

Prescribing for patients with heart failure with reduced ejection fraction. Information for Primary care.

The cornerstone of management is so-called “triple therapy” with an ACE inhibitor, beta-blocker and mineralocorticoid receptor antagonist. These are some guidelines for introducing and titrating therapy.

- Initial therapy will usually be started in secondary care, and an important part of treatment is to titrate therapy upward. The aim is to reach the dose shown to be effective in clinical trials, or to reach the maximal dose tolerated by the patient.
- It is probably true (although not proven) that in a patient who cannot reach targets for all drugs that a smaller dose of all three agents is better than a target dose of just one.
- The standard approach is to double the dose of an agent, wait 2-4 weeks and then double again until target is reached. Blood pressure, heart rate and renal function (ACE inhibitors and mineralocorticoid receptor antagonist) should be checked at each point.
- Which to increase in which order depends upon personal choice as well as clinical circumstance: the higher the blood pressure, the more ACEI titration is best; the faster the resting heart rate, the more β -blocker titration is indicated.
- It almost goes without saying that all patients are individuals, more fragile patients (particularly those with overt oedema or lower blood pressure) need to go more slowly and may never reach target dose.

ACE inhibitor.

The only ACE inhibitor shown to work in clinical trials is **enalapril** which should be used in preference to others. The target dose is 10 mg bd; typically a patient will be started on 2.5 or 5 mg bd; in patients who still have high blood pressure at the 10 mg bd dose, 20 mg bd is appropriate.

Ramipril is commonly used although has not been proven to be effective in chronic heart failure. It should **always** be used twice daily and the target dose is 5 mg bd.

Please note: although a dry cough is commonly cited as a reason for switching a patient to an angiotensin receptor antagonist (ARB), no ARB has been shown to increase survival, merely to reduce risk of admission to hospital for heart failure. If a patient complains of a cough, it is important to offer the patient the choice: they can continue to take a medication proven to prolong survival and bear with the cough; or change to a less effective medication.

A decline in eGFR is almost inevitable after starting ACE inhibitor. The fall is **not** a reason to stop ACE inhibitor, but if creatinine rises above $250 \mu\text{mol.L}^{-1}$, seek specialist advice.

Betablocker.

Carvedilol is the most widely used. It is a non-selective agent and has to be given twice daily. Bisoprolol has also been shown to be effective, and is β_1 -selective. In the only trial to

compare a selective to a non-selective β -blocker, carvedilol was more effective than metoprolol, and so is favoured.

A usual starting dose is 3.125 mg bd; and the target dose is 25 mg bd (or 50 mg bd in a patient weighing more than 85 kg).

Mineralocorticoid receptor antagonist (MRA).

Spironolactone and eplerenone are typically started at 25 mg od with a target dose of 50 mg od. Spironolactone commonly causes gynaecomastia and so eplerenone is commonly used in men.

The biggest concern with MRAs is the tendency to cause hyperkalaemia. Potassium **must** be checked after a week of initiation, before any dosage changes, and a minimum of 4-monthly. If potassium rises above 5.5 mmol.L^{-1} , then reduce dose. Some patients may only be on small dose such as 12.5 mg on alternate days.

	Starting dose	Target dose	Increase by	Frequency	Aims
Enalapril	2.5 mg bd	10 mg bd	Doubling	2 - 4 weekly	SBP>100 mmHg; creatinine <250 $\mu\text{mol.L}^{-1}$
Carvedilol	3.125 mg bd	25 mg bd	Doubling	2 - 4 weekly	Resting HR <70, >60 /min
MRA	25 mg od	50 mg od	Doubling	2 - 4 weekly	$\text{K}^+ \geq 4.0, \leq 5.5 \text{ mmol.L}^{-1}$

SBP=systolic blood pressure

HR=heart rate

Advice and Guidance

A number of departments at HEYHT offer an advice and guidance service which GPs can use to ask queries prior to or instead of making a referral to the department. The Cardiology Department can be contacted via 'Advice & Guidance' using e-Referrals.

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Suggested titration schedule:

<Patient sticker here>

Date seen

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Dose today	Suggested increase	Next step	Any comment	Aims
ACEI (Enalapril)				SBP > 100 mmHg; creatinine < 250 $\mu\text{mol.L}^{-1}$
B-blocker (Carvedilol)				Resting HR < 70, > 60 /min
MRA				K ⁺ ≥ 4.0 , ≤ 5.5 mmol.L ⁻¹

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