2: Cardiovascular System (7th edition 2023 amended Sept 2024)

2.1.1 Cardiac glycosides
Digoxin - *monitoring[1] required*

The likelihood of toxicity with digoxin increases progressively through the plasma range 1.5-3micrograms/litre. Digitalis toxicity is more likely to occur in the elderly and in patients suffering from hypokalaemia. If toxicity occurs, digoxin should be withdrawn; serious manifestations require urgent specialist management.

2.2 Diuretics
2.2.1 Thiazides & related diuretics - *monitoring[1] required*
Indapamide - *not m/r preparation*
Bendroflumethiazide (for existing patients and the treatment of oedema only)

Indapamide 2.5mg daily is the current recommended thiazide-like diuretic for treatment of hypertension (NICE NG136).

Metolazone is initiated on specialist advice from secondary care clinicians prior to continuation in primary care; AMBER G on SY IMOC TLD.
NOTE: Metolazone should only be prescribed by brand Xaqua® as the Xaqua® tablets are not directly interchangeable with other metolazone products due to higher bioavailability, which may differ significantly.
5mg Xaqua® tablet can be halved to make a 2.5mg Xaqua® dose

2.2.2 Loop diuretics – *monitoring[1] required.*
Furosemide
Bumetanide

2.2.3 Potassium sparing diuretics and aldosterone antagonists
– *monitoring[1] required*
Amiloride - *maximum dose is 10mg when used with other diuretics*.

- Hypokalaemia can occur with both thiazide and loop diuretics.
- Potassium sparing diuretics may be considered to treat hypokalaemia. Also consider optimising other therapies that may affect potassium levels.
- Increased risk of hyperkalaemia when potassium-sparing diuretics are given with ACEIs / A2RAs, especially in patients with additional risk factors. Stop if patient newly started on ACEI / A2RA due to risk of life-threatening hyperkalaemia. If amiloride is indicated and patient is already on an ACEI / A2RA, start with 2.5mg daily and monitor potassium levels closely.
- Potassium supplements **must not** be given with potassium-sparing diuretics.

Aldosterone antagonists
Spironolactone
Eplerenone- AMBER on TLDL for patients intolerant of spironolactone due to gynaecomastia
Finerenone – AMBER on SY IMOC TLD for use in CKD in Type 2 diabetes.
See NICE TA877 and SY ICB SCP

- Spironolactone daily improves the prognosis of NYHA grade III-IV heart failure (NICE NG106). Start at a low dose in heart failure 25mg once daily, to a maximum of 50mg once daily.
- Potassium supplements **must not** be given with aldosterone antagonists.

2.2.4 Potassium sparing diuretics with other diuretics

Fixed dose combination products only recommended for patients with compliance problems or to help reduce tablet load for the purpose of medicines optimisation.

2.3 Anti-arrhythmic drugs

2.3.1 Management of arrhythmias

For the management of atrial fibrillation, see NICE NG196

2.3.2 Drugs for arrhythmias – *drugs for arrhythmias are hospital-initiation only*

Amiodarone Amiodarone shared care guideline
Amiodarone patient passport

2.4 Beta-adrenoceptor blocking drugs

Bisoprolol *dose titration required in heart failure*
Atenolol
Carvedilol *dose titration required in heart failure*
Labetolol - *for hypertension during pregnancy*

Target doses for beta-blockers in heart failure

Bisoprolol	10mg once daily. (Increase in 1-2 week intervals)
Carvedilol	25mg twice daily in severe heart failure or weight < 85kg 50mg twice daily if weight > 85kg (Increase in 2 week intervals)
***Nebivolol (in adults ≥ 70yrs old with mild-moderate HF)**	10mg once daily. (Increase in 1-2 week intervals)

*Nebivolol is included in Sheffield guidelines for the Pharmacological management of chronic heart failure with reduced left ventricular ejection fraction (HFrEF) in adults in primary care.

Beta-blockers are step 4 in the management of resistant hypertension (see NICE NG136). However, they may be considered earlier in the pathway in younger people, particularly: a) those with intolerance or contraindication to ACEIs/A2RAs; b) women of child-bearing potential; c) people with evidence of increased sympathetic drive.
See NICE NG133 for place in management of hypertension in pregnancy.

Beta-blockers should not normally be co-prescribed with verapamil or diltiazem. Please see BNF or individual SPCs for advice on cautions and contraindications.

2.5 Hypertension and heart failure

Primary hypertension adults, including Type 2 diabetes: see NICE NG136 and NICE Visual summary for hypertension diagnosis and treatment
Type 1 diabetes: see blood pressure management NICE NG17
Chronic kidney disease: see blood pressure control NICE NG203
Pregnancy: see NICE NG133 and visual summaries

Chronic heart failure: NICE NG106
Sheffield prescribing guidelines –
Pharmacological management of chronic heart failure with reduced left ventricular ejection fraction (HFrEF) in adults in primary care

2.5.1 Vasodilator antihypertensive drugs
Hydralazine – *specialist initiation required in heart failure*
Treatment of pulmonary hypertension – specialist prescribing only

2.5.2 Centrally acting antihypertensive drugs
Methyldopa – *for hypertension during pregnancy (monitoring[1] required)*

Side-effects are minimised if the daily dose is kept below 1g; avoid in active liver disease.

2.5.4 Alpha-adrenoceptor blocking drugs
Doxazosin ***(do not prescribe modified release formulations)***
See also chapter 7 section 7.4.1 for prescribing in benign prostatic hyperplasia (BPH)

Hypertension- recommended as an option only in Step 4 for the management of resistant hypertension (NICE NG136). Use with caution in patients with heart failure.

2.5.5 Drugs affecting the renin-angiotensin system

Avoid use in pregnancy MHRA alert.

2.5.5.1 Angiotensin converting enzyme inhibitors (ACEIs) - *monitoring[1] required*
Ramipril
Enalapril
Lisinopril

2.5.5.2 Angiotensin-II receptor antagonists (A2RAs) - *monitoring[1] required*
Losartan
Candesartan
Valsartan - *licensed for use post-MI in patients with left ventricular systolic dysfunction (LVSD); target dose 160mg bd*
Sacubitril with valsartan (Entresto®) - AMBER on TLDL *specialist initiation required* for treating symptomatic chronic heart failure with reduced ejection fraction. See NICE TA388 and Sheffield HFrEF guidelines

Start with a low dose. Ensure correct dose titration in heart failure and post-myocardial infarction

Target doses for ACE Inhibitors & Angiotensin II Receptor Antagonists

	Enalapril	**Lisinopril**	**Ramipril**	**Losartan**	**Candesartan**
Heart Failure	10-20mg twice daily	35mg once daily	10mg daily	150 mg daily*	32 mg daily
Post-Myocardial Infarction	not licensed	BP-dependent. See BNF for details	5mg twice a day	not licensed	not licensed

*Note: dose of losartan beyond 100 mg per day is associated with excess hyperkalaemia and renal impairment

6.1.2.3 Sodium glucose co-transporter inhibitors (SGLT2 inhibitors)
Heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) or mildly reduced ejection fraction (HFmrEF):

AMBER on the TLDL - specialist initiation required for treating symptomatic chronic heart failure in line with NICE TA679, TA773 (HFrEF) and TA902,TA929 (HFpEF/HFmrEF).

Dapagliflozin 10mg daily
Empagliflozin 10mg daily

See Dapagliflozin and empagliflozin in HFrEF: guidance for primary care

Chronic kidney disease (CKD):
Green on the TLDL for management of CKD. See NICE TA775, TA942

Dapagliflozin 10mg daily
Empagliflozin 10mg daily

See Sheffield CKD management in adults: a guideline for primary care
(*under review finerenone*)

2.6 Nitrates, calcium-channel blockers, and other antianginal drugs
(See Stable angina: Management NICE CG126 and Sheffield stable angina treatment algorithm)

2.6.1 Nitrates
Glyceryl trinitrate spray – CFC Free
Isosorbide mononitrate (ISMN) MR 60mg tabs (Chemydur® 60XL) –
Chemydur® 60XL may be halved to give a 30mg dose

MR formulations should only be given **once daily** and used in this way do not produce tolerance.

2.6.2 Calcium channel blockers – dihydropyridines
BNF recommends branded prescribing for modified release preparations
Amlodipine
Nifedipine MR – twice daily (Adipine® MR)
Nifedipine XL – once daily: (Coracten XL®)
- *nifedipine for hypertension in pregnancy as per NICE NG133*

Calcium channel blockers – rate limiting
BNF recommends branded prescribing for modified release preparations

Diltiazem	Twice daily: (Angitil SR® caps) Once daily: (Slozem® caps)
Verapamil	***Securon SR® (240mg)** or Half Securon SR® (120mg) - if modified release required

*Securon SR® is scored and can be halved without affecting the slow-release profile of the drug, in line with the SPC. It is therefore more cost effective to use Securon SR® when prescribing 120mg doses compared with using Half Securon®.

Verapamil or diltiazem should not normally be co-prescribed with a beta-blocker and are contra-indicated with ivabradine. Please see current BNF or individual SPCs for advice on cautions and contraindications.

2.6.3 Other antianginal drugs
Nicorandil – second line due to the risks of ulcer complications MHRA alert
Ivabradine – AMBER on TLDL for: managing stable angina in people over 18yrs old (NICE CG126 and Sheffield stable angina treatment algorithm); and treating chronic heart failure (NICE TA267 and Sheffield HFrEF guidelines); MHRA alert – monitor for bradycardia.
Ranolazine- AMBER on TLDL for: managing stable angina in people who are

intolerant to other therapies, Sheffield stable angina treatment algorithm.

2.6.4 Peripheral Vasodilators and related drugs
(See NICE TA223 for place in therapy)
Naftidrofuryl oxalate

Cilostazol, pentoxifylline, and inositol nicotinate are not recommended for the treatment of intermittent claudication in patients with peripheral arterial disease; patients currently receiving these treatments should have the option to continue until they and their clinician consider it appropriate to stop (NICE TA223).

2.8 Anticoagulants and protamine

2.8.1 Parenteral anticoagulants
Dalteparin sodium in accordance with the Shared Care Protocol

2.8.2 Oral anticoagulants - *monitoring[1] essential.*
DOACs are recommended in preference to warfarin for stroke prevention in atrial fibrillation (SPAF)* see NICE NG196
Apixaban
Edoxaban
Rivaroxaban
Dabigatran
Warfarin tabs 1mg (brown), 3mg (blue)

Counsel patients regarding initiation of new anticoagulant. For AF patients see Sheffield SPAF guideline page 7.
Local agreement does **not** support the prescribing of warfarin 0.5mg or 5mg tablets.

*Choice of DOAC for SPAF should be in line with NHSE operational note for DOAC procurement; clinicians should use the best value DOAC that is clinically appropriate for the patient; see Sheffield SPAF guideline for further information.

Sheffield guidelines:
Anticoagulation for stroke prevention in atrial fibrillation (SPAF)
Calculating renal function for patients prescribed DOACs in primary care
Anticoagulant monitoring service SOP

2.9 Antiplatelet drugs
Sheffield guidelines:
Sheffield guidelines for the use of antiplatelets in the prevention and treatment of cardiovascular disease
Sheffield primary care guidelines for stroke and transient ischaemic attack

Dispersible Aspirin – e/c aspirin NOT recommended
Clopidogrel
Dipyridamole – M/R capsules 200mg
Prasugrel - AMBER on TLDL
Ticagrelor - AMBER on TLDL
Duration of treatment will depend on the indication-**avoid** unnecessary continuation.

Other anti-thrombotic drugs
Rivaroxaban 2.5mg- AMBER on TLDL

2.11 Antifibrinolytic drugs & haemostatics
Tranexamic acid tabs – *use mainly for menorrhagia*

2.12 Lipid-regulating drugs

See NICE Cardiovascular disease: risk assessment and reduction, including lipid modification NG238

Sheffield recommendations for lipid optimisation in the primary prevention and secondary prevention of CVD are under review. See also the raised triglycerides flow chart for recommendations on managing people with raised triglycerides.

Statins - *monitoring[1] required.*

Atorvastatin
Rosuvastatin tablets- do not prescribe capsules
Simvastatin
Pravastatin

Safety issues around the prescribing of simvastatin 80 mg tablets are detailed here: https://www.gov.uk/drug-safety-update/simvastatin-increased-risk-of-myopathy-at-high-dose-80-mg

Cholesterol absorption inhibitors
Ezetimibe
Bempedoic acid 180mg/ezetimibe 10mg (Nustendi® ▼)
Bempedoic acid (Nilemdo®) – AMBER on TLDL

Fibrates - AMBER on TLDL *monitoring[1] required.*
Bezafibrate MR
Fenofibrate

Fibrates are classified as amber on the TDL and should not be initiated by GPs Bezafibrate and fenofibrate are formulary choices, ciprofibrate is non-formulary and costly.

Inclisiran (Leqvio® ▼)

Omega-3 fatty acid compounds
Icosapent ethyl (Vazkepa® ▼) - AMBER on TLDL

Omega-3 fatty acid capsules are amber on TLDL in the management of hypertriglyceridaemia to prevent acute pancreatitis. They are not recommended for use in the primary and secondary prevention of cardiovascular events, except for icosapent ethyl which is approved for the secondary prevention of cardiovascular disease (NICE TA805). See the BLACK section of the TLDL.

PCSK-9 inhibitors
Alirocumab (Paluent®) - RED on TLDL
Evolocumab (Repatha SureClick ®) - RED on TLDL

Patients with familial hypercholesterolemia (see NICE CG71) need to be on agents to reduce their LDL cholesterol by at least 50%; this may include agents not in the formulary.

[1]where monitoring is recommended / required please refer to the:
Common Blood Monitoring Schedules

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