

# Annex 2

## Practical guidance: use of angiotensin-converting enzyme inhibitors in patients with heart failure with reduced ejection fraction<sup>60</sup>

### *Indications*

- First line treatment, along with beta blockers.

### *Contraindications*

- history of angioneurotic oedema
- known bilateral renal artery stenosis.

### *Cautions/seek specialist advice*

- significant hyperkalaemia ( $K^+ > 5.0$  mmol/l)
- significant renal dysfunction (creatinine  $> 221$  micromol/l)
- symptomatic or severe asymptomatic hypotension (systolic BP  $< 90$  mm Hg).

### *Drug interactions to look out for:*

- $K^+$  supplements /  $K^+$  sparing diuretics
- 'low salt' substitutes with a high  $K^+$  content.

### *Starting and target doses*

ACE inhibitor	Starting dose	Target dose
captopril	6.25 mg three times daily	50 mg three times daily
enalapril	2.5 mg twice daily	10–20 mg twice daily
lisinopril	2.5 mg once daily	20 mg once daily (up to 35mg in BNF) <sup>5</sup>
ramipril	2.5 mg once daily	5 mg twice daily

### *How to use ACE Inhibitors*

- Start with a low dose (*see starting and target doses*) and double the dose at not less than two-weekly intervals. Healthcare professionals with experience in the use of ACE inhibitors may wish to uptitrate the dose of ACE inhibitor more rapidly, taking account of the risk of adverse effects and the need for close monitoring of toleration and blood chemistry.
- Aim for the target dose or, failing that, the highest-tolerated dose.
- Monitor blood pressure and blood chemistry (urea, creatinine, and electrolytes).
- Check blood chemistry one to two weeks after initiation and one to two weeks after each dose titration.
- When to stop uptitration/reduce dose/stop treatment (*see problem solving*).
- A specialist HF nurse may assist with patient education, follow up (in person/by telephone), biochemical monitoring and dose uptitration.

### *Advice to the patient*

- Give written advice and explain the expected benefits, ie treatment is given to improve symptoms, to prevent worsening of HF thereby avoiding hospital admission and to increase survival.
- Symptoms improve within a few weeks to a few months of starting treatment.
- Advise patients to report principal adverse effects, ie dizziness/symptomatic hypotension, cough (*see problem solving*).
- Advise patients to avoid NSAIDs not prescribed by a physician (self purchased over the counter) and salt substitutes high in  $K^+$ .

## ***Problem Solving***

### *Asymptomatic low blood pressure*

- Does not usually require any change in therapy.

### *Symptomatic hypotension*

- If the patient has dizziness, light headedness and/or confusion and low blood pressure reconsider need for nitrates, calcium channel blockers and other vasodilators. Calcium channel blockers should be discontinued unless absolutely essential (eg, for angina or hypertension).
- If no signs/symptoms of congestion consider reducing diuretic dose.
- If these measures do not solve the problem seek specialist advice.

### *Cough*

- Cough is common in patients with heart failure, many of whom have smoking-related lung disease, including cancer.
- Cough is also a symptom of pulmonary oedema which should be excluded when a new or worsening cough develops.
- ACE inhibitor-induced cough rarely requires treatment discontinuation.
- When a very troublesome cough does develop (eg one stopping the patient sleeping) and can be proven to be due to ACE inhibition (ie recurs after ACE inhibitor withdrawal and rechallenge) substitution with an angiotensin receptor blocker should be made.

### *Worsening renal function*

- Some rise in urea, creatinine and potassium is to be expected after initiation of an ACE inhibitor; if an increase is small and asymptomatic no action is necessary.
- An increase in creatinine of up to 50% above baseline or 266 micromol/l, whichever is smaller, is acceptable.
- An increase in potassium to <5.5 mmol/l is acceptable.
- If urea, creatinine or potassium do rise excessively consider stopping concomitant nephrotoxic drugs (eg NSAIDs), other potassium supplements/retaining agents (triamterene, amiloride, spironolactone/ eplerenone) and, if there are no signs of congestion, reducing the dose of diuretic. The safety and efficacy of an ACE inhibitor used with an ARB and spironolactone (as well as beta blocker) is uncertain and the use of all three inhibitors of the renin-angiotensin-aldosterone system together is not recommended.
- If greater rises in creatinine or potassium than those outlined above persist despite adjustment of concomitant medications, the dose of the ACE inhibitor should be halved and blood urea, creatinine and electrolytes rechecked within one to two weeks; if there is still an unsatisfactory response specialist advice should be sought.
- If potassium rises to >5.5 mmol/l or creatinine increases by >100% or to above 310 micromol/l the ACE inhibitor should be stopped and specialist advice sought.
- Blood urea, creatinine and electrolytes should be monitored frequently and serially until potassium and creatinine have plateaued.

*Reproduced from: McMurray J, Cohen-Solal A, Dietz R, Eichhorn E, Erhardt L, Hobbs FD, et al. Practical recommendations for the use of ACE inhibitors, beta blockers, aldosterone antagonists and angiotensin receptor blockers in heart failure: putting guidelines into practice. Eur J Heart Fail. 2005;7(5):710-21, with permission from John Wiley and Sons.<sup>60</sup>*