

## Prescribing ACE Inhibitors for patients with heart failure due to left ventricular dysfunction

The guidance does *not* override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Evidence from clinical trials demonstrates that patients with heart failure, due to left ventricular dysfunction, show an improvement in symptom control and a reduction in morbidity and mortality when treated with an ACE inhibitor (ACEI). Therefore, all patients diagnosed with heart failure due to left ventricular systolic dysfunction (ejection fraction  $\leq 40\%$ ) should be considered for an ACEI.

Contra-indications	Cautions
<ul style="list-style-type: none"> <li>- Haemodynamically relevant bilateral renal artery stenosis</li> <li>- Renal artery stenosis in a single functioning kidney</li> <li>- Aortic or mitral valve stenosis or outflow obstruction – except under specialist supervision</li> <li>- Known hypersensitivity to ACEI or excipients or to any other ACEI</li> <li>- History of angioedema of any cause</li> <li>- Pregnancy</li> <li>- Baseline potassium <math>&gt; 5.5</math> mmol/L</li> </ul>	<ul style="list-style-type: none"> <li>- Symptomatic or severe asymptomatic hypotension (systolic blood pressure (BP)<math>&lt; 90</math>mmHg)</li> <li>- Patients with a documented intolerance of ACEI due to symptomatic hypotension - consider re-challenging with a longer acting ACEI (such as ramipril)</li> <li>- Patients on high dose diuretics (i.e. furosemide <math>&gt; 80</math>mg daily) – increased risk of hypotension and renal dysfunction</li> <li>- Breastfeeding – seek specialist advice</li> <li>- Moderate to severe renal impairment: creatinine <math>&gt; 150\mu\text{mol/L}</math> or eGFR <math>&lt; 50</math>ml / min. See individual SPCs for dose adjustment requirements.</li> <li>- Baseline potassium <math>&gt; 5</math> to <math>5.5</math>mmol/l</li> </ul>

Seek specialist advice prior to initiation:
<ul style="list-style-type: none"> <li>- Hypertrophic cardiomyopathy</li> <li>- Hyponatraemia (serum Na <math>&lt; 135</math>mmol/L)</li> <li>- Symptomatic or severe asymptomatic hypotension (systolic BP<math>&lt; 90</math>mmHg)</li> <li>- Significant renal dysfunction/renovascular disease e.g. creatinine <math>&gt; 150</math> micromol/L or eGFR <math>&lt; 50</math>ml/min or hyperkalaemia (serum K<math>&gt; 5.0</math>mmol/L)</li> <li>- Renovascular disease (diagnosed as well as undiagnosed and clinically silent disease) e.g. PAD or severe generalised atherosclerosis</li> <li>- Patients undergoing dialysis/extracorporeal treatments or having desensitisation with wasp or bee venom</li> </ul>

### Initiation and monitoring

- Check baseline blood chemistry. (e.g. serum creatinine, urea, potassium, sodium and eGFR) and blood pressure (BP)
- Discontinue potassium supplements/potassium sparing diuretics (with the exception of aldosterone antagonists) and review need for concomitant nephrotoxic drugs e.g. NSAIDs
- Review dose of diuretic therapy to the minimum necessary to control oedema
- Start with the lowest recommended dose of ACEI and titrate as suggested below. Aim for the target dose, failing that, the maximum tolerated dose. **Some ACEI is better than no ACEI**

### Dose titration

- BP and blood chemistry (e.g. serum creatinine, urea, potassium, sodium and eGFR) should be checked within **two weeks** of initiation and any change of dose. Recheck at 1, 3, and 6 months after achieving maintenance dose, then at least 6 monthly thereafter. More frequent monitoring may be required especially if patients are on combined loop and thiazide diuretic therapy, or are taking aldosterone antagonists. Reduce dose/stop according to “worsening renal function” and “symptomatic hypotension” in “problem solving” below.
- ACEI dose should be doubled at no less than **2 weekly** intervals (if appropriate) - smaller dose increments may be more clinically suitable for certain patients

Licensed ACEI	Starting Dose (mg)	Target Dose (mg)
Ramipril	1.25mg once daily	5mg twice daily or 10mg once daily
Lisinopril	2.5mg-5mg once daily	30-35mg once daily
Enalapril	2.5mg twice daily	10-20mg twice daily

- **Ramipril** and **lisinopril** are the ACEI of choice for heart failure, however some patients will require titration of existing ACEI therapy.

## Problem Solving

- a. **Angioedema:** Rare but life threatening. Discontinue therapy and seek immediate advice from accident and emergency.
- b. **Worsening renal function:** An increase in urea, creatinine and K<sup>+</sup> is to be expected after initiation/titration of ACEI. If the increase is small and asymptomatic, no action is necessary. Please see the table below for recommended actions.

### Recommendations for monitoring ACEI therapy in patients with normal renal function\*

Blood Chemistry	Action
<b>Creatinine</b> ↑ up to <b>50%</b> above baseline or to <b>265µmol/L</b> (whichever is smaller). <b>OR K<sup>+</sup></b> ↑ to <b>≤5.5 mmol/L</b>	<b>No action required.</b> Repeat blood chemistry (urea, creatinine and potassium) within 2-4 weeks.
<b>Creatinine</b> ↑ > <b>50%</b> but < <b>100%</b> above baseline or between <b>265µmol/L</b> and <b>310µmol/L</b> (whichever is smaller). <b>OR K<sup>+</sup></b> ↑ to <b>≥ 5.5 - ≤5.9 mmol/L</b>	<b>Review required-</b> consider: <ol style="list-style-type: none"> <li>a) Stopping concomitant nephrotoxic drugs e.g. NSAID's, non essential vasodilators (e.g. calcium antagonists, nitrates) and if no signs of fluid retention, reduce the dose of diuretic.</li> <li>b) Review causes of high potassium. Stop other agents that cause hyperkalaemia e.g. potassium sparing diuretics.</li> </ol> Recheck renal function within 2 weeks. If despite adjusting medication the creatinine and K <sup>+</sup> remain higher than above the dose of ACEI should be halved and the blood chemistry re-checked in 5-7days. If the response to this is not satisfactory, seek specialist advice. Blood chemistry should be monitored closely until K <sup>+</sup> and Creatinine concentrations are stable
<b>Creatinine</b> ↑ by > <b>100%</b> (from baseline) or to <b>above 310µmol/L</b> . <b>OR K<sup>+</sup> ≥ 6mmol/l</b>	<b>Discontinue ACEI and discuss with cardiologist</b> <b>Note: It is very rarely necessary to stop an ACEI and clinical deterioration is likely if treatment is withdrawn; ideally, specialist advice should be sought before treatment discontinuation.</b>

\*[Additional recommendations for monitoring ACEI therapy in patients with chronic kidney disease \(CKD\) Stage 3 and above.](#)

- c. **Asymptomatic hypotension:** Does not usually warrant a change in therapy
- d. **Symptomatic hypotension:**
  - Consider dehydration and address as appropriate
  - Review diuretic dose with a view to decreasing dose if patient free of symptoms suggestive of fluid retention.
  - If dizziness, light-headedness and/or confusion occur in the setting of low blood pressure, consider stopping nitrates, calcium channel blockers and other vasodilators.
  - Monitor closely and allow longer intervals between dose titrations.
  - Aim to maintain treatment with both ACEI and beta-blockers, at a reduced dose if necessary
  - Seek specialist advice if measures do not resolve symptomatic hypotension
- e. **Persistent dry cough:**
  - Review aetiology of cough e.g. due to smoking, worsening heart failure/pulmonary oedema, respiratory disease, respiratory tract infection or ACEI therapy.
  - Review cough tolerability against benefits of an ACEI in chronic heart failure. Some patients may tolerate re-institution of the ACEI after a drug free period.

ACEI cough is harmless and every effort should be made to maintain treatment. If ACEI cough is significantly affecting the patient's quality of life, an Angiotensin Receptor Blocker (ARB) licensed for heart failure may be considered as an alternative to ACEI (see separate ARB guideline).

### Information for Patients

- ACEI treatment will improve day to day symptoms, prevent heart failure worsening, reduce risk of hospital admission and prolong life
- It may take a few weeks for symptoms to significantly improve after starting therapy
- Hypotension and dizziness are the most common side effects
- Should a dry, unproductive cough occur, this should be reported to your GP / heart failure nurse as this may be a sign of worsening heart failure and requires further investigation to establish the cause.
- Avoid over the counter anti-inflammatory drugs (NSAIDs), such as ibuprofen, soluble tablets and salt substitutes high in K.<sup>+</sup>

### References

- [Chronic Heart Failure. NICE clinical Guideline CG108. Issued Aug 2010](#)
- [ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012.](#)

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