NEW DRUGS

New drugs

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Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Patiromer sorbitex calcium

Approved indication: hyperkalaemia

Veltassa (Vifor)
sachets containing 8.4 g powder for oral suspension

High concentrations of potassium can induce fatal cardiac arrhythmias. Hyperkalaemia can be an adverse effect of drugs which inhibit the renin–angiotensin–aldosterone system, such as the ACE inhibitors and the angiotensin receptor antagonists. This can be a particular problem in patients with chronic kidney disease. One approach to the problem is to use potassium-binding substances. While binders, such as sodium resonium, have been available for many years, they are poorly tolerated so better alternatives are needed.

Patiromer is an ion exchange polymer made up of beads of patiromer sorbitex calcium. It is mixed in water, apple or cranberry juice to form a suspension. This should be taken with food. In the gut, patiromer exchanges potassium for calcium. By binding potassium, the free concentration of potassium for absorption is reduced and faecal excretion of potassium increases. This lowers serum potassium. No patiromer is absorbed, but it could affect the absorption of other drugs including metformin, thyroxine and ciprofloxacin. The daily dose of patiromer should therefore be separated from other oral drugs by at least three hours.

The OPAL-HK trial enrolled 243 patients who had chronic kidney disease (estimated glomerular filtration rate 15–60 mL/min/1.73m^2) and serum potassium concentrations of 5.1–6.5 mmol/L. They were all taking inhibitors of the renin–angiotensin–aldosterone system, mainly ACE inhibitors. According to the severity of their hyperkalaemia, the patients started on either 4.2 g or 8.4 g of patiromer twice daily. The dose could be adjusted in response to the concentration of serum potassium. After four weeks the mean change in potassium was a decline of 1 mmol/L. The concentration fell into the target range in 76% of the patients.[1]

In the second phase of the trial, patients who had a potassium concentration within the target range were randomised to continue patiromer or switch to a placebo. After four weeks there was no change in the 55 patients who continued treatment, but the potassium concentration climbed by a median of 0.72 mmol/L in the 52 patients who switched to placebo. A potassium concentration of 5.5 mmol/L or above was reported in 60% of the placebo group compared with 15% in the patiromer group.[1]

A phase II trial investigated the doses needed to treat hyperkalaemia in patients with chronic kidney disease and type 2 diabetes.[2] All patients were treated with inhibitors of the renin–angiotensin–aldosterone system. Depending on the potassium concentration, the 306 participants were randomised to receive different doses of patiromer. After an eight-week treatment period there was a maintenance phase of 44 weeks during which the dose of patiromer was adjusted to control the concentration of potassium. All doses of patiromer reduced the mean potassium concentration within the first four weeks of the trial. For example, a dose of 12.6 g twice daily resulted in a mean reduction of 0.55 mEq/L (0.55 mmol/L) in patients with mild hyperkalaemia and 0.97 mEq/L (0.97 mmol/L) in those with moderate hyperkalaemia. During the maintenance phase approximately 77–95% of all patients had potassium concentrations in the target range at each monthly visit. Concentrations rose after treatment ceased.[2]

Patiromer has also been studied in patients with heart failure. The 120 patients in the trial either had chronic kidney disease or a history of hyperkalaemia that had required discontinuation of treatment with, for example, an ACE inhibitor. Patients took 15 g patiromer or a placebo twice a day, plus spironolactone. After four weeks of treatment potassium concentrations had increased in the placebo group and decreased with patiromer. The difference between the groups was 0.45 mEq/L (0.45 mmol/L). Hyperkalaemia occurred in 7% of the patients taking patiromer and 25% of the placebo group.[3]

During the clinical trials, most adverse effects were related to the gut. In the OPAL-HK trial 11% of patients experienced constipation, but diarrhoea also occurred in some patients (3%).[1] The action of patiromer will cause hypokalaemia in some patients. As well as reducing potassium concentrations, patiromer can cause a fall in magnesium. Serum concentrations of magnesium therefore need to be monitored for at least the first month of treatment. As patiromer releases calcium in exchange for potassium, some patients may be at risk of hypercalcaemia.

Patiromer could enable patients who have had to cease taking drugs that inhibit the renin–angiotensin–aldosterone system because of hyperkalaemia to continue treatment. While patiromer reduces serum

potassium, it is unknown if this will eventually improve clinical outcomes. Most of the trials were short term, but treatment may need to be long term as the potassium rises once patiromer is stopped. The main trials used twice-daily doses, but the product information recommends a once-daily dose. Longer term safety also needs to be confirmed. Other ion exchange substances have been associated with intestinal necrosis and patients with a history of bowel surgery or obstruction were excluded from the trials of patiromer. As there is a delayed onset of effect, patiromer should not be used alone in the emergency management of hyperkalaemia.

TT manufacturer provided additional useful information

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.