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Medicines Commissioning Group recommendations on the Monitoring Requirements for a Combination of Spironolactone and a Renin-Angiotensin Drug

Recent Safety Guidance

The February 2016 MHRA Drug Safety Update (DSU) highlights the risk of potentially fatal hyperkalaemia when spironolactone and renin-angiotensin drugs are used together in heart failure. The risk of hyperkalaemia is increased in patients with impaired renal function. Spironolactone should not be used in patients with severe renal impairment or pre-existing hyperkalaemia.
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/500974/DSU_Feb_2016_pdf__2_.pdf

The DSU contains the following reminders for healthcare professionals:

- Concomitant use of spironolactone with an Angiotensin Converting Enzyme Inhibitor (ACEi) or Angiotensin Receptor Blocker (ARB) is not routinely recommended because of the risks of severe hyperkalaemia, particularly in patients with marked renal impairment.
- Use the lowest effective doses of spironolactone and ACEi or ARB if coadministration is considered essential
- Regularly monitor serum potassium levels and renal function
- Interrupt or discontinue treatment in the event of hyperkalaemia
- Suspected adverse reactions should be reported to us on a Yellow Card

The Issue: Frequency of Monitoring

- The DSU emphasises that monitoring of blood electrolytes is essential in patients prescribed a potassium-sparing diuretic and an ACEi or ARB for heart failure.
- The advice is to 'regularly monitor serum potassium levels and renal function' but there is no indication about the frequency of this.
- No national recommendation about the frequency of monitoring for this combination of drugs has been identified.

Recommendation for Monitoring

In the absence of any tightly defined monitoring guidelines for potassium when a combination of a RAS and spironolactone is used it may be pragmatic to ensure that:

- The frequency of monitoring should depend on the clinical status and stability of the patient. The monitoring interval should be short (days to 2 weeks) if the clinical condition or medication has changed, but is required at least 6-monthly for stable patients with proven heart failure.

  Chronic heart failure in adults: management NICE guidelines [CG108] Published date: August 2010.
- Is done monthly for those patients with a clinical status that is likely to fluctuate.
- Is done more frequently for any patient in times of acute illness (e.g. AKI etc)
- Refer to appendix 1 “Practical recommendations for the use of spironolactone taken from the NICE Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care (CG5 July 2003)” for further advice on monitoring spironolactone, particularly when starting treatment, and if potassium levels are raised.

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Agreed at the MCG on 6th September 2016

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Appendix 1

Practical recommendations for the use of spironolactone taken from:
Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care

NICE Clinical Guideline 5
July 2003

Which dose of spironolactone? **Dose (mg)** 12.5–25 daily * * 50 mg may be advised by a specialist if heart failure deteriorates and no problem with Hyperkalaemia
How to use • Start at 25 mg once daily • Check blood chemistry at: 1, 4, 8 and 12 weeks; 6, 9 and 12 months; 6 monthly thereafter • If K+ rises to between 5.5 and 5.9 mmol/litre or creatinine rises to 200 µmol/litre reduce dose to 25 mg on alternate days and monitor blood chemistry closely • If K+ rises to ≥ 6.0 mmol/litre or creatinine to > 200 µmol/litre stop spironolactone and seek specialist advice
Advice to patient • Explain expected benefits • Treatment is given to improve symptoms, prevent worsening of heart failure and to increase survival • Symptom improvement occurs within a few weeks to a few months of starting treatment • Avoid NSAIDs not prescribed by a physician (self-purchased 'over the counter' treatment, e.g. ibuprofen) • Temporarily stop spironolactone if diarrhoea and/or vomiting and contact physician
Problem solving ***Worsening renal function/hyperkalaemia:*** • See 'How to use section above' • Major concern is hyperkalaemia (≥ 6.0 mmol/litre) though this was uncommon in the RALES clinical trial; a potassium level at the higher end of the normal range may be desirable in patients with heart failure, particularly if taking digoxin • Some 'low salt' substitutes have a high K+ content • Male patients may develop breast discomfort and/or gynaecomastia
Adapted from *European Journal of Heart Failure* 2001, 3, 495-502 (McMurray et al. Practical recommendations for the use of ACE inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice), copyright (2001), with permission from European Society of Cardiology.