
  - If 200 J fails, use 360 J.

3.3.2.3 NON-SUSTAINED (<30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

I47.0-2/I47.9

These tachycardias are usually ventricular. They are common in acute myocardial infarction. Check serum potassium level and correct if low.

MEDICINE TREATMENT

LoE:IIIb[iii]

- Amiodarone, IV, 5 mg/kg infused over 30 minutes.

Follow with:

- Amiodarone, oral, 200 mg three times a day for 7 days.
  - Then 200 mg 12 hourly for 7 days.
  - Follow with a maintenance dose of 200–400 mg daily, depending upon clinical judgement. Consult specialist before instituting long-term (>1 week) therapy.

Precautions:

- If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.
- Monitor heart rate closely when patient is on concomitant digoxin.
- Monitor thyroid function every 6months as thyroid abnormalities may develop.
- Ophthalmological examination every 6 months.

OR

Only in haemodynamically stable patients: LoE:IIIb[iv]

- Lidocaine (lignocaine), IV, 50–100 mg (1–2 mg/kg) initially as a slow IV injection over 2 minutes.
  - Repeat at 5-minute intervals if required to a total of 200–300 mg.

Thereafter, for recurrent ventricular tachycardia only:

- Lidocaine (lignocaine), IV infusion, 1–3 mg/minute for 24–30 hours.

» Lidocaine will only terminate ± 30% of sustained ventricular tachycardias, and may cause hypotension, heart block or convulsions.
» For emergency treatment of ventricular tachycardia, DC cardioversion is first line therapy, even if stable.

In the absence of acute ischaemia or infarction, consider torsades de pointes, due to QT prolonging medicines.

3.3.2.4 TORSADES DE POINTES VENTRICULAR TACHYCARDIA (VT)

I47.2

Torsades de pointes Ventricular Tachycardia (VT) has a twisting pattern to the QRS complexes and a prolonged QT interval in sinus rhythm. It is usually due to a QT-prolonging medication, active myocardial ischaemia and/or hypokalaemia and/or a history of alcohol abuse/malnutrition.

GENERAL MEASURES

Defibrillation, as necessary.
Torsades complicating bradycardia: temporary pacing.

MEDICINE TREATMENT

Stop all QT-prolonging medicines (a list of medicines that cause QT prolongation can be viewed at https://www.sads.org.uk/drugs-to-avoid/?doing_wp_cron=1672916576.0519239902496337890625
Correct serum potassium.

- Magnesium sulphate, IV, 2 g administered over 5–10 minutes.

If recurrent episodes after initial dose of magnesium sulphate:

- Magnesium sulphate, IV, 2 g administered over 24 hours.

Torsades complicating bradycardia:

- Adrenaline (epinephrine) infusion to raise heart rate to >100 bpm (if temporary pacing unavailable). *LoE:IVb*

REFERRAL

All cases of wide QRS tachycardia, after resuscitation and stabilisation.

3.3.3 HEART BLOCK (SECOND OR THIRD DEGREE)

I44.1/I44.2

DESCRIPTION

The majority of cases occur in patients >60 years of age and are idiopathic, with an excellent long-term prognosis, provided a permanent pacemaker is implanted. Acute, reversible AV block commonly complicates inferior myocardial infarction. Heart block may also be induced by metabolic and electrolyte disturbances, as well as by certain medicines.

GENERAL MEASURES

Emergency cardio-pulmonary resuscitation (if necessary).
External pacemaker should be available in all secondary hospitals and must be preceded by appropriate analgesia.

MEDICINE TREATMENT

Analgesia if external pacemaker:

- Morphine, IM, 10–15 mg 3–6 hourly.

Apply relevant precautions as indicated in Appendix II (i.e. monitoring for response and toxicity).

AV nodal block **with narrow QRS complex escape rhythm only:**

- Atropine, IV bolus, 0.6–1.2 mg.
  - May be repeated as needed until a pacemaker is inserted.
  - Use in patients with inferior myocardial infarct and hypotension and second- degree AV block, if symptomatic.

- It is temporary treatment of complete AV block before referral (urgently) for pacemaker.

OR

For resuscitation of asystole in combination with CPR:

I46.0-1/I46.9+(I44.1-2)

- Adrenaline (epinephrine) 1:10 000, slow IV, 5 mL (0.5 mg).
  - Used as temporary treatment of complete heart block when other medicines are not effective.

REFERRAL

» All cases with a heart rate <40 bpm after resuscitation and stabilisation.
» All cases of 2nd or 3rd degree AV block, whether or not myocardial infarct or other reversible cause is suspected, and whether or not the patient is thought to be symptomatic.
» A permanent pacemaker is the definitive form of treatment. These are only available in tertiary institutions. Refer all symptomatic patients with significant bradyarrhythmias for evaluation.

3.3.4 SINUS BRADYCARDIA

R00.1

DESCRIPTION

This rhythm does not require treatment, unless it is causing symptoms, i.e. syncope, dizziness, tiredness and poor effort tolerance.

Sinus bradycardia <50 bpm or sinus arrest with slow escape rhythm, accompanied by hypotension, strongly suggest a treatable underlying cause such as:

» acute inferior myocardial infarct,
» hyperkalaemia, especially if wide QRS and/or peaked T waves,
» medicines, especially combination of verapamil and ß-blocker or digoxin,
» hypothermia,
» hypoxia, or
» hypothyroidism.

Treat the cause. Consider atropine if inferior myocardial infarct.

3.3.5 SINUS ARREST

I49.5

Refer all urgently to a cardiologist.

3.4 CONGESTIVE CARDIAC FAILURE (CCF)

I50.0

DESCRIPTION

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

Potentially reversible causes include:

- » hypertension
- » thyroid disease
- » valvular heart disease
- » constrictive pericarditis
- » thiamine deficiency
- » ischaemic heart disease
- » haemochromatosis
- » tachycardia

GENERAL MEASURES

Patient and family education.
Monitor body weight to assess changes in fluid balance.
Limit fluid intake to 1–1.5 L/day if fluid overloaded despite diuretic therapy.
Limit alcohol intake to a maximum 2 drinks per day if at all.

LoE:IIIb[lv]

Salt restriction (dietician guided when possible).
Regular exercise within limits of symptoms.
Avoid NSAIDs as these may exacerbate fluid retention.
Counsel that pregnancy may exacerbate heart failure, and some medicines used in treatment of heart failure are contraindicated in pregnancy e.g. ACE-inhibitors, angiotensin-receptor blockers, spironolactone.

LoE:IVb[lvi]

Advise on contraception or refer for such advice.

MEDICINE TREATMENT

Where heart failure is due to left ventricular systolic dysfunction, mortality is significantly reduced by the use of ACE-inhibitors, beta-blockers and spironolactone and every effort should be made to ensure eligible patients receive all these agents in appropriate doses.

Note: All the guideline evidence presented here relates to treatment of patients in whom the heart failure syndrome is due to left ventricular systolic dysfunction and cannot necessarily be extrapolated to patients in whom heart failure is due to other causes of the syndrome.

Digoxin has only been shown to improve symptoms and reduce hospitalisation.

LoE:Ia[lvii]

Diuretic

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

LoE:IIIb[lviii]

- Hydrochlorothiazide, oral, 25–50 mg daily.
  - Caution in patients with gout.

LoE:IIIb[lix]

- Less effective in impaired renal function.
- 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 or hepatic function, loop diuretic:

- Furosemide, oral, daily.
  - Initial dose: 40 mg/day.
  - Higher dosages may be needed, especially if comorbid renal failure.
  - Advise patients to weigh themselves daily and adjust the dose if necessary.

LoE:IVb

Note:

» Unless patient is clinically fluid overloaded, reduce the dose of diuretics before adding an ACE-inhibitor. After introduction of an ACE-inhibitor, try to reduce diuretic dose and consider a change to hydrochlorothiazide.

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

LoE:Ia[ix]

Renin-angiotensin-aldosterone system (RAAS) blockers

- ACE-inhibitor, e.g.:
- Enalapril, oral, 2.5 mg 12 hourly, titrated to 10 mg 12 hourly.
  - In the absence of significant side-effects always try to increase the dose to the level shown to improve prognosis (i.e. 10 mg 12 hourly).

LoE:Ia[ix]

If ACE-inhibitor intolerant, i.e. intractable cough or angio-oedema:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated

Spironolactone

Use with an ACE-inhibitor and furosemide in patients presenting with Class III or IV heart failure.

Do not use if eGFR <30 mL/minute.

Monitoring of potassium levels is essential if spironolactone is used with an ACE-inhibitor or other potassium sparing agent or in the elderly.

- Spironolactone, oral, 25–50 mg once daily.

LoE:IVb[lxii]

Beta-blockers

For all stable patients with heart failure who tolerate it:

Note: Patients should not be fluid overloaded or have a low BP before initiation of therapy.

- Carvedilol, oral.
  - Initial dose: 3.125 mg 12 hourly.

- Increase at 2-weekly intervals by doubling the daily dose until a maximum of 25 mg 12 hourly, if tolerated.

LoE:Ia[lxiii]

- If not tolerated, i.e. worsening of cardiac failure symptoms, reduce the dose to the previously tolerated dose.
- Up-titration should take several weeks or months.
- If > 85 kg: maximum of 50 mg 12 hourly.

LoE:IIIb[lxiv]

Digoxin
Patients in sinus rhythm remaining symptomatic despite the above-mentioned agents (specialist consultation):

- Digoxin, oral, 0.125 mg daily, adjust according to response and trough plasma level.
  - Digoxin trough plasma levels (before the morning dose) should be maintained between 0.6-1 nmol/L.
  - Patients at high risk of digoxin toxicity: the elderly, patients with renal dysfunction, hypokalaemia and patients with low lean body mass.

LoE:IIIb[lxv]

Anticoagulants
Heparin: for DVT prophylaxis for patients admitted to hospital, unless contraindicated: See Section 2.14: Venous thrombo-embolism.

Warfarin: See Section 3.3.1: Narrow QRS complex (supraventricular) tachydysrhythmias.

Anti-dysrhythmic medicines
Only for potentially life-threatening ventricular dysrhythmias. See Section 3.3: Cardiac Dysrhythmias.
Always exclude electrolyte abnormalities and medicine toxicity first.

Thiamine
Consider as a trial of therapy in all unexplained heart failure:

- Thiamine, oral/IM, 100 mg daily for 4 weeks.

Prophylaxis (Z29.2)

- Annual influenza vaccine. See Section 9.2: Adult vaccination.

REFERRAL

» Where specialised treatment and diagnostic work-up is needed and to identify treatable and reversible causes.
» All patients with audible cardiac murmurs should undergo specialist evaluation, as should all patients with potentially reversible causes of the heart failure syndrome and those with persistent and severe symptoms and signs of fluid overload despite adequate doses of diuretic.

» Patients who have LBBB on the ECG are potential candidates for cardiac resynchronization therapy and should be discussed with a specialist. An ECG should be recorded at baseline and repeated at 6-monthly intervals.

3.5 ENDOCARDITIS, INFECTIVE

I33.0

GENERAL MEASURES

Bed rest.

Early surgical intervention in acute fulminant and prosthetic valve endocarditis is often indicated. Consider surgery if there is heart failure, embolism, large vegetations on echocardiography, heart block, evidence of persistent infection despite antibiotics or renal impairment. Refer these patients promptly.

LoE:IVb

MEDICINE TREATMENT

Treat accompanying complications, e.g. cardiac failure. Such treatment should not delay referral.

Antibiotic therapy

» It is essential to do at least 3 blood cultures, taken by separate venipunctures, before starting antibiotics.
» In patients with subacute presentation and no haemodynamic compromise, wait for the results of blood culture before starting antibiotics.
» Empiric treatment (Table 4.6) is indicated in patients with a rapidly fulminant course or with severe disease only.
» Aminoglycoside therapy should be monitored with trough levels for safety.
» Duration of therapy listed is the minimum and may be extended based on the response (clinical and laboratory).
» Severe penicillin-allergic patients (Z88.0), or methicillin resistant staphylococcal infections (U80):

LoE:IVb[lxvi]

- Vancomycin, IV, 15–20 mg/kg 12 hourly, is the antibiotic of choice. W It is essential to monitor trough concentrations of vancomycin regularly and adjust doses, accordingly, starting after the third dose. (See Appendix II for guidance on prescribing and therapeutic drug monitoring.)

Empiric therapy

Native valve	• Ampicillin, IV, 2 g 6 hourly for 4 weeks. A **AND** LoE:IIIb[lxvii] Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks. (See Appendix II, for guidance on prescribing). A **AND** • Cloxacillin, IV, 3 g, 6 hourly. A **OR** Cefazolin, IV, 2 g, 8 hourly. A
Prosthetic valve*	• Vancomycin, IV, 15–20 mg/kg 12 hourly for 6 weeks. (See Appendix II for guidance on prescribing and therapeutic drug monitoring.) W **AND** • Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks. W **AND** LoE:IIIb[lxviii] • Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks. (See Appendix II for guidance on prescribing). A

* All cases of prosthetic valve endocarditis should be referred.

LoE:IIIb[lxix]

Table 3.6: Empiric therapy for valve endocarditis

Directed therapy (native valve)

Streptococcal	
Fully susceptible to penicillin MIC: ≤0.12 mg/L	• Ampicillin, IV, 2 g 6 hourly for 4 weeks. A **OR** Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks. A
Moderately susceptible MIC: >0.12–2 mg/L	• Ampicillin, IV, 2 g 6 hourly for 4 weeks. A **OR** Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks. A **AND** LoE:IIIb[lxx] • Gentamicin, IV, 3 mg/kg daily for 2 weeks (see Appendix II for guidance on prescribing). A

Fully resistant MIC: ≥4 mg/L	• Vancomycin, IV, 15–20 mg/kg 12 hourly for 6 weeks. W **AND** • Gentamicin, IV, 3 mg/kg daily for 6 weeks (see Appendix II for guidance on prescribing). A *LoE:IIIb*[lxxi]
Enterococcal	
Susceptible to penicillin	• Ampicillin, IV, 2 g 6 hourly for 4-6 weeks. A **OR** Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4-6 weeks. A ○ 6 weeks of therapy may be required in cases with a history of >3 months, or when the regimen is combined with ceftriaxone. **AND** • Gentamicin, IV, 3 mg/kg daily for 2-6 weeks. A ○ 6 weeks of therapy may be required in cases with a history of >3 months (see Appendix II for guidance on prescribing). Check high level gentamicin susceptibility before prescribing. *LoE:IIIb*[lxxii] **OR** *LoE:IIIb*[lxxiii] • Ceftriaxone 2 g 12-hourly for 6 weeks. W
Penicillin-resistant MIC ≥ 4 mg/L **or** *significant β-lactam allergy*	Refer.
Staphylococcal	
Cloxacillin-susceptible (methicillin-susceptible)	• Cloxacillin, IV, 3 g, 6 hourly for 4 weeks. A *LoE:IIIb*[lxxiv] **OR** Cefazolin, IV, 2 g, 8 hourly for 4 weeks. A
Cloxacillin-resistant (methicillin resistant) or methicillin sensitive with significant beta-lactam allergy	• Vancomycin, IV, 15–20 mg/kg 12 hourly for 4 weeks. W

LoE:IIIb[lxxv]

Table 3.7.: Directed therapy for valve endocarditis

Directed therapy for prosthetic valve endocarditis
Duration of therapy is usually a minimum of at least 6 weeks.
Seek expert opinion on antibiotic choice and the need for referral for repeat cardiac surgery early in the course of treatment.

Endocarditis prophylaxis
Cardiac conditions
Patients with the following cardiac conditions are at high risk of developing infective endocarditis:
» Acquired valvular heart disease with stenosis or regurgitation.
» Patients with prosthetic heart valves.
» Structural congenital heart disease, including surgically corrected or palliated structural conditions, but excluding isolated atrial septal defect, fully repaired ventricular septal defect or fully repaired patent ductus arteriosus.
» Patients who have suffered previous endocarditis.

Procedures requiring prophylaxis
Antibiotic prophylaxis is recommended for all dental procedures that involve manipulation of either the gingival tissue or the peri-apical region of the teeth.
Antibiotic prophylaxis is not recommended for patients who undergo a gastro-intestinal or genitourinary procedure.

Prophylaxis (Z29.2)
Maintain good dental health.
This is the most important aspect of prophylaxis.
Refer all patients to a dental clinic/dental therapist for assessment and ongoing dental care.

- Amoxicillin, oral, 2 g one hour before the procedure. A

<u>If patient cannot take oral:</u>

- Ampicillin, IV/IM, 2 g one hour before the procedure. A

<u>Severe penicillin allergy:</u> (Z88.0)

- Clindamycin, oral, 600 mg one hour before the procedure. A

<u>If patient with severe penicillin allergy cannot take oral:</u>

- Clindamycin IV, 600 mg one hour before the procedure. A

LoE:IIIb[lxxvi]

Note: The NICE review noted the lack of a consistent association between interventional procedures and development of infective endocarditis, and that the efficacy of antibiotic prophylaxis is unproven. It further commented that because the antibiotic is not without risk, there is a potential for a greater mortality from severe hypersensitivity than from withholding antibiotics.

It is very difficult to extrapolate from these guidelines to a South African situation where good dental hygiene may be lacking and valvular heart disease is common. Practitioners need to weigh the risk of the underlying heart disease (particularly previous successfully treated endocarditis) and the essential need for ongoing antibiotic stewardship.

3.6 HYPERTENSION

I10

KEY POINTS

Hypertension control has significant benefit for patients. Detect and treat co-existent risk factors. Assess cardiovascular risk (see Figure 4.1). Lifestyle modification and patient education is essential for all patients.

Classification of hypertension based on office blood pressure			
Category	***Systolic (mmHg)***		***Diastolic (mmHg)***
Normal BP	<130	and	<85
High - Normal	130 - 139	and/or	85 - 89
Mild	140 - 159	and/or	90 - 99
Moderate	160 - 179	and/or	100 - 109
Severe	≥ 180	and/or	≥ 110

LoE:IIIb[lxxvii]

Table 3.8: Classification of hypertension (office-based blood pressures)

Medicine treatment is needed for SBP ≥140 mmHg and DBP ≥90 mmHg that remains elevated despite lifestyle modification.

LoE:IIb[lxxviii]

See medicine treatment choices below.

Immediate medicine treatment is needed for DBP ≥110 mmHg and/or SBP ≥180 mmHg (defined as severe hypertension - see Sections 3.6.1, 3.6.2 and 3.6.3) or for patients with 3 or more risk factors, hypertension mediated organ damage (HMOD) and/or associated clinical conditions.

Patients should be evaluated for cardiovascular risk factors, HMOD and associated clinical conditions.

Other major risk factors for ischaemic cardio- and cerebrovascular disease (see Section 3.1: Ischaemic heart disease and atherosclerosis, prevention).

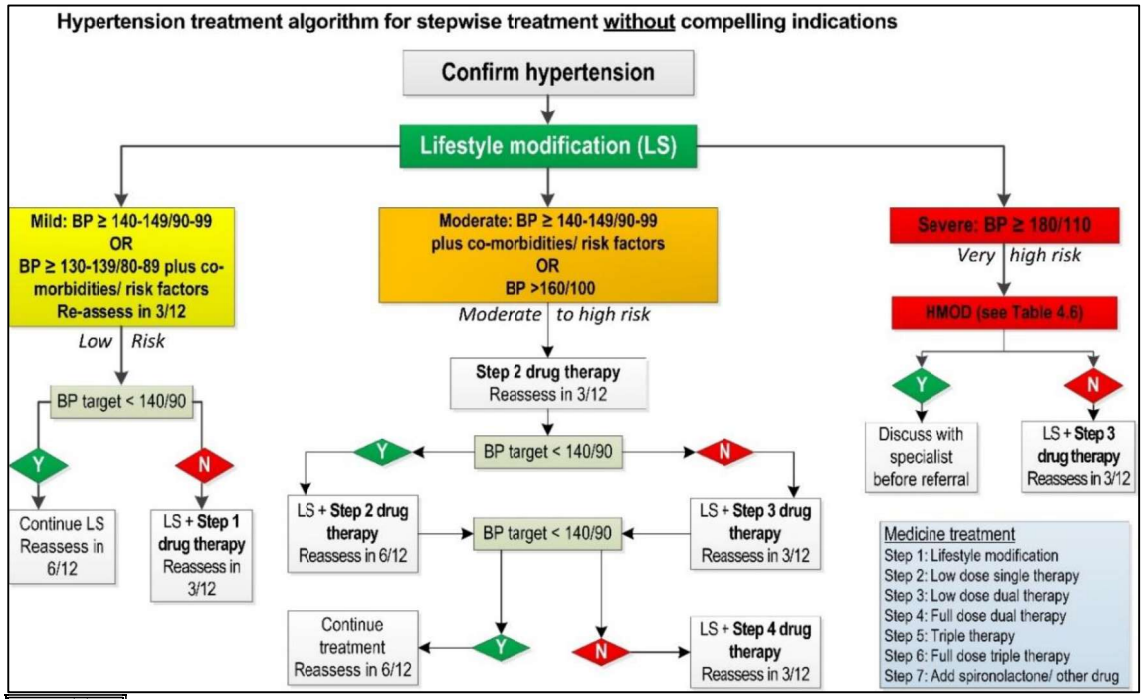
Hypertension mediated organ damage:
» left ventricular hypertrophy,
» hypertensive retinopathy,
» microalbuminuria, or positive dipsticks for albuminuria or elevated albumin/creatinine ratio, or
» elevated creatinine level (or eGFR <60 mL/minute).

Associated clinical conditions:
» ischaemic heart disease,

» heart failure,
» stroke or transient ischaemic attack,
» chronic kidney disease,
» peripheral arterial disease.

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 3.1: 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.



LoE:IIIb[xxx]

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

Figure 3.2: Algorithm for the stepwise approach of treating hypertension without compelling indications

Investigations

If overweight, record body weight and waist circumference at each visit when BP is measured. Central obesity is defined as waist circumference:

» >102 cm in men, and
» >88 cm in women.

Do urine test strip analysis for protein, blood and glucose at presentation.

» If normal, repeat urine test strip every 6 months.
» If abnormal, do spot urine ACR. Repeat yearly.
» If haematuria >1+, investigate further.
» If glycosuria, exclude diabetes mellitus.

Other investigations at presentation:

» If known diabetic, HbA1c.
» Random total cholesterol.
» Perform a resting ECG to exclude left ventricular hypertrophy or ischaemia.
» Assess renal function (serum creatinine and eGFR).

Goals of treatment

Aim for SBP <140 mmHg and DBP <90 mmHg.

GENERAL MEASURES

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 18.5 kg/m^2 to 25 kg/m^2. Weight reduction *LoE:IVb*[lxxx] in the overweight patient.
» 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. (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 adequate fresh fruit and vegetables. Dietician's advice recommended.
» Regular moderate aerobic exercise, e.g. 30 minutes brisk walking 5-7 times/week (150 minutes/week).

MEDICINE TREATMENT

Initial medicine choice in patients qualifying for treatment is dependent on the presence of compelling indications (see Table 3.9); the severity of the elevated BP; and the presence of target organ damage, cardiovascular risk factors, and associated clinical conditions.

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 may improve adherence and such agents should be used when they are available.

LoE:IIIb[lxxxi]

» Monitor patients monthly and adjust therapy, if necessary, until the BP is controlled.

» After target BP is achieved, patients can be seen at 3–6 monthly intervals.

MEDICINE TREATMENT CHOICES WITHOUT COMPELLING INDICATIONS

Stepped-care approach to BP treatment

Note:

» In low risk (high-normal or mild hypertensive patents) lifestyle intervention may be considered initially, for 3-6 months.

» If lifestyle modification failed to achieve BP control: counsel patient on the risk of major cardiovascular events associated with elevated BP; and initiate monotherapy.

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

LoE:IIIb[lxxxii]

remaining on monotherapy and/or suboptimal doses.

» The timing of the dose 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.

» In 60–80% of patients a combination of antihypertensive therapy is needed. Combination therapy, i.e. hydrochlorothiazide plus a calcium channel blocker or ACE-inhibitor should be considered at the outset in patients with BP >160/100 mmHg. Refer to Figures 4.1 and 4.2, above.

» Initiate combination medicine therapy in cases of severe hypertension (see Section 3.6.1) and hypertension urgency (see Section 3.6.2).

BP 140-159/90-99 mmHg:

» < 3 risk factors, no target organ damage or associated clinical conditions:

– Lifestyle modification for 3–6 months.

– Start antihypertensive therapy with a single medicine if target BP not achieved.

» ≥3 risk factors, target organ damage and/or associated clinical conditions:
  – Start antihypertensive therapy immediately (together with lifestyle modification).

BP 160-179/100-109 mmHg:

» Even in absence of risk factors, or target organ damage or associated clinical conditions:
  – Start antihypertensive therapy (together with lifestyle modifications) with a combination of two medicines.

BP ≥180/100 mmHg: this is severe hypertension: see Sections 3.6.1, 3.6.2 and 3.6.3.

Initial antihypertensive medicine:

- thiazide/thiazide-like diuretic e.g.:
- Hydrochlorothiazide, oral, 12.5 mg daily.
  - Caution in patients with gout.
  - Less effective in impaired renal function.
  - Caution in patients with a history or family history of skin cancer; and counsel all patients on sun avoidance and sun protection.

LoE:IIIb[lxxxiii]

If target BP is not reached after one month despite adequate adherence (or immediately in patients with BP 160-179/100-109 mmHg), add one of the following: ACE-inhibitor or calcium channel blocker.

ADD

- Long-acting calcium channel blocker, e.g.:

LoE:IIa[lxxxiv]

- Amlodipine, oral, 5 mg daily.

OR

- ACE-inhibitor, e.g.:

LoE:IIIb[lxxxv]

- Enalapril, oral, 10 mg daily.

If ACE-inhibitor intolerant, i.e. intractable cough:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50 mg daily. Specialist initiated.

If target BP is still not achieved after one month despite adequate adherence, increase the dose of medication, one medicine every month, to their maximal levels: amlodipine 10 mg daily, enalapril 20 mg daily (losartan 100 mg daily) hydrochlorothiazide 25 mg daily.

If target BP is not reached after one month despite adequate adherence on two medicines, add one of ACE-inhibitor or calcium channel blocker,

whichever has not already been used.

If target BP is not reached after one month despite adequate adherence:
ADD

LoE:Ia[lxxxvi]

- Spironolactone, oral 25–50 mg daily.

For refractory hypertension:
ADD

LoE:IIb[lxxxvii]

- Beta-blocker, e.g.:
- Atenolol, oral, 50 mg daily.

Medicine treatment choices with compelling indications

Compelling indications	Medicine class
Angina	Beta-blocker Calcium channel blocker
Post myocardial infarction	Beta-blocker ACE-inhibitor
Heart failure	ACE-inhibitor Carvedilol Spironolactone Hydrochlorothiazide or furosemide
Left ventricular hypertrophy	ACE-inhibitor
Stroke	Hydrochlorothiazide Calcium channel blocker
Diabetes type 1 or 2 with/without evidence of microalbuminuria or proteinuria	ACE-inhibitor, usually in combination with a diuretic
Chronic kidney disease	ACE-inhibitor, usually in combination with a diuretic
Isolated systolic hypertension	Hydrochlorothiazide Calcium channel blocker
Pregnancy	See Chapter 6: Obstetrics.

Table 3.9: Medicine treatment choices with compelling indications

CAUTION
Lower BP over a few days.
A sudden drop in BP can be dangerous, especially in the elderly.
BP should be controlled within 1–3 months.

Assess for risk of ischaemic disease. See Section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

REFERRAL

Referrals or consultation with a specialist are indicated when:

» Patients are adherent to therapy, and BP is resistant i.e., >140/90 mmHg, while on medicines from 3-4 different classes at appropriate doses, one of which is a diuretic.
» All cases where secondary hypertension is suspected.
» Complicated hypertensive urgency e.g. malignant/accelerated hypertension, severe heart failure with hypertension and hypertensive emergency.

3.6.1 HYPERTENSION, ASYMPTOMATIC SEVERE

I10

DESCRIPTION

These patients have severe hypertension (DBP ≥110 mmHg and/or SBP ≥180 mmHg), are asymptomatic and have no evidence of acute target organ damage.

Keep the patient in the care setting and repeat BP measurement after resting for 1 hour.

If the second measurement is still elevated at the same level, start oral therapy using two medicines together, one of which should be low dose hydrochlorothiazide. The second medicine is either a long-acting calcium channel blocker, e.g., amlodipine, or an ACE-inhibitor, e.g. enalapril.

Follow up carefully and refer as needed.

3.6.2 HYPERTENSIVE URGENCY

I10

DESCRIPTION

Severe hypertension (DBP ≥110 mmHg and/or SBP ≥180 mmHg) which is **symptomatic** and/or with evidence of acutely progressive target organ damage. There are no immediate life threatening neurological or cardiac complications such as are seen in the hypertensive emergencies.

> Do not lower BP in acute stroke or use antihypertensive medication unless SBP >220 mmHg or the DBP >120 mmHg, as a rapid fall in BP may aggravate cerebral ischaemia and worsen the stroke – see Section 14.1.1: Stroke.

Treatment may be given orally but in patients unable to swallow, use parenteral medicines.

MEDICINE TREATMENT

Ideally, all patients with hypertensive urgency should be treated in hospital. Commence treatment with two oral agents and aim to lower the DBP to 100 mmHg slowly over 48–72 hours. Specialist should be consulted.

This BP lowering can be achieved by:

- Long-acting calcium channel blocker.
- ACE-inhibitor.

Note: Avoid if there is severe hyponatraemia, i.e. serum Na <130 mmol/L.

- Spironolactone.
- Beta-blocker.

Diuretics may potentiate the effects of the other classes of medicines when added. Furosemide should be used if there is renal insufficiency or signs of pulmonary congestion.

3.6.3 HYPERTENSIVE CRISIS, HYPERTENSIVE EMERGENCY

I10

DESCRIPTION

This is a **life-threatening situation** that requires immediate lowering of BP usually with parenteral therapy. Grade 3-4 hypertensive retinopathy is usually present, together with impaired renal function and proteinuria.

The true emergency situation should preferably be treated by a specialist.

Life-threatening complications include:

» Hypertensive encephalopathy, i.e. severe headache, visual disturbances, confusion, seizures and coma that may result in cerebral haemorrhage.
» Unstable angina or myocardial infarction.
» Acute left ventricular failure with severe pulmonary oedema (extreme breathlessness at rest).
» Eclampsia and severe pre-eclampsia.
» Acute kidney failure with encephalopathy.
» Acute aortic dissection.

MEDICINE TREATMENT

Admit the patient to a high care setting for intravenous therapy and close monitoring. Do not lower the BP by >25% within 30 minutes to 2 hours.
In the next 2–6 hours, aim to decrease the BP to 160/100 mmHg.
This may be achieved by the use of intravenous or oral medicines.

Intravenous therapy

- Labetalol, IV, 2 mg/minute to a total dose of 1–2 mg/kg, while trying to achieve control with other agents.

- Caution in acute pulmonary oedema.

OR

If myocardial ischaemia and CCF:

- Glyceryl trinitrate, IV, 5–10 mcg/minute.
  - Refer to dosing table in Section 3.2.1: ST elevation myocardial infarction (STEMI).

AND

- Furosemide, IV, 40–80 mg.
  - Duration of action: 6 hours.
  - Potentiates all of the above medicines.

Oral therapy

- ACE-inhibitor, e.g.:
- Enalapril, oral, 2.5 mg as a test dose.
  - Increase according to response, to a maximum of 20 mg daily.
  - Monitor renal function.

If ACE-inhibitor intolerant, i.e. intractable cough or angio-oedema:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated.

3.7 RHEUMATIC HEART DISEASE

I01.0-2/I01.8-9, I02.0, I05, I05.1, I06.0-2, I06.8-9, i09.0-2/I09.8-9

DESCRIPTION

These are chronic sequelae of rheumatic fever consisting of valvular damage, usually involving left heart valves, with progression and complications.

GENERAL MEASURES

Acute stage of rheumatic fever: bed rest and supportive care.

MEDICINE TREATMENT

Acute rheumatic fever

For eradication of streptococci in throat:

- Benzathine benzylpenicillin (depot formulation), IM, 1.2 MU as a single dose. A

  LoE:IIIb[lxxxviii]

  - 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.

OR

LoE:IIb[lxxxix]

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

Severe penicillin allergy: (Z88.0) LoE:IIIa[xc]

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

For arthritis and fever: LoE:IVb

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

Prevention of recurrent rheumatic fever

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: LoE:IVb[xci]

» Treat lifelong.

- Benzathine benzylpenicillin (depot formulation), IM, 1.2 MU every 3–4 weeks (preferred treatment). A
  - 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.

OR LoE:IIIb[xcii]

- Phenoxymethylpenicillin, oral, 250 mg 12 hourly. A LoE:IVb

OR

- Amoxicillin, oral, 250 mg daily. A LoE:IVb

Severe penicillin allergy: (Z88.0)

- Macrolide, e.g.:
- Azithromycin, oral, 250 mg daily. W

Prophylaxis for infective endocarditis

See Section 3.5: Endocarditis, infective.

REFERRAL

» Any patient with rheumatic valvular heart disease who requires a significant dose of diuretic to control fluid overload or who has had an episode of pulmonary oedema should be discussed with a specialist and referred for possible valve surgery.

» Pregnancy poses a particular problem in women with symptomatic rheumatic valvular heart disease, and all should be referred for specialist consultation.

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SOUTH AFRICAN NATIONAL DEPARTMENT OF HEALTH
NEMLC SUMMARY REPORT ON UPDATES MADE TO THE
THE STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINE LIST GUIDANCE PRODUCTS
AHC Chp 3 Cardiovascular System (CVS)

Document Version Control

Report Version	Date	Detail
V1.0	*14/08/2026*	• *Updates to statins and DOACs in response to latest HP09 tender*

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 3.1 Ischaemic heart disease and atherosclerosis, prevention	√	√			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 statin-related muscle pain	Added	Yes

	√	√			Simvastatin 10mg, oral – secondary prevention for statin-related muscle pain	Retained	Yes
Section 3.2.1 ST elevation myocardial infarction (STEMI)	√	√			Oxygen supplementation	Guidance amended	No
Section 3.3.1.1 Atrial fibrillation		√			DOACs e.g. rivaroxaban 20mg, oral	Added	Yes
		√			Apixaban 5mg, oral	Added to TI database	Yes
		√			Dabigatran 150mg, oral	Added to TI database	Yes
Section 3.3.1.1 Atrial fibrillation – non-valvular		√			Warfarin 5mg, oral	Retained	No
Section 3.4 Congestive cardiac failure					SGLT2 inhibitors	Not added	

*Therapeutic Interchange

Report V1.0
AH Cardiovascular System Chapter 3

Section 3.1 ISCHAEMIC HEART DISEASE AND ATHEROSCLEROSIS, PREVENTION

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:

<table>
<tr>
<td>AMENDED FROM:

Management is based on the patient's 10-year risk of a cardiovascular event:
– <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.

Note:
» Lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.
▪ HMGCoA reductase inhibitors (statins), according to table below:</td>
<td>AMENDED TO:

Management is based on the patient's 10-year risk of a cardiovascular event:
– <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.

Note:
» Lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.
▪ HMGCoA reductase inhibitors (statins), according to table below:

<table>
<tr><th>INDICATION</th><th>HMGCOA REDUCTASE INHIBITOR (STATIN) DOSE</th></tr>
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</td>
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</table>

[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.

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. » ≥ 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.

Table 3.1: Management with HMGCoA reductase inhibitors
Note: Lipid-lowering medicines must always be used in conjunction with ongoing lifestyle modification.

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.

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.
» 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 3.1: Management with HMGCoA reductase inhibitors
Note: Lipid-lowering medicines must always be used in conjunction with ongoing lifestyle modification.

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.

» 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. » 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.	» 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 VIII: 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 3.1 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 AH chapter. Additionally, the table below detailing NEMLC approved comparative dosing of statins has been included in the newly developed Appendix VIII: 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		20mg	80mg	PI: Max dose 10mg/day**
Pravastatin	20mg	80mg		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		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 3.2 Acute coronary syndromes

Section 3.2.1 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]

An additional caution has been added advising against the use of oxygen if the patient is not hypoxic, in accordance with the previously ratified NEMLC review[4].

STG guidance has been amended as tabulated below:

AMENDED FROM	**AMENDED TO:**
3.2.1 ST elevation myocardial infarction (STEMI) I21.0-I21.3/I21.9/I22.0-1/I22.8-9	**3.2.1 ST elevation myocardial infarction (STEMI) I21.0-I21.3/I21.9/I22.0-1/I22.8-9**
MEDICINE TREATMENT **Note:** The following guidance is not for primary percutaneous coronary intervention (PCI). **MEDICINE TREATMENT** **Note:** The following guidance is not for primary percutaneous coronary intervention (PCI). • Oxygen if saturation <94%.	**MEDICINE TREATMENT** **Note:** The following guidance is not for primary percutaneous coronary intervention (PCI). • Oxygen if saturation <90%, or shock. **CAUTION** Do not administer oxygen if the patient is not hypoxic as evidence indicates that liberal oxygen therapy does not improve patient-important outcomes and may actually increase mortality.

Interaction between clopidogrel and proton pump inhibitors (PPIs)

In response to an external comment received on the clinical significance of the drug-drug interaction (DDI) between clopidogrel and omeprazole (*PPI awarded on the most recent HP09 tender circular*[5]), the NEMLC recommendation is as follows:

DDI: Clopidogrel and omeprazole

- A pharmacological interaction between omeprazole and clopidogrel has been reported in the literature, i.e. omeprazole inhibits the cytochorome P450 (CYP) 2C19 enzyme thus inhibiting the bioactivation of clopidogrel, prompting medicine regulatory authorities to advise against the concomitant use of clopidogrel and omeprazole[6].
- Since then, several RCTs and observational studies were published to assess the clinical significance of this interaction.
- Outcomes from a recent systematic review and meta-analysis assessed the risk of CV events with the concomitant use of clopidogrel and PPIs[7], and concluded that the concurrent use of PPIs with clopidogrel

[3] 2023 ESC guidelines for the management of acute coronary syndromes. 25 Aug 2023.
[4] NEMLC evidence review. Oxygen therapy for ST elevated myocardial infarction. 22 Feb 2022.
[5] P09-2026SD: supply and delivery of solid dosage forms to the Department of health for the period 1 May 2026 to 30 April 2029.
[6] US Food and Drug Administration, Plavix Prescribing Information, 2022 and European Medicines Agency, Plavix Summary of Product Characteristics, 2008.
[7] Axelsson MAB, Parodi López N, Wikström Jonsson E, Wallerstedt SM. Efficacy and Safety of Clopidogrel With and Without a Proton Pump Inhibitor: A Systematic Review and Meta-Analysis. Basic Clin Pharmacol Toxicol. 2025 Aug;137(2):e70087. doi: 10.1111/bcpt.70087. PMID: 40685887; PMCID: PMC12277936.

probably does not largely affect the risk of CV events, but probably reduces the risk of overt GI bleeding. Importantly, these results are mainly applicable to dual antiplatelet therapy (DAPT) i.e. aspirin + clopidogrel. The authors were unable to draw conclusions regarding the safety and efficacy of omeprazole versus other PPIs due to very low certainty evidence.

- The lack of reported adverse CV effects related to the concurrent use of clopidogrel and PPIs is noted in several international clinical guidelines, such as the American Heart Association guideline for chronic coronary artery disease[8], the ESC Guidelines for the Management of Acute Coronary Syndromes[9], American college of Gastroenterology Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease.[10]

The NEMLC therefore recommends that the use of omeprazole as the current PPI on tender, not be limited in patients on clopidogrel when used as DAPT in accordance with the STG recommendations.

Section 3.3.1.1 Atrial fibrillation

Direct-acting oral anticoagulants (DAOCs) – treatment of atrial fibrillation: Added
Rivaroxaban: Added as example of a therapeutic alternative
Warfarin – treatment of atrial fibrillation for patients in whom DOACs not clinically appropriate: Retained

Following the price reduction of rivaroxaban as included in the most recent HP09 contract circular[11], NEMLC has extended the STG indications for rivaroxaban to the management of atrial fibrillation. This is an update to the previous NEMLC recommendation (2020-4 review cycle)[12], where the use of DOACs for the management of atrial fibrillation was not supported, based on medicine costs at the time[13].

STG updates as tabulated below:

AMENDED FROM:	**AMENDED TO:**
3.3.1.1 ATRIAL FIBRILLATION I48.0-I48.2/I48.9	3.3.1.1 ATRIAL FIBRILLATION I48.0-I48.2/I48.9
Acute onset (<48 hours) Assess clinically, e.g.: heart failure, mitral stenosis, thyrotoxicosis, hypertension, age and other medical conditions. Consider anticoagulation with warfarin (see table below on CHA_2DS_2-VASc Score). Synchronised direct current (DC) cardioversion is occasionally necessary in haemodynamic instability.	**DEFINITION** Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial electrical activation and chaotic, ineffective atrial contraction. On ECG, it is defined by the absence of distinct P waves and replacement with irregular fibrillatory waves alongside an irregularly irregular ventricular response. Risk factors

[8] Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. Circulation. 2023; 148:e9-e119
[9] Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur Heart J. 2023; 44:3720–3826
[10] Katz PO, Dunbar KB, Schnoll-Sussman FH, et al. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. Am J Gastroenterol. January 2022; 117(1):p 27-56
[11] HP09-2026SD: supply and delivery of solid dosage forms to the Department of Health for the period 01 May 2026 to 30 April 2029. (Ref: HP09-2026SD)
[12] NDoH evidence summary. DOACS for chronic non-valuvular atrial fibrillation_8 December 2022_final.
[13] NDoH Pharmacoeconomics and Budget impact analysis: rivaroxaban for stroke prevention in AF. 8 Dec 2022.

Non-acute/chronic (>48 hours)
As above, but not immediate DC cardioversion, unless there is haemodynamic instability.

MEDICINE TREATMENT
The main aims of therapy for patients with atrial fibrillation should be:

1. Reduction of stroke and systemic embolic risk.
2. Rate or rhythm control.
3. Relief of symptoms attributed to the atrial fibrillation.

A simple scoring system allows calculation of risk of stroke in patients with non-valvular atrial fibrillation.

A simple scoring system allows calculation of risk of stroke in patients with non-valvular atrial fibrillation.
CHA_2DS_2-VASc Score:

Risk Factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75 years of age	2
Diabetes mellitus	1
Stroke/TIA/Thromboembolism	2
Vascular disease	1
Age 65–74 years of age	1
Sex (female gender)	1

Table 3.4: CHA_2DS_2-VASc Score
Source: Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest. 2010 Feb;137(2):263-72. http://www.ncbi.nlm.nih.gov/pubmed/19762550

» When the score is ≥2, use warfarin or equivalent. The higher the score the greater the risk of stroke and therefore the more compelling the use of effective anticoagulation.
» **Note:** This score has been developed on patients with non-valvular atrial fibrillation and may not be applicable to patients with atrial fibrillation and rheumatic mitral valve disease. Anticoagulation has not been tested in this population, but most authorities favour anticoagulation.

HAS-BLED Score:
The potential risk for bleeding needs to be assessed using the HAS-BLED score when initiating oral anticoagulation therapy.

Risk factor and definitions		Score
H	Uncontrolled hypertension » SBP >160 mmHg	1
A	Abnormal renal and/or hepatic function » Dialysis, transplant, serum creatinine >200 mmol/L, cirrhosis, bilirubin >2xULN, AST/ALT/ALP >3xULN	1 point each
S	Stroke » Previous ischaemic or haemorrhagic stroke[a]	1
B	Bleeding history or predisposition » Previous major haemorrhagic, anaemia, severe thrombocytopenia	1
L	Labile INR » TTR ≤60% in patient receiving warfarin	1
E	Elderly » Aged >65 years or extreme frailty	1

– Hypertension - Physical Inactivity
– Cardiac failure - Hyperthyroidism
– Diabetes Mellitus - Advancing age
– Obesity - Male sex
– Obstructive sleep apnoea -Genetics

MEDICINE TREATMENT

Acute onset (<48 hours)
» Assess clinically, e.g., heart failure, mitral stenosis, thyrotoxicosis, hypertension, age and other medical conditions.
» Consider anticoagulation with warfarin (see table below on CHA_2DS_2-VASc Score).
» Synchronised direct current (DC) cardioversion is occasionally necessary in haemodynamic instability.

Non-acute/chronic (> 48 hours)
As above, but not immediate DC cardioversion, unless there is haemodynamic instability.

The main aims of therapy for patients with atrial fibrillation should be:

1. Reduction of stroke and systemic embolic risk.
2. Rate or rhythm control.
3. Relief of symptoms attributed to the atrial fibrillation.

A simple scoring system allows calculation of risk of stroke in patients with non-valvular atrial fibrillation.

Table 3.4: CHA_2DS_2-VASc Score:

Risk Factor	Score
Congestive heart failure/ Left ventricular dysfunction	1
Hypertension	1
Age ≥ 75 years of age	2
Diabetes mellitus	1
Stroke/TIA/Thromboembolism	2
Vascular disease	1
Age 65**–**74 years of age	1
Sex **C**ategory (female gender)	1

Source: Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest. 2010 Feb;137(2):263-72.
http://www.ncbi.nlm.nih.gov/pubmed/19762550

» When the score is ≥ 2, use DOAC, warfarin, or equivalent. The higher the score, the greater the risk of stroke and therefore the more compelling the use of effective anticoagulation.
» **Note:** The CHA_2DS_2-VASc risk stratification tool applies specifically to non-valvular atrial fibrillation. Due to the high baseline risk of thromboembolism in patients with atrial fibrillation and rhematic mitral valve disease, long-term anticoagulation (preferably warfarin) is advisable, irrespective of risk score.

Table 3.5: HAS-BLED Score:
The potential risk for bleeding needs to be assessed using the has-bled score when initiating oral anticoagulation therapy.

Risk factor and definitions		Score
H	**Uncontrolled hypertension** » **Sbp > 160 mmhg**	**1**
A	Abnormal renal function » **Dialysis, transplant, serum creatinine > 200 mmol/l**	**1 point for renal, 1**

D	Drugs or excessive alcohol » Concomitant use of antiplatelet or NSAID, excessive alcohol per week	1 point each
Maximum score		9

Table 3.5: HASBLED Score

a: Haemorrhagic stroke would also score 1 point under the "B" criterion.

b: Only relevant if patient receiving warfarin or other vitamin K antagonists

c: Alcohol excess/abuse refers to a high intake (e.g. >14 units per week) where the clinician assesses there would be an impact on health or bleeding risk

Source: Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al.; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021 Feb 1;42(5):373-498. https://pubmed.ncbi.nlm.nih.gov/32860505/

» The formal assessment of bleeding risk identifies modifiable bleeding risk factors that should be managed, and patients should be assessed at every visit.
» The higher the score the greater the risk of bleeding.
» A high bleeding risk score should not lead to withholding oral anticoagulation therapy.

Initial therapy aimed at stroke reduction
Anticoagulate with warfarin:

- Warfarin, oral, 5 mg daily.
  - INR should be done after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to initiation dosing tables in Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to maintenance dosing tables in Appendix II).
  - Every effort should be made to keep the time in therapeutic range (TTR) >65%. If TTR ≤65% there is less benefit of warfarin therapy and a greater risk of stroke and haemorrhage.

See Appendix II for guidance on calculating TTR for management with warfarin.

For therapy aimed at rate control

- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

OR

If in CCF: (I50.0)

- Carvedilol, oral. See Section 3.4: Congestive cardiac failure.

AND

If control not adequate add:

- Digoxin, oral, 0.125 mg daily, adjust according to rate response and trough plasma level
  - Digoxin trough plasma levels (before the morning dose) should be maintained between 0.6-1 nmol/L.
  - Patients at high risk of digoxin toxicity: the elderly, patients with renal dysfunction, hypokalaemia, and patients with low lean body mass.

	Abnormal hepatic function » **Cirrhosis, bilirubin >2XULN, AST/ALT/ALP >3XULN**	**for hepatic**
S	Stroke[a] » **Previous ischaemic or haemorrhagic stroke**	**1**
B	Bleeding history or predisposition[a] » **Previous major haemorrhagic, anaemia, severe thrombocytopenia**	**1**
L	Labile INR[b] » **TTR ≤ 60% in patient receiving warfarin**	**1**
E	Elderly » **Aged > 65 years or extreme frailty**	**1**
D	Drugs predisposing to bleeding » **Concomitant use of antiplatelet or NSAID**	**1 point for drugs, 1 for alcohol**
	Alcohol use[c] » **Excessive alcohol per week**	
Maximum score		9

A: HAEMORRHAGIC STROKE WOULD SCORE 1 ADDITIONAL POINT UNDER THE "B" CRITERION FOR BLEEDING HISTORY OR PREDISPOSITION.

B: ONLY RELEVANT IF PATIENT RECEIVING WARFARIN OR OTHER VITAMIN K ANTAGONISTS

C: ALCOHOL EXCESS/ABUSE REFERS TO A HIGH INTAKE (E.G. >14 UNITS PER WEEK) WHERE THE CLINICIAN ASSESSES THERE WOULD BE AN IMPACT ON HEALTH OR BLEEDING RISK

***SOURCE:* HINDRICKS G, POTPARA T, DAGRES N, ARBELO E, BAX JJ, BLOMSTRÖM-LUNDQVIST C ET AL; ESC SCIENTIFIC DOCUMENT GROUP. 2020 ESC GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF ATRIAL FIBRILLATION DEVELOPED IN COLLABORATION WITH THE EUROPEAN ASSOCIATION FOR CARDIO-THORACIC SURGERY (EACTS): THE TASK FORCE FOR THE DIAGNOSIS AND MANAGEMENT OF ATRIAL FIBRILLATION OF THE EUROPEAN SOCIETY OF CARDIOLOGY (ESC) DEVELOPED WITH THE SPECIAL CONTRIBUTION OF THE EUROPEAN HEART RHYTHM ASSOCIATION (EHRA) OF THE ESC. EUR HEART J. 2021 FEB 1;42(5):373-498. DOI: 10.1093/EURHEARTJ/EHAA612. PMID: 32860505.**

» The HAS-BLED assessment identifies modifiable bleeding risk that can be managed. Patients should therefore be assessed at every visit.
» The higher the score, the greater the risk of bleeding. However, a high HAS-BLED score **is not a contraindication** for oral anticoagulation.
» Instead, use the HAS-BLED score to identify and correct modifiable bleeding risks (e.g., control blood pressure, stop unnecessary NSAIDs/aspirin, advise reduced alcohol use), and to schedule more frequent clinical reviews.

Initial therapy aimed at stroke reduction

1. Anticoagulation

a) Non-valvular atrial fibrillation:

- Direct-acting oral anticoagulant (DOAC), e.g.:
- Rivaroxaban, oral, 20 mg daily with food.
  - Reduce dose in moderate renal impairment (eGFR 30–50mL/min) to 15 mg daily.

Drug-drug interactions with rivaroxaban

Some common drug interactions with rivaroxaban are listed below. Evidence on potential drug-drug interactions is still evolving, so consult the latest literature if uncertain of potential drug interactions. The risk of some drug interactions may be increased in patients with renal impairment and require careful anticoagulation risk assessment.

Medicine groups	Interaction information	Recommendation

If beta-blockers are contra-indicated, e.g. asthma or severe peripheral vascular disease:

- Verapamil, oral, 40–120 mg 8 hourly.
  - Titrate against ventricular rate (verapamil is negatively inotropic, therefore avoid in heart failure due to LV dysfunction).

If not controlled on these agents, refer to specialist for consideration of alternative therapy, e.g.: amiodarone or atrioventricular node ablation and pacemaker insertion.

DC cardioversion may be needed in selected cases, after 4 weeks effective warfarin anticoagulation.

Long-term therapy

Continue warfarin anticoagulation long-term, unless contra-indicated:

- Warfarin, oral, 5 mg daily.
  - Control with INR to therapeutic range:
    - INR between 2–3 and patient stable: monitor every 2 months.
    - INR <1.5 or >3.5: monitor monthly.

CAUTION

Warfarin use requires regular INR monitoring and dose adjustment according to measured INR.

For rate control:

- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

If in CCF: (I50.0)

- Carvedilol, oral. See Section 3.4: Congestive cardiac failure.

AND

If control not adequate add:

- Digoxin, oral, start at 0.125 mg daily and adjust according to rate response and trough plasma level.
  - In patients with impaired renal function (eGFR <60 mL/minute), consider 0.125 mg daily and adjust according to trough level monitoring.
  - In all patients, digoxin trough level monitoring is required at all doses.

If beta-blockers are contra-indicated, e.g. asthma or severe peripheral vascular disease:

- Verapamil, oral, 40–120 mg 8 hourly.
  - Titrate against ventricular rate (verapamil is negatively inotropic, avoid in heart failure due to left ventricular dysfunction).

If not controlled on these agents, refer to specialist for consideration of alternative therapy.

CAUTION

Note: The risk of thromboembolic complications and stroke in those with paroxysmal AF is similar to that of patients with persistent AF and similar recommendations as to anticoagulation apply.

Strong inhibitors of both CYP3A4 & P-glycoprotein • Ketoconazole, • Protease Inhibitors e.g. Ritonavir	Increased rivaroxaban concentrations with risk of bleeding	Contraindicated Use warfarin with INR monitoring instead
Moderate inhibitors of CYP3A4 • Fluconazole	Interaction not significant	May be co-administered with rivaroxaban
Strong inducers of CYP3A4 Medicines intended for long term use • Phenytoin, • Carbamazepine:	Decreased rivaroxaban concentrations with risk of clotting	Refer to doctor to switch to safer alternative anti-seizure medicines, e.g., lamotrigine (see PHC STG & EML, Section 15.7.2: Epilepsy in Adolescents and Adults). *Consider warfarin with INR monitoring if a switch to alternative anti-seizure medicine is not possible.*
Strong inducers of CYP3A4 Medicines intended for limited duration • Rifampicin	Decreased rivaroxaban concentrations with risk of clotting	Use warfarin with INR monitoring for the duration of TB treatment instead.

b) Valvular heart disease (e.g., rheumatic heart disease), prosthetic heart valves (e.g. transcatheter aortic valve replacement), renal impairment (eGFR < 15mL/min) or hypersensitivity to DOAC,

Anticoagulation with warfarin is required:

- Warfarin, oral, 5 mg daily.
  - INR should be done after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to initiation dosing tables in Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to maintenance dosing tables in Appendix II).
  - Every effort should be made to keep the time in therapeutic range (TTR) > 65%. TTR ≤ 65% is associated with decreased benefit of warfarin therapy and a greater risk of stroke and haemorrhage.

See Appendix II for guidance on calculating TTR for management with warfarin.

2. **Rate control**

- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

OR

If in CCF:(I50.0)

- Carvedilol, oral. See Section 3.4: Congestive cardiac failure.

If control is not adequate, **ADD**:

- Digoxin, oral, 0.125 mg daily, adjust according to rate response and trough plasma level
  - Measure digoxin trough plasma levels (before the morning dose) – Maintain levels between 0.6–1 nmol/L.

Only in patients with severe symptoms despite the above measures:

- Amiodarone, oral, 200 mg 8 hourly for 1 week. Specialist initiated.
  - Followed by 200 mg 12 hourly for one week.
  - Thereafter, 200 mg daily.

Precautions:

- If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.
- Monitor heart rate closely when patient is on concomitant digoxin.
- Monitor thyroid function every 6 months as thyroid abnormalities may develop.
- Ophthalmological examination every 6 months.

For management of pregnant women with valvular disease and atrial fibrillation, see Section 6.3: Heart disease in pregnancy.

- Patients at high risk of digoxin toxicity: the elderly, patients with renal dysfunction, hypokalaemia, and patients with low lean body mass.

<u>If beta-blockers are contraindicated, e.g., asthma or severe peripheral vascular disease:</u>

- Verapamil, oral, 40–120 mg 8 hourly.
  - Titrate against ventricular rate (verapamil is negatively inotropic, therefore avoid in heart failure due to LV dysfunction).

If not controlled on these agents, refer to specialist for consideration of alternative therapy, e.g., amiodarone or atrioventricular node ablation and pacemaker insertion.

DC cardioversion may be needed in selected cases, after 4 weeks of effective warfarin anticoagulation.

3. Long-term therapy

» Continue with anticoagulation long-term, unless contraindicated.

a) <u>Non-valvular atrial fibrillation:</u>

▪ Direct acting oral anticoagulant (DOAC), e.g.:

- Rivaroxaban, oral, 20 mg once daily with food.
  - Reduce dose in moderate renal impairment (eGFR 30-50mL/min) to 15 mg daily.

If on warfarin, consider converting to DOAC:

» Ensure no contraindications to DOACs:
  – Active bleeding
  – Severe risk of bleeding: Recent GI ulcer, malignant neoplasms, recent brain/spinal/ophthalmic surgery, recent intracranial haemorrhage, oesophageal varices, vascular aneurysm
  – Severe hepatic disease
  – Severe renal impairment (eGFR < 15 ml/min)

» Stop warfarin treatment and monitor INR until INR is ≤ 3 mmol/L, then initiate treatment with:

▪ Direct acting oral anticoagulant (DOAC), e.g.:

- Rivaroxaban, oral, 20 mg once daily with food.
  - INR values may be falsely elevated following the initiation of rivaroxaban.
  - Reduce dose in moderate renal impairment (eGFR 30–50mL/min) to 15 mg daily.

●

b) <u>Valvular heart disease (e.g. rheumatic heart disease), prosthetic heart valves (e.g. transcatheter aortic valve replacement), renal impairment (eGFR < 15mL/min):</u>

- Warfarin, oral, 5 mg daily.
  - Monitor dose to ensure therapeutic INR:
    – INR between 2–3 and patient stable: monitor every 2 months.
    – INR <1.5 or >3.5: monitor monthly.

CAUTION
Warfarin use requires regular INR monitoring and dose adjustment according to measured INR.

For rate control:

- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

OR

If in CCF: (I50.0)

- Carvedilol, oral. See Section 3.4: Congestive cardiac failure.

If control not adequate **ADD**:

- Digoxin, oral, start at 0.125 mg daily and adjust according to rate response and trough plasma level.
  - In patients with impaired renal function (eGFR <60 mL/min), consider 0.125 mg daily and adjust according to trough level monitoring.
  - In all patients, digoxin trough level monitoring is required at all doses.

If beta-blockers are contra-indicated, e.g., asthma or severe peripheral vascular disease:

- Verapamil, oral, 40–120 mg 8 hourly.
  - Titrate against ventricular rate (verapamil is negatively inotropic, avoid in heart failure due to left ventricular dysfunction).

If not controlled on these agents, refer to specialist for consideration of alternative therapy.

CAUTION

The risk of thromboembolic complications and stroke in those with paroxysmal AF is similar to that of patients with persistent AF and similar recommendations as to anticoagulation apply.

Only in patients with severe symptoms despite the above measures:

- Amiodarone, oral, 200 mg 8 hourly for 1 week. (Specialist initiated).
  - Follow with 200 mg, 12 hourly for one week.
  - Thereafter, 200 mg, daily.

Precautions:

» If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.
» Monitor heart rate closely when patient is on concomitant digoxin.
» Monitor thyroid function every 6 months as thyroid abnormalities may develop.
» Ophthalmological examination every 6 months.

For management of pregnant women with valvular disease and atrial fibrillation, see Section 6.3: Heart disease in pregnancy.

The following updates to the therapeutic interchange database were supported by the Committee:

Section (Description)	Indication	Therapeutic class	INN	Strength	Unit	Formulation	Daily dose
Atrial Fibrillation – non-valvular heart disease	Reduction of stroke and systemic embolic risk	Direct oral anticoagulants (DOAC)	Rivaroxaban	20	mg	oral	20mg once daily[14]
Atrial Fibrillation - non-valvular heart disease	Reduction of stroke and systemic embolic risk	Direct oral anticoagulants (DOAC)	Apixaban	5	mg	oral	5mg twice daily[15]
Atrial Fibrillation- non-valvular heart disease	Reduction of stroke and systemic embolic risk	Direct oral anticoagulants (DOAC)	Dabigatran	150	mg	oral	150mg twice daily[16]

Section 3.4 Congestive cardiac failure

Sodium-Glucose Transport 2 (SGLT2) Inhibitors – management of congestive cardiac failure**:** Not added

In response to an external comment received that NEMLC consider the use of SGLT2 inhibitors for the management of CCF, this request has been included on the list of topics for prioritisation for NEMLC's consideration during the next review cycle.

Appendix VII: 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

[14] SAHPRA approved product information (PI). Xarelto®. Bayer (Pty) Ltd. Text revised 12 May 2022
[15] SAHPRA approved product information (PI). Eliquis®. Pfizer Laboratories (Pty) Ltd. Text revised 11 July 2022
[16] SAHPRA approved product information (PI). Pradaxa®. Ingelheim Pharmaceuticals (Pty) Ltd. Text revised 28 Feb 2025