Doncaster & Bassetlaw Medicines Formulary

Section 2.5.1: Vasodilator Antihypertensives

Hydralazine 25mg and 50mg Tablets
Hydralazine 20mg Injection

Sodium Nitroprusside 50mg Injection

Minoxidil 2.5mg, 5mg, and 10mg Tablets

Section 2.5.2: Central Antihypertensives

Clonidine hydrochloride 100microgram Tablets
Clonidine hydrochloride 150microgram/ml Injection

Methyldopa 250mg and 500mg Tablets

Moxonidine 200microgram, 300microgram and 400microgram Tablets

Section 2.5.4: Alpha-Adrenoceptor Blocking Drugs

Doxazosin 1mg, 2mg and 4mg Tablets

Section 2.5.5: Drugs Affecting the Renin-Angiotensin System

Lisinopril 2.5mg, 5mg, 10mg and 20mg Tablets
Ramipril 1.25mg, 2.5mg, 5mg and 10mg Capsules

Candesartan 2mg, 4mg, 8mg, 16mg and 32mg tablets
Irbesartan 75mg, 150mg and 300mg tablets

Approved by Drug and Therapeutics Committee: Sept 2014
Reviewed Date: Sept 2017

Prescribing Guidance:

Specialist advice should be sought for the management of hypertensive emergencies.

For dosage information, refer to the current edition of the BNF.

KEY: [UL] Unlicensed Preparation; Drug – first line choice; Drug – hospital only; Drug – Amber (TLS), Drug – Red (TLS), see http://medicinesmanagement.doncasterpct.nhs.uk/
Hydralazine is a direct acting arteriolar dilator used in the treatment of resistant hypertension especially in the 3rd trimester of pregnancy, and can be given parenterally in hypertensive crises (see BNF, via www.bnf.org.uk). It is rarely used alone for hypertension, as it causes tachycardia and fluid retention. Risk of side effects are lowered if the dose is kept below 100mg daily, but systemic lupus erythematosus (SLE) should be suspected if unexplained weight loss, arthritis or other unexpected ill health occurs.

Hydralazine can also be used in heart failure (in combination with a nitrate) as an alternative for patients intolerant of ACE inhibitors (ACEIs) and angiotensin receptor blockers (ARBs).

Sodium nitroprusside is used in hypertensive crises and now only available from 'special-order manufacturers'. It acts within 1 to 2 minutes, with the rate being adjusted (see BNF, via www.bnf.org.uk) to control the blood pressure. The infusion should be withdrawn gradually over 10 to 30 minutes to prevent a rebound increase in blood pressure. It has also been used in the treatment of heart failure and other cardiac disorders where it is necessary to quickly reduce left ventricular outflow (afterload) and lower raised ventricular pressure (preload). The infusion must be wrapped in foil to protect it from light.

Prolonged use can cause cyanide toxicity and in general the infusion should not continue for longer than 3 days. If required for several days, blood and plasma concentrations of cyanide and thiocyanate concentrations in serum should be monitored, for details see product data sheet. Signs of cyanide toxicity may include tachycardia, sweating, hyperventilation, arrhythmias and profound metabolic acidosis.

Minoxidil should be reserved for the treatment of severe hypertension resistant to other drugs. Vasodilatation is accompanied by increased cardiac output and tachycardia and patients develop fluid retention. For this reason the addition of a beta-blocker and a diuretic (usually furosemide, in high dosage) are mandatory. Hypertrichosis is troublesome and renders this drug unsuitable for women.

Clonidine is an imidazoline antihypertensive that appears to act centrally to reduce sympathetic tone, resulting in a fall in diastolic and systolic blood pressure and a reduction in heart rate. It is used in the management of hypertension and hypertensive crisis although other drugs with fewer adverse effects are now generally preferred.

Clonidine is sometimes used in the intensive care setting as an intravenous infusion (unlicensed use) as a sedative agent or to control withdrawal symptoms from opioids. Further information regarding the prescribing of clonidine in this indication can be obtained via the critical care intranet site.

Moxonidine is a centrally acting drug licensed for mild to moderate hypertension. It should only be considered when the usual first and second line antihypertensives have failed to control blood pressure adequately.
Methyldopa is not recommended as a first line agent due to adverse effects. It is, however, a safe option for use in pregnancy.

Doxazosin is used for treatment of hypertension where other drugs have failed to control blood pressure, or in patients with contraindications to other antihypertensive drugs.

Alpha-blockers have post-synaptic alpha-blocking and vasodilator properties and rarely cause tachycardia. However, they can cause a rapid fall in blood pressure so the first dose should be given with caution, preferably at bedtime.

Doxazosin XL should not be prescribed as there is insufficient evidence suggesting that it is better than the cheaper generic preparation (also given as a single daily dose)

**ACE Inhibitors:**

ACE inhibitors (ACEIs) are indicated post myocardial infarction (post MI), and in the treatment of heart failure and hypertension.

Dosage (Post Myocardial Infarction):

Ramipril (Start 3 to 10 days post-MI): 2.5mg twice daily increased after 2 days to 5mg twice daily. If 2.5mg dose not tolerated give 1.25mg twice daily for 2 days before increasing to 2.5mg twice daily, then 5mg twice daily

Lisinopril (Usually started within 24 hours of an MI):

- **Systolic BP greater than 120mmHg**: 5mg within 24 hours followed by further 5mg 24 hours later, then increasing to a maintenance dose of 10mg once daily after a further 24 hours
- **Systolic BP 100 to 120mmHg**: 2.5mg once daily increasing to a maintenance dose of 5mg once daily
- **Systolic BP less than 100mmHg**: not to be used

Dosage (Heart Failure and Hypertension):

When used in the treatment of heart failure, ACE inhibitors should be titrated to the maximum tolerated dose over a period of one to two months. In hypertension, doses are titrated to achieve target blood pressure control.

Ramipril: Initially 1.25mg once daily increased gradually at intervals of 1 to 2 weeks to maximum of 10mg daily

Lisinopril: Initially 2.5mg daily increased gradually to a maximum dose of 40mg daily

Prescribing outside this formulary should only take place via a New Product Request
ACE inhibitor therapy should be considered in patients with established diabetic nephropathy (in patients with normal or near normal creatinine and no hyperkalaemia) and also in those patients having either vascular disease or diabetes with one other cardiovascular risk factor (HOPE Study, 2000).

Diabetic patients are particularly prone to the hyperkalaemia and deterioration in renal function with ACE inhibitor therapy and must be monitored closely. ACE inhibitor therapy is contraindicated in known or suspected renovascular disease.

**Initiation and Monitoring:**
- There is no need to give a captopril test dose unless the patient is at a particularly high risk of renal artery stenosis or any other side effect. ACE inhibitors should be started at the lowest recommended dose (with the first dose given at night) and the dosage increased gradually.
- Urea and electrolytes (particularly creatinine and potassium) should be monitored closely for the first 3 months after initiating an ACE inhibitor. They should be checked (as a minimum) before initiation, 2 weeks after either initiation or a dose change, if the patient becomes unwell with

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deteriorating heart failure and following initiation of additional diuretic therapy.

- ACE inhibitors can cause a very rapid fall in blood pressure in patients who are volume depleted. If diuretic dose is greater than 80mg furosemide (or equivalent), the ACE inhibitor should be initiated under close supervision and the diuretic dose may need reducing 24 hours beforehand. However, this is rarely possible in heart failure due to the risk of pulmonary oedema.

Care must be taken to stop all potassium sparing diuretics prior to starting an ACE inhibitor.

### Treating heart failure

[Diagram showing the steps of treating heart failure]

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2 For more information on drug treatment see appendix D of the NICE guideline and ‘Chronic kidney disease’ (NICE clinical guideline 73).

3 Consider an ICD in line with ‘Implantable cardiovascular defibrillators for arrhythmias’ (NICE technology appraisal guidance 95).

4 NYHA class III-IV.

5 Not all ARBs are licensed for use in heart failure in combination with ACE inhibitors.

6 NYHA class II-III.

7 This does not include mixed race. For more information see the full guideline at www.nice.org.uk/guidance/CG108

8 Consider CRT in line with ‘Cardiac resynchronisation therapy for the treatment of heart failure’ (NICE technology appraisal guidance 120).
Angiotensin Receptor Blockers:

Angiotensin Receptor Blockers (ARBs) are generally only used in patients who need to discontinue ACE inhibitors due to intolerance. They should be used with caution in renal artery stenosis, mitral or aortic valve stenosis, and obstructive hypertrophic cardiomyopathy.

ARBs exhibit many properties similar to ACE inhibitors. However, as they do not inhibit the breakdown of bradykinin they are less likely to cause persistent, dry cough. They are therefore a useful alternative in those patients who have to discontinue an ACEI for this reason.

Candesartan has the strongest evidence in heart failure (see below) and both have evidence in treating hypertension, but irbesartan has most evidence of the two agents in type II diabetes.

Initiation and Monitoring (see above for ACE inhibitors)

Candesartan:

Dosage (Hypertension):
8mg once daily (in renal impairment and intravascular volume depletion – start with 4mg), adjusted (at four weekly intervals) according to response to a maximum dose of 32mg once daily

Dosage (Heart Failure):
Initiate at 4mg once daily, doubled every 2 weeks up to a target dose of 32mg once daily (or to the maximum tolerated dose)

Candesartan should be considered for use in heart failure in the following situations:
- As an alternative to ACE inhibitors in patients who are truly intolerant of an ACE inhibitor due to persistent cough (cough is a symptom of heart failure – the ACE inhibitor-induced cough is a dry, tickly cough)
- In addition to an ACE inhibitor when standard maximum tolerated treatment has been achieved (under Consultant Cardiologist advice)
Prescribing outside this formulary should only take place via a New Product Request.

See also NICE Clinical Guideline 108 (via [http://www.nice.org.uk/cg108](http://www.nice.org.uk/cg108))

**Irbesartan:**

Initiate at 150mg once daily and increase to 300mg once daily if needed (In haemodialysis or in elderly patients – initial doses of 75mg once daily may be needed)

**Irbesartan** is of particular use in the treatment of hypertension in type II diabetics where it has been show to be renoprotective in patients with nephropathy.
Items for Restricted Prescribing:

**Olmesartan** is restricted to prescribing in the renal hypertension clinic, where it will be used as an alternative to first-line formulary antihypertensives. Patients already controlled on formulary ARBs will not be switched.