Health and Social Care in Northern Ireland

NI Medicines Management Formulary (Adult)

BNF Chapter 2 Cardiovascular System v4.0

Cardiovascular System

BNF Chapter 2

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2.1 Positive inotropic drugs

For more information see BNF Chapter 2

2.1.1 Cardiac glycosides

Choice	Drug
1st choice	Digoxin tablets 62.5 micrograms, 125 micrograms, 250 micrograms

Prescribing Notes

- **Seek specialist advice before initiating digoxin in heart failure.**
- Refer to NICE NG106 Chronic heart failure in adults and NICE NG196 Atrial fibrillation.
- Digoxin may be a useful adjunct to a beta-blocker for heart rate control but assessment of heart rate/rhythm is required and doses more than 125 micrograms in this setting are generally best avoided.
- Regular measurements of plasma digoxin concentrations are not usually required except to confirm toxic levels, or to check compliance. Blood should be taken at least 6 hours after the last dose of digoxin. Laboratories in NI offer a normal range. Refer to the Digoxin monitoring guidance for further information.
- There is no therapeutic dose response relationship for digoxin in heart failure. Increasing doses >250 micrograms just increases toxicity.
- If toxicity occurs, digoxin should be withdrawn; serious manifestations require urgent specialist management. For further information on the management of toxicity see Toxbase or contact UK National Poisons Information Service on 0844 892 0111.
- Digoxin should not be used in the treatment of patients with pre-excitation syndromes, e.g. Wolff-Parkinson-White Syndrome, unless specifically prescribed by a specialist.

Cautions

- Loading and maintenance doses of digoxin should be adjusted according to renal function. Age, sex and weight need to be considered. Seek specialist advice if there is any clinical uncertainty. A maintenance dose of ≤125 micrograms daily is adequate in most patients. A lower maintenance dose (i.e. 62.5 micrograms daily) is often adequate in older patients, in patients with renal failure and in patients taking potentiating therapy.
- Digoxin should be used with particular caution in the elderly and patients with renal impairment.
- Hypokalaemia predisposes to digoxin toxicity. Care should be taken to monitor the electrolytes when prescribing diuretics. Consider use of appropriate potassium-sparing diuretics, or combination with ACE inhibitor/ARB as appropriate.

2.2 Diuretics

2.2.1 Thiazide and related diuretics

Choice	Drug
1st choice	Indapamide tablets 2.5mg
2nd choice	Indapamide tablets m/r 1.5mg

Prescribing Notes

- Modified release indapamide 1.5mg SR is second line if patients develop side-effects, in particular hypokalaemia, on the IR preparation.
- Allow 4 weeks for maximal antihypertensive effect of thiazide-like diuretics.
- Both thiazide and loop diuretics can cause sodium and potassium depletion, glucose intolerance and gout. These effects are dose-related and may be more dramatic with thiazides because of their relatively long duration of action. Regular monitoring of potassium, sodium, glucose and uric acid is

recommended, particularly with high doses, long term use, or in renal impairment. If potassium is persistently low, consider also measuring magnesium.

- Diuretics should not be used on a long term basis to treat simple gravitational oedema. This will usually respond to increased ambulation, raising the legs and support stockings.
- Counsel patients on 'sick day guidance' with diuretics (add link to section 6.1.2).
- Bendroflumethiazide is no longer a routine choice of diuretic for hypertension, but there is no need to change patients already taking it whose blood pressure is stable and well controlled. A dose of 5mg bendroflumethiazide is not recommended for hypertension.

Metolazone

- **Metolazone** should ideally only be initiated by a specialist.
- Profound diuresis can occur and the patients should therefore be monitored carefully.
- Metolazone should be prescribed by brand. Metolazone (Xaqua®) is not interchangeable with the generic unlicensed metolazone. Exercise caution when switching patients between different metolazone preparations – for further information see MHRA
- Xaqua® tablets cannot be divided into quarters. When necessary to split tablets, this should only be into halves using the tablets score-line.

Cautions

- Thiazide and related diuretics can exacerbate diabetes, gout, and systemic lupus erythematosus.
- Thiazides are ineffective if eGFR is less than 30ml/minute/1.73m^2 and should be avoided; metolazone remains effective but with a risk of excessive diuresis and should only be initiated by a specialist.
- Thiazide and related diuretics should be used with caution in nephrotic syndrome, hyperaldosteronism and malnourishment

- Elderly patients are particularly susceptible to the side-effects of diuretics including increased risk of postural hypotension, collapse and falls. Confusion, dehydration, urinary incontinence and hyponatraemia may be particular problems.

2.2.2 Loop diuretics

Choice	Drug
1st choice	Furosemide tablets 20mg, 40mg
2nd choice	Bumetanide tablets 1mg

Prescribing Notes

- Furosemide and bumetanide produce a dose-dependent diuresis within 1 hour if given orally or 30 minutes if given intravenously; duration of action is 6 hours and thus can be given twice daily without interfering with sleep (second dose preferably no later than 4pm).
- 1mg bumetanide is equivalent to 40mg furosemide.
- 5mg bumetanide should only be initiated with specialist input, and should not be given as a single dose.
- Diuretics should not be used on a long term basis to treat simple gravitational oedema. This will usually respond to increased ambulation, raising the legs and support stockings.
- Counsel patients on 'sick day guidance' with diuretics (add link to section 6.1.2).

Cautions

- Elderly patients are particularly susceptible to the side-effects of diuretics including increased risk of postural hypotension, collapse and falls. Confusion, dehydration, urinary incontinence and hyponatraemia may be particular problems.

- Loop diuretics can cause sodium and potassium depletion, glucose intolerance and gout. The hypokalaemia which may occur can be dangerous in patients with severe ischaemic heart disease or when cardiac glycosides are used. Combination with a potassium-sparing diuretic, ACE inhibitor or ARB should be considered in these patients. Oral potassium supplementations are relatively inefficient.

2.2.3 Potassium-sparing diuretics and mineralocorticoid receptor antagonists

Potassium-sparing diuretics

Choice	Drug
1st choice	Amiloride tablets 5mg

Mineralocorticoid Receptor Antagonists [MRAs] (Aldosterone antagonists)

Choice	Drug
1st choice	Eplerenone tablets 25mg, 50mg
	Spironolactone tablets 25mg, 50mg, 100mg

Prescribing Notes

- These agents have a weak diuretic effect if given alone but their effects are additive with thiazides and loop diuretics.
- Amiloride is usually reserved for those already receiving thiazide or loop diuretics in whom hypokalaemia is a concern. Amiloride may take 2 to 3 days for full effect.
- Amiloride is also used in resistant hypertension under specialist supervision.
- Spironolactone may be associated with significant hyperkalaemia or renal impairment particularly in combination with ACE inhibitors, angiotensin-II receptors, angiotensin

receptor/neprilysin inhibitor, or other diuretics. U&Es should be checked at baseline, 1 week after initiation (and after every dose increase), monthly for first 3 months, then every 3 months for 1 year, and then every 6 months thereafter. Patients should be warned of the risk of hyperkalaemia in the setting of volume depletion and of the signs and symptoms of hyperkalaemia. See MHRA for further information.

- Eplerenone is less likely to produce sexual side effects such as gynaecomastia, breast pain or menstrual irregularities.
- Finerenone is available for patients who meet criteria in NICE TA877. See NI Managed Entry decisions.
- Counsel patients on 'sick day guidance' with diuretics (link to section 6.1.2).
- Diuretics should not be used on a long term basis to treat simple gravitational oedema. This will usually respond to increased ambulation, raising the legs and support stockings.

Cautions

- Potassium-sparing diuretics and MRAs should be used with caution in renal impairment.
- Elderly patients are particularly susceptible to the side-effects of diuretics, including increased risk of postural hypotension, collapse and falls. Confusion, dehydration, urinary incontinence and hyponatraemia may be particular problems.
- Caution with concurrent NSAID due to risk of acute kidney injury (avoid over-the-counter use of NSAIDs).
- Potassium-sparing diuretics should be used with caution when co-administered with ACE inhibitors or angiotensin-II receptor antagonists due to the risk of hyperkalaemia. See BNF for other interactions e.g. trimethoprim, clarithromycin.
- Potassium supplements should not (unless under close supervision and monitoring) be given with: potassium sparing diuretics, MRAs, in the presence of renal failure, with ACE inhibitors or with angiotensin-II receptor antagonists, due to the danger of hyperkalaemia. Ask about potassium-containing salt substitutes that a patient may be taking: one serving of common

salt substitutes can contain around the potassium content of one oral potassium supplement tablet.

2.2.4 Potassium-sparing diuretics with other diuretics

Choice	**Drug**
1st choice	Co-amilofruse tablets 2.5/20 (amiloride 2.5mg, furosemide 20mg) 5/40 (amiloride 5mg, furosemide 40mg)

Prescribing Notes

- Where combinations of diuretics with amiloride are prescribed generically, the prescriber must state the dose and strength required.
- Combination products containing a diuretic plus potassium do not contain sufficient potassium to reliably correct hypokalaemia and are **not recommended.**
- Diuretics should not be used on a long-term basis to treat simple gravitational oedema. This will usually respond to increased ambulation, raising the legs and support stockings.
- Counsel patients on 'sick day guidance' with diuretics (link).

Cautions

Add jump to 2.2.2 and 2.2.3

2.3 Anti-arrhythmic drugs

2.3.2 Drugs for arrhythmias

Apart from beta-blockers, other anti-arrhythmics should only be initiated on specialist advice

Prescribing Notes

- Shared care guidelines are available for:
  - Amiodarone
  - Dronedarone
  - Mexiletine
- Anti-arrhythmics are complex agents; intravenous injections or infusions should be given according to specialist advice.
- The management of a cardiac arrhythmia requires a precise diagnosis and electrocardiographic evidence is essential.
- Dronedarone is recommended for AF rhythm control in the setting of normal/mildly impaired stable LV function, HFpEF, ischaemic or valvular heart disease [ESC AF guideline]. It requires annual review with a specified cardiologist as per SCG and should be discontinued only heart rate control is required (e.g. permanent AF) or the patient has heart failure.
- Amiodarone has a very long half-life and interacts with many drugs (see SCG). There is a potential for drug interactions to occur for several weeks (or even months) after treatment with it has been stopped.
- Propafenone is contraindicated in patients with significant structural heart disease or in patients with an incident of myocardial infarction within the last 3 months.
- Flecainide has a negative inotropic effect and can increase the electrical threshold in patients with pacemakers. It should be avoided after myocardial infarction.
- Sotalol is a non-selective beta-blocker with additional Class III anti-arrhythmic properties. Sotalol may cause polymorphic VT (torsades de pointes); it should be given with extreme caution with drugs known to prolong the QT interval, e.g. erythromycin, clarithromycin, chloroquine, haloperidol, lithium, tricyclic antidepressants, chlorpromazine. Sotalol should be used with

caution in patients on diuretics and avoided in hypokalaemia. It is normally reserved for use in paroxysmal atrial fibrillation ‘For further information on drugs that can prolong the QT interval – see https://www.crediblemeds.org.

- The negative inotropic effects of anti-arrhythmic drugs tend to be additive. Therefore, special care is needed if two or more are used, especially in impaired myocardial function.
- Verapamil may be used in paroxysmal supraventricular tachycardia. It is also used to slow the ventricular rate in atrial fibrillation. However, it should be avoided in atrial fibrillation or flutter complicating Wolff-Parkinson-White syndrome where it may promote antero-grade conduction, which can potentially lead to ventricular fibrillation. It should be avoided in patients with impaired left ventricular function. There is a risk of potentially serious bradycardia if co-administered with beta-blockers or digoxin.

2.4 Beta-adrenoceptor blocking drugs (Beta-blockers)

Choice	Drug
1st choice	Bisoprolol tablets 1.25mg, 2.5mg, 3.75mg, 5mg, 7.5mg, 10mg
2nd choices	Carvedilol tablets 3.125mg, 6.25mg, 12.5mg, 25mg
	or
	Nebivolol tablets 2.5mg, 5mg Note: prescribe 5mg tablets for doses from 2.5mg to 10mg (see Beta-blockers in Heart Failure below). If a 1.25mg dose is required, prescribe 2.5mg tablets and request half tablet dosing.

Prescribing Notes

- As per NICE CG126, a beta-blocker +/- a calcium channel blocker is a first-line option to reduce symptoms of stable angina.
- Beta-blocker choice is dependent on individual patient factors (co-morbidities, contra-indications, preference) and the primary indication for use. Once-a-day drugs may improve compliance.
- As per NICE NG136, beta-blockers are no longer preferred as a routine initial therapy for hypertension (unless the patient has a co-morbidity for which a beta-blocker is indicated). In the past beta-blockers were sometimes used along with thiazides for hypertension, either as separate agents or as combination product. This is now discouraged to reduce the risk of developing diabetes.
- Beta-blockers are contra-indicated in those with second or third degree heart block.
- Patients currently prescribed atenolol should be reviewed opportunistically and a switch considered to an alternative formulary choice of beta-blocker unless specifically indicated due to intolerance of other beta-blocker.

- Propranolol is a choice for other indications, see 4.9.3 and 4.7.2 [add jumps].
- Labetalol is recommended as first line antihypertensive for the treatment of hypertension in pregnancy. Refer to NICE NG133
- For information on the use of beta-blockers post MI, please refer to NICE NG185 Acute Coronary Syndromes.
- It may be reasonable to stop beta-blocker one year after MI, provided LV function is normal and there is full revascularisation. Discuss with rehabilitation nurse or specialist.

Beta-blockers in heart failure

- Refer to NICE NG106 Chronic heart failure in adults.
- The beta-blockers bisoprolol and carvedilol reduce mortality in patients with stable heart failure and left ventricular systolic dysfunction.
- Nebivolol is licensed for use in stable mild to moderate heart failure in patients aged ≥70 years.
- Beta-blocker treatment should be started at a very low dose and titrated very slowly over a period of weeks. Aim for the target dose or failing that, the maximum tolerated dose. Symptoms may deteriorate initially, calling for adjustment of concomitant therapy. Please follow recommendations given by heart failure specialist teams and contact them for advice if necessary.
- Patients should be monitored for heart rate, oedema, breathlessness and blood pressure after each dose increment.
- Due to the high cost of other nebivolol strengths, **nebivolol 5mg tablets should be prescribed where possible** for doses 2.5 to 10mg. Please see table for dosing:

Nebivolol Dose Required	**Prescribe (where appropriate)**
2.5mg	5mg tablets: Take half a tablet daily
5mg	5mg tablets: Take one daily
10mg	5mg tablets: Take two tablets daily
1.25mg*	2.5mg tablets: Take half a tablet daily
*** due to the *very high* cost of nebivolol 1.25mg tablets** **NB: heart failure titration dose only**	

Cautions

- Beta-blockers, including those considered to be cardioselective, should usually be avoided in patients with a history of asthma, bronchospasm or a history of obstructive airways disease. However, when there is no alternative, a cardioselective beta-blocker can be given to these patients with caution and under specialist supervision.
- Elderly patients are particularly susceptible to the side-effects of beta-blockers which include cold extremities, bradycardia, conduction disorders, heart failure and fatigue. Reduced doses of beta-blockers may be required in the elderly.
- There is some evidence that sudden withdrawal may cause an exacerbation of angina or transitory worsening of heart failure and therefore gradual reduction of dose is preferable when beta-blockers are to be stopped, unless there is a need to stop treatment immediately.

2.5 Hypertension and heart failure

Hypertension

- See NICE NG136 and ESC hypertension guidelines.
- Choice of hypertensive drug and BP targets is summarised in the NICE 2-page visual summary.
- Offer antihypertensive drug treatment to women of child-bearing potential in line with the recommendations on management of pregnancy with chronic hypertension and breastfeeding in 'Hypertension in Pregnancy' (NICE NG133).

Heart failure

See NICE NG106 and ESC for the management of chronic heart failure in adults**.** Pharmacological treatment should be used as per NICE NG106 recommendations. Refer to relevant formulary sections, for example: *(add jumps below)*

- ACE inhibitors and ARBs – refer to section 2.5.5
- Beta-blockers – refer to section 2.4
- Mineralocorticoid Receptor Antagonists – refer to section 2.2.3

Specialist treatments include:

- Ivabradine – refer to section 2.6.3
- Sacubitril / valsartan – refer to section 2.5.5
- Dapagliflozin and empagliflozin – refer to section 6.1.2.5

2.5.2 Centrally acting antihypertensive drugs

Prescribing Notes

- Moxonidine may be considered as a fourth line antihypertensive drug.
- Methyldopa may be used in the management of hypertension in pregnancy, although labetolol is recommended as first line treatment by NICE.

2.5.4 Alpha-adrenoceptor blocking drugs (alpha-blockers)

Choice	Drug
1st choice	Doxazosin tablets 1mg, 2mg, 4mg (immediate release tablets)

Prescribing Notes

- Refer to NICE NG136 hypertension guidance.
- Alpha-blockers are a fourth-line agent in the treatment of hypertension. Doxazosin should be used with caution in patients with heart failure, impaired left ventricular function or coronary artery disease.
- Doxazosin may cause postural hypotension and first dose hypotension. Treatment should be initiated at the lowest possible dose.
- Immediate release doxazosin has a long half-life and is taken as a single daily dose. Doxazosin m/r formulations are generally more expensive than the immediate release formulation with no clinical advantage and are therefore not recommended. Do not start new patients on doxazosin m/r; review existing patients for a switch to immediate release – see switch SOP on primary care intranet.

2.5.5 Drugs affecting the renin-angiotensin system

2.5.5.1 Angiotensin-converting enzyme (ACE) inhibitors

Hypertension

Choice	Drug
1st choices	Perindopril (erbumine) tablets 2mg, 4mg, 8mg
	or
	Lisinopril tablets 2.5mg, 5mg, 10mg or 20mg

General Notes (Hypertension)

- Refer to NICE NG136 hypertension guidance.
- In hypertension associated with diabetes, ACE inhibitors are the drugs of first choice. They reduce proteinuria and slow the deterioration in renal function.

Prescribing Notes (ACE inhibitors)

- First dose hypotension may occur when ACE inhibitors are introduced to patients who are already receiving diuretics. Temporary withdrawal of the diuretic may reduce this risk (see BNF).
- Monitoring is required for all patients. Patient should have their electrolytes and renal function (creatinine and eGFR) checked:
  - before initiating treatment
  - within 2 weeks of commencing treatment
  - within 2 weeks of last dose increase
  - annually
- Treatment with ACE inhibitors can be initiated in the community but close medical supervision is required. ACE inhibitors should be initiated under specialist supervision and with careful monitoring in those with severe heart failure or in those with a number of co-morbidities (see BNF).
- ACE inhibitors tend to cause potassium retention. To avoid dangerous hyperkalaemia, potassium supplements or potassium-sparing diuretics should not be used with ACE inhibitors. If spironolactone is prescribed, serum potassium must be monitored. Ask about potassium-containing salt substitutes that a patient may be taking: one serving of common salt substitutes can contain around the potassium content of one oral potassium supplement tablet.
- ACE inhibitors cause cough in some patients. In patients who are intolerant of ACE inhibitors, an ARB may be considered as an alternative (see section 2.5.5.2).

- ACE inhibitors and ARBs are contra-indicated in pregnancy and should be avoided in patients who become pregnant.
- Prescribe perindopril as perindopril erbumine rather than perindopril arginine, as perindopril arginine has no clinical benefit over perindopril erbumine and is more costly.

Cautions (ACE inhibitors)

- Patients taking ACE inhibitors or ARBs should be informed that they are at an increased risk of Acute Kidney Injury (AKI) if they develop an illness associated with hypovolaemia and hypotension. ACE inhibitors and ARBs should be stopped temporarily Refer to 'sick day guidance' for further information (link to section 6.1.2).
- As elderly patients are at particular risk of renal impairment, renal function should be monitored pre-treatment in patients taking ACE inhibitors. Regular U&E checks may be needed after initiation.
- Initiation of ACE inhibitors or ARBs may precipitate hypotension in patients with severe aortic stenosis or outflow obstruction. Therefore use with caution and under the direction of a specialist.
- Caution is required in patients who may have renovascular disease. ACE inhibitors are contra-indicated in patients with renal artery stenosis.

Heart failure

Choice	**Drug**
1st choices	Ramipril capsules, tablets 1.25mg, 2.5mg, 5mg, 10mg
	or
	Perindopril (erbumine) tablets 2mg, 4mg
	or
	Lisinopril tablets 2.5mg, 5mg, 10mg, 20mg

General Notes (Heart failure)

- Refer to NICE heart failure guidance NG106.
- In heart failure, ACE inhibitors have been shown to improve symptoms and prolong life. They also improve outcome after myocardial infarction, particularly in patients with left ventricular dysfunction.
- For further Prescribing Notes on ACE inhibitors see (link)
- Cough is common in heart failure. ACE inhibitors cause cough in some patients. Do not rule out an ACE inhibitor until you are certain it is causing the cough.
- Every patient with heart failure as a result of left ventricular systolic dysfunction and who has no contra-indications should be prescribed RAAS inhibition with either ACEi/ARB/ARNI.
- For the prescribing of sacubitril/valsartan (Entresto®) refer to NICE TA388. Treatment with sacubitril valsartan should be started by a heart failure specialist with access to a multidisciplinary heart failure team.
- Sacubitril /valsartan should not be co-administered with an ACE inhibitor. Due to the potential risk of angioedema when used concomitantly: sacubitril/valsartan must not be started until 36 hours after taking the last dose of ACE inhibitor therapy; ACE inhibitor therapy must not be started until 36 hours after the last dose of sacubitril/valsartan.

Cautions [add link to ACE inhibitors cautions]

Secondary Prevention

Choice	**Drug**
1st choices	Perindopril (erbumine) tablets 2mg, 4mg, 8mg
	or
	Ramipril tablets, capsules 1.25mg, 2.5mg, 5mg, 10mg

Prescribing Notes – link to ACE inhibitor prescribing notes

Cautions – link to ACE inhibitor cautions

2.5.5.2 Angiotensin-II receptor antagonists (AIIRAs/ARBs)

Hypertension

Choice	**Drug**
1st choices	Candesartan tablets 2mg, 4mg, 8mg, 16mg, 32mg
	or
	Losartan tablets 12.5mg, 25mg, 50mg, 100mg

Heart Failure

Choice	**Drug**
1st choice	Candesartan tablets 2mg, 4mg, 8mg, 16mg, 32mg
2nf choice	Valsartan capsules 40mg, 80mg, 160mg

Diabetic nephropathy in type II diabetes mellitus

Choice	**Drug**
1st choice	Losartan tablets 12.5mg, 25mg, 50mg, 100mg
2nd choice	Irbesartan tablets 75mg, 150mg, 300mg

Prescribing Notes

- Refer to NICE NG136 hypertension guidance.
- Monitoring requirements are the same for ACE inhibitors and ARBs.
- ACE inhibitors and ARBs are contra-indicated in pregnancy and should be avoided in patients who become pregnant.

- The combination of an ACE inhibitor and ARB may cause increased adverse events and is not recommended. Refer to MHRA advice.
- For the prescribing of sacubitril/valsartan (Entresto®) see 2.5.5.1 under General notes *(add jump).*

Cautions

- Patients taking ACE inhibitors or ARBs should be informed that they are at an increased risk of Acute Kidney Injury (AKI) if they develop an illness associated with hypovolaemia and hypotension. ACE inhibitors and ARBs should be stopped temporarily. Refer to 'sick day guidance' for further information (link to section 6.1.2).
- As elderly patients are at particular risk of renal impairment, renal function should be monitored pre-treatment in patients taking ARBs. Regular U&E checks may be needed after initiation
- Initiation of ACE inhibitors or ARBs may precipitate hypotension in patients with severe aortic stenosis or outflow obstruction. Therefore use with caution and under the direction of a specialist.
- Caution is required in patients who may have renovascular disease. ARBs should be used with caution in patients with renal artery stenosis.

2.6 Nitrates and calcium-channel blockers, and other antianginal drugs

2.6.1 Nitrates

Choice	Drug
Acute relief	Glyceryl trinitrate spray 400 micrograms per metered dose
Ongoing treatment	Isosorbide mononitrate m/r capsules 25mg, 40mg, 50mg, 60mg; m/r tablets 25mg, 40mg, 50mg, 60mg

Prescribing Notes

- NICE CG126 covers the management of Stable Angina.
- Nitrates are used in the management of angina pectoris, unstable angina, heart failure and acute myocardial infarction.
- **Modified release nitrates should not be given more than once daily as nitrate tolerance will develop**. A daily nitrate-free period is necessary to minimise tolerance. The length of the nitrate-free period required varies, and depends on the pharmacokinetic properties of each preparation.
- Therapy should not be discontinued suddenly. Both dosage and frequency should be tapered gradually
- Asymmetric dosing regimens with standard-release nitrate preparations can be confusing to patients and could lead to non-compliance and nitrate tolerance. Consider a switch to modified release preparation.
- Phosphodiesterase type 5 inhibitors (e.g. sildenafil, vardenafil and tadalafil) have been shown to potentiate the hypotensive effects of nitrates (possibly resulting in collapse, unconsciousness and even death), and coadministration with glyceryl trinitrate is therefore contraindicated.
- Nitrates may occasionally aggravate angina in hypertrophic cardiomyopathy and increase intra-ocular pressure in glaucoma.

2.6.2 Calcium-channel blockers (CCBs)

CCBs are divided into two subtypes which have important pharmacological differences:

i. Rate-limiting non-dihydropyridine CCBs - verapamil and diltiazem - which are negatively inotropic and should be avoided in heart failure or reduced left ventricular function

ii. Dihydropyridine CCBs - amlodipine, felodipine, lacidipine, lercanidipine, nicardipine, nifedipine and nimodipine

Hypertension

Choice	Drug
1st choice	Amlodipine tablets 5mg, 10mg
2nd choice	Lercanidipine tablets 10mg, 20mg

Angina

Choice	Drug
1st choice CCB (patient taking a beta-blocker)	Amlodipine tablets 5mg, 10mg
2nd choice CCB (patient unable to tolerate a beta-blocker)	Diltiazem m/r tablets 60mg, 90mg, 120mg,; m/r capsules 90mg, 120mg, 180mg, 200mg, 240mg, 300mg, 360mg **Prescribe by brand name**

Supraventricular arrhythmias – to be used under secondary care guidance only

Choice	Drug
1st choice	Verapamil m/r tablets 120mg, 240mg **Prescribe by brand name***
*patients switched between brands due to medicines shortages may require closer monitoring of BP in the initial stages	

Prescribing Notes

- The commonest problem with amlodipine is ankle oedema, which may necessitate stopping as the oedema responds poorly to leg elevation or diuretics.

- A switch to lercanidipine may be reasonable to try if a patient develops ankle oedema with amlodipine.
- Felodipine m/r is still a reasonable choice, and there is no need to switch patients already stable on felodipine m/r.
- The treatment of patients currently receiving concomitant simvastatin 40 mg and amlodipine or diltiazem should be reviewed at their next routine appointment. Switch to atorvastatin 20mg and monitor lipid levels to ensure lowest necessary dose of atorvastatin is used. See MHRA and 2.12 lipid regulating drugs (ADD jump).
- The rate limiting CCBs diltiazem or verapamil may be considered for angina or following myocardial infarction if a beta-blocker cannot be used.
- Diltiazem and verapamil have negative inotropic effects and should be avoided in patients with LV dysfunction or heart failure.
- A long-acting formulation should be used if diltiazem is prescribed. Different versions of modified-release preparations may not have the same clinical effect. Therefore prescribe by brand, taking care to prescribe either the once or twice daily option as appropriate.
- Diltiazem should only be used under specialist advice if given with beta-blockers due to risk of bradycardia.
- Verapamil may be used to treat supraventricular arrhythmias or occasionally, atrial fibrillation (see section 2.3.2).
- The combination of a beta-blocker and verapamil should only be used under specialist advice because bradycardia, asystole, severe hypotension, and heart failure can occur. **It must be avoided in patients with heart block or heart failure.**
- Standard release nifedipine may be harmful and is no longer recommended for angina or hypertension.

2.6.3 Other anti-anginal drugs

These drugs are not first line agents and should be reserved for the indications outlined.

NICE CG126 on the management of stable angina advises that if the person cannot tolerate beta-blockers and calcium channel blockers, or both are contraindicated, monotherapy with one of the following drugs can be considered:

- long-acting nitrate (link to 2.6.1 Nitrates)
- ivabradine
- nicorandil
- ranolazine

The decision on which drug to use should be based on comorbidities, contraindications, the person's preference and drug costs.

(i) Ivabradine

General Notes ivabradine

Heart Failure

- NICE recommend that ivabradine, in combination with standard therapy including a beta-blocker (unless contraindicated or not tolerated), or when beta-blocker therapy is contraindicated or not tolerated, is an option for treating New York Heart Association (NYHA) class 2 to 4 stable heart failure in patients who
    - Have a left ventricular ejection fraction of ≤ 35% and
    - Are in sinus rhythm with a heart rate of ≥ 75 beats/min
- Ivabradine should be initiated only by a heart failure specialist after 4 weeks of stable optimal standard therapy; monitoring and dose titration should be carried out by heart failure specialist, or a GP with a specialist interest in heart failure, or by a heart failure specialist nurse.

Angina

- Ivabradine should only be initiated by specialists for angina as per NICE CG126 Management of Stable Angina.

- Treatment with ivabradine should be discontinued if there is no improvement in symptoms of angina within 3 months.

Off-label use

- Ivabradine is sometimes used by specialists to manage postural orthostatic tachycardia syndrome (POTS) or inappropriate sinus tachycardia with initiation by specialist in secondary care.

Cautions

- Ivabradine may be associated with bradycardia, atrial fibrillation, and other cardiovascular risks:
  - Only start ivabradine in adults with normal sinus rhythm if the resting heart rate is at least 70 beats per minute.
  - Do not prescribe ivabradine with verapamil, diltiazem, or strong CYP3A4 inhibitors
  - See MHRA for further details.

(ii) Nicorandil

General Notes nicorandil

- Nicorandil should be reserved for the treatment of stable angina in patients where treatment with rate-limiting agents, nitrates or dihydropyridine CCBs are ineffective, contra-indicated or not tolerated.
- Gastrointestinal ulcerations, skin and mucosal ulceration have been frequently reported with nicorandil. These are refractory to treatment and most only respond to withdrawal of nicorandil treatment. If ulcerations develop, nicorandil should be discontinued.
- If prescribed, quantities should be in multiples of 10 to ensure stability of the product.

(iii) Ranolazine

General Notes ranolazine

- Ranolazine is indicated for treatment of stable angina in patients inadequately controlled or intolerant of first-line antianginal therapies.
- Ranolazine is sometimes used in patients with microvascular angina (ESC 2024).
- Ranolazine inhibits myocardial late sodium current (hence reduces calcium influx) but does not affect heart rate or BP, thus may be particularly useful in patients with low BP and/or low heart rate.

Caution

- Caution in patients with body weight <60kg or borderline renal function (avoid if eGFR less than 30mL/minute/1.73m^2).
- Ranolazine is largely metabolised by the CYP3A4 system thus there is a potential for serious drug interactions, especially at higher doses (see BNF).

2.6.4 Peripheral vasodilators and related drugs

General Notes

- There is currently insufficient evidence to recommend the routine use of peripheral vasodilators.
- See NICE CG147 on Lower Limb Peripheral Arterial Disease and ESC Guideline for the management of peripheral arterial and aortic diseases.
- The use of vasodilators may increase blood flow at rest, but the few controlled studies carried out have shown little improvement in walking distance or sustained increase in muscle flow during exercise.

- Symptoms in patients with intermittent claudication are often improved through the use of treatments and lifestyle interventions to reduce cardiovascular risk. First line advice is to exercise and stop smoking. Those remaining symptomatic may be considered for treatment with naftidrofuryl and assessed for improvement after 3 to 6 months (discontinue if no symptomatic benefit).
- First-line management of Raynaud's phenomenon includes avoiding exposure to cold and stopping smoking. A calcium channel blocker such as nifedipine m/r [off-label] may be useful for reducing the frequency and severity of vasospastic attacks.
- Patients suffering intermittent claudication or Raynaud's phenomenon should be specifically advised to exercise and stop smoking.

Cautions

- The MHRA Drug Safety Update December 2014 detailed the risk of cardiovascular and bleeding events linked to cilostazol. (Pletal®). Cilostazol is restricted to second line treatment under the guidance of a secondary care specialist and is contraindicated with some cardiovascular conditions and medicines.

2.7 Sympathomimetics

For specialist use in secondary care only.

2.8 Anticoagulants and protamine

2.8.1 Parenteral anticoagulants

General Notes

- Parenteral anticoagulants are for specialist initiation in secondary care only. Patient factors such as weight, renal function and indication will impact on dosing.
- Refer to NICE NG158 Venous Thromboembolic diseases.
- Refer to enoxaparin shared care guideline.
- Unfractionated heparin use in the elderly – caution is required in the frail/very elderly, in whom daily doses of 20,000 units may be sufficient for full heparinisation.

2.8.2 Oral anticoagulants

2.8.2.1 Atrial Fibrillation (AF)

Prophylaxis of stroke and systemic embolism in non-valvular AF

Choice	**Drug**
1st choice	Apixaban tablets 2.5mg, 5mg
2nd choice	Rivaroxaban **tablets** 15mg, 20mg
	or
	Dabigatran capsules 110mg, 150mg
	or
	Edoxaban tablets 15mg, 30mg, 60mg
3rd choice	Warfarin tablets 1mg, 3mg

Doses of DOACs for AF (reduce dose in renal impairment based on Cockcroft Gault calculation of CrCl. Do not use estimated GFR)				
Drug	Creatinine Clearance			
	≥ 50 ml/min	30-49 ml/min	15-29 ml/min	<15ml/min
Apixaban	5 mg twice daily Reduce to 2.5 mg twice daily in patients with two or more of the following characteristics: o Age ≥80 years o Body weight ≤60kg o Serum creatinine ≥1.5mg/dL (133 micromoles/L)		Reduce dose to 2.5mg twice daily	Do not use
Dabigatran	Usual dose is 150mg twice daily Consider reducing to 110mg twice daily in patients aged 75-80years, or with moderate renal impairment, gastritis/ GORD or at increased risk of bleeding Always reduce to 110mg twice daily in patients >80 years or if taking verapamil		Do not use	Do not use
Edoxaban	60mg once daily Reduce to 30mg edoxaban once daily in patients with one or more of the following clinical factors: • Low body weight ≤60kg • Concomitant use of ciclosporin, dronedarone, erythromycin or ketoconazole	30mg once daily		Do not use
Rivaroxaban	20 mg once daily with food	Reduce dose to 15mg daily with food		Do not use

SPS

Anticoagulation General Notes

- Refer to NICE NG196 and ESC guidelines on atrial fibrillation.
- Clinical Knowledge Summaries provide a comprehensive overview in relation to oral anticoagulation and includes information that patients should be given prior to treatment and monitoring that should be carried out. Information on switching between anticoagulant regimens is also included.
- Anticoagulation should not be withheld solely because of a person's age or their risk of falls.
- Indication and duration of treatment should be clearly recorded at initiation of treatment; the patient-held anticoagulant treatment booklet should be used. See BNF for details.
- Patients should be warned of the hazards of treatment with anticoagulants. In particular, they should be aware of the need to report symptoms such as bruising. Patients should be provided with safety netting advice on signs of clinically relevant bleeding or clotting (e.g. FAST mnemonic) and when it is important to represent to hospital.
- Anticoagulant alert cards must be carried by patients and can be ordered by e-mailing the HSC Business Services Organisation at the following address pharmacystationeryorders@hscni.net.
- The anticoagulant effect of DOACs fades rapidly 12 to 24 hours after the last intake. Therefore **strict compliance** by the patient is crucial for adequate protection. Refer to individual SPC for 'missed dose' guidance for each DOAC. In contrast, the anticoagulant effect of warfarin persists for several days after the last warfarin dose.

Prescribing Notes

DOAC prescribing notes

- Apixaban is recommended as first choice DOAC for AF.
- Where compliance is an issue, rivaroxaban is the most cost-effective once-daily choice.
- Rivaroxaban must be taken with food. The MHRA has received a small number of reports suggesting a lack of efficacy

(thromboembolic events) in people taking 15 mg or 20 mg rivaroxaban tablets on an empty stomach.

- Patients at extremes of body weight (i.e. <50kg or >120kg) were under-represented in initial DOAC clinic trials. For patients weighing more than 120kg, there has historically been a degree of caution surrounding the use of DOACs due to concerns of sub-therapeutic effect. Evidence is now available to support the use of apixaban and rivaroxaban at standard doses in patients weighing 120kg to 150kg as recommended by the International Society of Thrombosis and Haemostasis (ISTH). There is no need for DOAC therapeutic monitoring checks. Warfarin is generally preferable >150kg (BMI approximately 50kg/m^2).
- Calculating creatinine clearance (CrCl) for DOACs:
    - CrCl calculators embedded within GP IT systems do not give a reliable estimate of CrCl for the adjustment of DOAC doses and are not recommended
    - The use of a web based application such as MDCalc is suggested where actual bodyweight is used to calculate the CG CrCl. If in addition the patient's height is added the different weight method calculations (modified for body weight) can be seen giving a range of possible values for CrCl.
- Renal function should be monitored at initiation and at least annually for patients taking DOACs. Ensure any necessary dose reductions are made.
- Dabigatran capsules cannot be crushed or opened and cannot be used in standard compliance aids due to the instability of the drug. Some packs have short expiry dates once opened, therefore prescribers should, where possible, prescribe in full packs.

Warfarin prescribing notes

- Warfarin is recommended where DOACs are contraindicated, not tolerated or not suitable in patients with AF. This includes:
    - patients with mechanical prosthetic valves or significant mitral stenosis
    - patients with severe renal dysfunction (CrCl<15mL/min)
- Only warfarin 1mg and 3mg tablets should be prescribed.

- Vitamin K (phytomenadione) can be given to reverse the effects of warfarin but takes 6 to 12 hours to become effective. If rapid reversal of warfarin is required, specialist haematological advice on the agreed regional policy should be sought. See also BNF.

Cautions

- A lower initial loading dose of warfarin is recommended in patients aged over 70 years.
- There are many clinically important interactions with warfarin - consult BNF before prescribing.
- The MHRA reminds healthcare professionals of the bleeding risk with DOACs and of the importance that patients receive an appropriate dose based on renal function.
- DOACs are contraindicated in the setting of mechanical (metallic) valves. They may be used in bioprosthetic valves after 3 months post operatively. This is in line with EHRA guidance (see Table 1); recommendations in SPC may differ.
- DOACs are contraindicated in the setting moderate to severe mitral stenosis but may be used with other native valvular disease (see EHRA guidance, Table 1).
- Guidance on the management of dental patients taking anticoagulants or antiplatelet drugs by the Scottish Dental Clinical Effectiveness Programme (SDECP) has been adopted for use in Northern Ireland and is available at www.sdcep.org.uk.
- Specialist haematological advice should be sought regarding strategies for the reversal of the anticoagulant effects of DOACs.
    - Specific reversal agents for dabigatran (idarucizumab) and the factor Xa inhibitors apixaban and rivaroxaban (andexanet alfa▾) are now available. These are for **hospital only use** – see Managed Entry Decisions for further details on when they can be used. A specific anticoagulant reversal agent for edoxaban is not available.
    - For information on the management of bleeding complications see 'EHRA Practical Guide to NOAC use in AF.'

- Refer to BNF for full details of cautions, contraindications and interactions with DOACs.

2.8.2.2 Treatment of Pulmonary Embolism (PE) and Deep Vein Thrombosis (DVT) and prevention of recurrent DVT and PE

Choice	**Drug**
1st choices	Apixaban tablets 2.5mg, 5mg
	or
	Rivaroxaban tablets 15mg, 20mg
2nd choices	Dabigatran capsules 110mg, 150mg
	or
	Edoxaban tablets 30mg, 60mg
	or
	Warfarin tablets 1mg, 3mg

Prescribing notes

- Refer to NICE NG158 guidance on anticoagulation treatment for venous thromboembolism. Choice of anticoagulant depends on co-morbidities / clinical features.
- Apixaban or rivaroxaban are recommended first line in patients with no relevant co-morbidities or significant clinical features.
- Please note differing initial dose periods and dosing schedules; dose adjustment may be needed. Refer to BNF and CKS.
- Indication and duration of treatment should be clearly recorded at initiation of treatment; the patient-held anticoagulant treatment booklet should be used. See BNF for details.
- Estimated glomerular filtration rate (eGFR) can overestimate renal function and increase the risk of bleeding events.

Creatinine clearance (CrCl) should be calculated using the Cockcroft-Gault formula to determine dosage adjustments for DOACs. Refer to BNF for dosage adjustments in renal impairment. Do not use DOACs if CrCl is < 15ml/min (<30ml/min for dabigatran):
    - CrCl calculators embedded within GP IT systems do not give a reliable estimate of CrCl and are not recommended
    - The use of a web based application such as MDCalc is suggested where actual bodyweight is used to calculate the CG CrCl.
- Renal function should be monitored at initiation and at least annually for patients taking DOACs. Ensure any necessary dose reductions are made.
- The anticoagulant effect of DOACs fades rapidly 12 to 24 hours after the last intake. Therefore **strict compliance** by the patient is crucial for adequate protection. Refer to individual SPC for 'missed dose' guidance for each DOAC.
- Clinical Knowledge Summaries provide a comprehensive overview in relation to oral anticoagulation and includes information that patients should be given prior to treatment and monitoring that should be carried out. Information on switching between anticoagulant regimens is also included.
- Patients should be warned of the hazards of treatment with anticoagulants. In particular, they should be aware of the need to report symptoms such as bruising. Patients should be provided with safety netting advice on signs of clinically relevant bleeding or clotting (e.g. FAST mnemonic) and when it is important to represent to hospital.
- Anticoagulant alert cards must be carried by patients and can be ordered by e-mailing the HSC Business Services Organisation at the following address pharmacystationeryorders@hscni.net.
- Dabigatran capsules cannot be crushed or opened and cannot be used in standard compliance aids due to the instability of the drug.
- Rivaroxaban must be taken with food. The MHRA has received a small number of reports suggesting a lack of efficacy

(thromboembolic events) in people taking 15 mg or 20 mg rivaroxaban tablets on an empty stomach.

Cautions

- The MHRA reminds healthcare professionals of the bleeding risk with DOACs and of the importance that patients receive an appropriate dose based on renal function.
- Guidance on the management of dental patients taking anticoagulants or antiplatelet drugs by the Scottish Dental Clinical Effectiveness Programme (SDECP) has been adopted for use in Northern Ireland and is available at www.sdcep.org.uk.
- Specialist haematological advice should be sought regarding strategies for the reversal of the anticoagulant effects of DOACs.
    - Specific reversal agents for dabigatran (idarucizumab) and the factor Xa inhibitors apixaban and rivaroxaban (andexanet alfa▾) are now available. These are for **hospital only use** – see Managed Entry Decisions for further details on when they can be used. A specific anticoagulant reversal agent for edoxaban is not available.
- Refer to BNF for full details of cautions, contraindications and interactions.

2.8.2.3 Prophylaxis of venous thromboembolism in orthopaedics

Specialist initiation in secondary care only

Choice	**Drug**
1st choice oral anticoagulant for VTE in orthopaedic surgery	Apixaban tablets 2.5mg
2nd choices	Dabigatran capsules 75mg, 110mg
	or
	Rivaroxaban tablets 10mg

	(note: rivaroxaban capsules are high cost)

Prescribing Notes

- Refer to NICE NG89 Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism.
- Apixaban, dabigatran and rivaroxaban are approved for **specialist initiation only**, in hip and knee replacement surgery, for prophylaxis of venous thromboembolism.
- NICE have issued a number of pieces of guidance in relation to the DOACs and the prophylaxis of venous thromboembolism - these are listed below for information:
    - NICE TA 157 (September 2008) Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee surgery in adults
    - NICE TA 170 (April 2009) Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults
    - NICE TA 245 (January 2012) Apixaban for the prevention of venous thromboembolism after total hip or knee replacements in adults.

Cautions

- Refer to BNF for full details of cautions, contraindications and interactions with DOACs.

2.8.2.4 Acute Coronary Syndrome

Rivaroxaban in acute coronary syndrome

- Refer to NICE TA335 - Rivaroxaban for preventing adverse outcomes after acute management of acute coronary syndrome.
- In patients after acute coronary syndrome with elevated cardiac biomarkers, low dose rivaroxaban 2.5mg twice daily may be considered as an option, co administered with aspirin 75mg once daily, or with aspirin 75mg once daily plus clopidogrel 75mg once daily.
- This should only be undertaken under specialist guidance.
- Co-administration as per NICE TA335 may significantly increase bleeding risk and clinicians should carefully assess if bleeding risk outweighs potential benefit in individual patients.
- Co-administration of rivaroxaban with newer P2Y12 drugs (prasugrel or ticagrelor) is not currently recommended.
- Treatment discontinuation may be considered at 12 months because experience of treatment beyond this is limited.

2.8.2.5 Prevention of Atherothrombotic events

Rivaroxaban for preventing atherothrombotic events in people with coronary or peripheral artery disease

- Refer to NICE TA607.
- Low dose rivaroxaban 2.5mg twice daily (i.e. a quarter of the usual daily anticoagulant dose) plus aspirin 75mg daily is recommended as an option (**under specialist guidance**) for preventing atherothrombotic events in adults with coronary artery disease or symptomatic peripheral artery disease who are at high risk of ischaemic events.
- Clinicians should carefully assess if bleeding risk outweighs potential benefit in individual patients.

2.9 Antiplatelet drugs

(i) Management of Myocardial Infarction (STEMI or NSTEMI)

Refer to NICE NG185 and local trust protocol for early management / initial drug therapy.

Initial drug therapy and secondary prevention after myocardial infarction:

Choice	Drug	Dose
1st choice	Aspirin tablets 75mg, 300mg	initial loading dose of 300mg as a single dose, then 75mg daily

Dual antiplatelet therapy secondary prevention after myocardial infarction:

Choice	Drug	Dose
1st choice	Aspirin indefinitely plus:	Aspirin 75mg daily plus:
	$P2Y_{12}$ inhibitor for up to 12 months then stopped. The $P2Y_{12}$ inhibitors are listed below and should be **prescribed according to local trust protocol**: • Ticagrelor • Clopidogrel • Prasugrel (for patients undergoing PCI only)	
	Ticagrelor	Ticagrelor: Initially 180mg as a single dose, then 90mg twice daily for up to 12 months
		or
	Clopidogrel	Clopidogrel: Initially 300 to 600mg as a single dose, then 75mg daily for up to 12 months
		or

	Prasugrel	Prasugrel: Adult 18–74 years (body-weight up to 60kg) Initially 60mg for 1 dose, then 5mg once daily usually for up to 12 months. Adult 18–74 years (body-weight 60kg and above) Initially 60mg for 1 dose, then 10mg once daily usually for up to 12 months. Adult 75 years and over Initially 60mg for 1 dose, then 5mg once daily usually for up to 12 months. Aged 75 and older - consider whether person's risk of bleeding with prasugrel outweighs effectiveness, in which case offer ticagrelor or clopidogrel as alternatives.

(ii) Secondary prevention in cerebrovascular disease, peripheral arterial disease or multivascular disease

Choice	Drug	Dose
1st choice	Clopidogrel 75mg tablets	Secondary prevention of ischaemic stroke and transient ischaemic attacks, 75mg daily

Prescribing Notes

- The use of aspirin for *primary* prevention of cardiovascular events, in patients with or without diabetes, is of unproven benefit.
- Refer to NICE NG185 Acute Coronary Syndromes (ACS).
- There is no conclusive evidence that enteric-coated (e/c) preparations of aspirin are better tolerated. Therefore the e/c formulation of aspirin is not recommended.
- In acute myocardial infarction, a loading dose of 300mg of dispersible or crushed (if enteric-coated) aspirin is given as early as possible after the onset of symptoms. Thereafter, a daily maintenance dose of 75mg aspirin is suggested.
- Secondary prevention drug treatments are initiated in hospital after an acute myocardial infarction (MI). Dual antiplatelet therapy (DAPT) with aspirin plus a second antiplatelet is offered (unless contraindicated) and continued for up to 12 months after an MI). After DAPT, treatment with aspirin is usually continued indefinitely (unless the person is aspirin intolerant or has an indication for anticoagulation).
- The combination of anticoagulant and antiplatelet therapy is sometimes used in selected patients, where an indication for anticoagulation co-exists, e.g. atrial fibrillation. This should be prescribed under the care of a specialist. The combination significantly increases the bleeding risk so the duration of therapy should be clearly stated by secondary care. For further details refer to NICE NG185 Acute Coronary Syndromes.
- Dual antiplatelet therapy with aspirin and clopidogrel is sometimes initiated by neurovascular specialists after a high risk TIA or a minor ischaemic stroke. Treatment is initiated within 24 hours of the onset of symptoms and continued for 10 to 21 days, at which point patients should continue with single antiplatelet therapy (usually clopidogrel). For further details see CKS.
- An interaction between PPIs and clopidogrel leading to reduction of antiplatelet effect has been reported, but the clinical significance is uncertain. If co-prescribing a PPI with clopidogrel is thought necessary, lansoprazole or pantoprazole are preferred to omeprazole or esomeprazole See MHRA.

- Ticagrelor, co-administered with aspirin, is indicated for the prevention of atherothrombotic events in adult patients with acute coronary syndromes (ACS) for up to 12 months. Extended treatment with ticagrelor (following an initial 12 months course for ACS) is an option in those who have a history of MI and who are deemed to be at high risk of a future atherothrombotic event:. Refer to BNF or CKS for dosing regimens.
- A high risk of developing atherothrombotic events is defined as presence of at least one of the following five risk factors:
  - Age ≥65 years or
  - Diabetes mellitus requiring medication or
  - A second prior MI or
  - Evidence of multivessel coronary artery disease or
  - Chronic non-end stage renal dysfunction (creatinine clearance <60ml/min)
- Extended treatment is most clinically effective if it commences immediately after the initial course rather than after a gap in treatment. However it can be started within 1 year of stopping previous P2Y12 inhibitor treatment.
- Extended treatment should be stopped after 3 years of 60mg twice daily, or earlier if clinically indicated, e.g. if bleeding concern develops. See NICE TA420 for full details
- Guidance on the management of dental patients taking anticoagulants or antiplatelet drugs by the Scottish Dental Clinical Effectiveness Programme (SDECP) has been adopted for use in Northern Ireland and is available at www.sdcep.org.uk.
- The HSC Cardiology Network has issued Post-Coronary Stenting: Dual Antiplatelet Therapy Discharge Information Leaflet for professional staff.

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DAPT Professional staff information leafl

Link added to the PDF in document library on website

Caution

- Aspirin and clopidogrel are contra-indicated in patients with active peptic ulceration and bleeding disorders.
- Prasugrel is contraindicated in active bleeding, history of stroke or transient ischaemic attack.

- Ticagrelor is contraindicated in active bleeding or history of intracranial haemorrhage.
- Dyspnoea has been associated with the use of ticagrelor. If this is intolerable to the patient it is important to discuss treatment options with the Cardiologist as switching therapies may require reloading.

2.10 Stable angina, acute coronary syndromes and fibrinolysis – Refer to NICE CG126 for the management of Stable Angina

Refer to NICE NG185 Acute Coronary Syndromes, includes visual summaries on STEMI, unstable angina NSTEMI and secondary prevention

See also Rivaroxaban in Acute Coronary Syndrome (*ADD JUMP*)

2.11 Antifibrinolytic drugs and haemostatics

Choice	Drug
1st choice	Tranexamic acid tablets 500mg

Prescribing Notes

- The manufacturer recommends regular eye examinations and liver function tests when tranexamic acid is used long-term for hereditary angioneurotic oedema.

2.12 Lipid-regulating drugs

Choice	Drug	Dose
1st choices	Atorvastatin tablets 20mg, 40mg, 80mg	Aim for doses below (see BNF for full dosage information). Note: starting dose of 20mg once daily is not licensed for the primary prevention of cardiovascular events, but is in line with NICE NG238. Primary prevention (including type 1 and 2 diabetes): 20mg daily Secondary prevention: 80mg daily* Primary and secondary prevention of CKD: 20mg daily** *use a lower dose if potential drug interactions, high risk of adverse effects or patient preference. **increase the dose if the lipid target for primary or secondary prevention of CVD is not achieved and eGFR ≥30ml/min. Agree the use of higher doses with a renal specialist if eGFR < 30ml/min.
	or	
	Rosuvastatin tablets 5mg, 10mg, 20mg, 40mg (note: rosuvastatin capsules higher cost)	Refer to BNF

Prescribing Notes

- Refer to NICE NG238 and Lipid Management Pathways for NI (Lipid Management Pathway and Statin Intolerance Pathway).
- Other statins (simvastatin, pravastatin, fluvastatin) **may occasionally** be used if there are tolerability issues or, under secondary care guidance, for complex lipid management
- Simvastatin 80mg is no longer recommended due to the risk of adverse effects. People currently taking simvastatin 80mg should be advised to contact their doctor to arrange a switch to an alternative statin, usually atorvastatin. See MHRA.
- For place in therapy of ezetimibe, refer to Lipid Management Pathways | NI Formulary. Ezetimibe should be considered for use in combination therapy for all patients, in particular those who do not meet target LDL-C levels on statin treatment alone or where statin therapy is not tolerated or contra-indicated.
- Bempedoic acid is available for patients who meet the criteria outlined in NICE TA694. See NI Managed Entry decisions.
    - Bempedoic acid with ezetimibe can be used as separate tablets or a fixed-dose combination. The fixed-dose combination is the same price as bempedoic acid.
- Inclisiran is available for patients who meet criteria in SMC2358. See NI Managed Entry decisions.
- Two PCSK9 inhibitors are available (alirocumab and evolocumab) for patients who meet criteria outlined in NICE TA 393/ 394.
    - Alirocumab is an AMBER list medicine. A GP information sheet is available on the Interface Pharmacy website.
    - Evolocumab is an AMBER list medicine. A GP information sheet is available on the Interface Pharmacy website.

Cautions

- Caution should be exercised when prescribing other drugs with statins. Statins interact with many drugs including azole anti-fungals, macrolide antibiotics, HIV protease inhibitors, amiodarone, verapamil, grapefruit juice, and warfarin. See BNF for full details of drug interactions.

- Statins have been associated with new onset diabetes. See MHRA for further information.
- There have been some suspected (very infrequent) reports of new-onset or aggravation of pre-existing myasthenia gravis or ocular myasthenia associated with statin use. See MHRA for further information.

Lipid Management Pathways

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Editorial note: on conclusion of chapter review complete summary sheet and tagging updates.