

Annex 5

Practical guidance: Use of mineralocorticoid receptor antagonist in patients with heart failure reduced ejection fraction⁶⁰

Indications

- Second-line treatment (after optimisation of ACE inhibitor and beta blocker) in patients with NYHA class II-IV HF. The safety and efficacy of spironolactone used with an ACE inhibitor and an ARB (as well as beta blocker) is uncertain and the use of all three inhibitors of the renin-angiotensin-aldosterone system together is not recommended.

Cautions/seek specialist advice

- significant hyperkalaemia ($K^+ > 5.0$ mmol/l).
- significant renal dysfunction (creatinine > 220 micromol/l or CKD stage > 3).

Drug interactions to look out for

K^+ supplements/ K^+ sparing diuretics

ACE inhibitors, ARBs, NSAIDs (avoid unless essential)

- 'low salt' substitutes with a high K^+ content.

Starting and target doses

Mineralocorticoid receptor antagonist	Starting dose	Target dose
spironolactone	25 mg once daily or on alternate days	25–50 mg once daily
eplerenone	25 mg once daily	50 mg once daily

How to use mineralocorticoid receptor antagonists

- Start with a low dose (*see starting and target doses*).
- Check urea, creatinine and electrolytes at one, four, eight and 12 weeks; six, nine and 12 months; six monthly thereafter.
- If K^+ rises above 5.5 mmol/l or creatinine rises to > 220 micromol/l reduce the dose to 25 mg on alternate days and monitor blood chemistry closely.
- If K^+ rises ≥ 6.0 mmol/l or creatinine to 310 micromol/l stop spironolactone immediately and seek specialist advice.
- A specialist HF nurse may assist with patient education, follow up (in person/by telephone), biochemical monitoring and dose up titration.

Advice to the patient

- 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 should improve within a few weeks to a few months of starting treatment.
- Advise patients to report principal adverse effects, ie dizziness/symptomatic hypotension.
- Advise patients to avoid NSAIDs not prescribed by a physician (self purchased 'over the counter') and salt substitutes high in K^+ .
- If diarrhoea and/or vomiting occurs, patients should stop the MRA and contact their physician.

Problem solving

Worsening renal function/hyperkalaemia

- See the *how to use mineralocorticoid receptor antagonists* section.
- The major concern is hyperkalaemia (≥ 6.0 mmol/l); conversely, a high normal potassium may be desirable in patients with HF, especially if they are taking digoxin.
- It is important to avoid other K^+ retaining drugs (eg K^+ sparing diuretics such as amiloride and triamterene) and nephrotoxic agents (eg NSAIDs).
- The safety and efficacy of an MRA used with an ACE inhibitor and an ARB (as well as a beta blocker) is uncertain and the use of all three inhibitors of the renin-angiotensin-aldosterone system together is not recommended.
- Be aware that some 'low salt' substitutes have a high K^+ content.
- Male patients treated with spironolactone may develop breast discomfort and/or gynaecomastia. These problems are significantly less common with eplerenone.

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.⁶⁰