Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	3rd September 2019
Appraisal & Details	The Northern (NHS) Treatment Advisory Group considered an appraisal of **Patiromer (as patiromer sorbitex calcium) for the treatment of hyperkalaemia in adults.**
Recommendation	**The Northern (NHS) Treatment Advisory Group <u>does not</u> recommend the use of patiromer (as patiromer sorbitex calcium) for the treatment of hyperkalaemia in adults.** The group was concerned about the following: • The NICE Apprasial Consultation Document (Oct 2018) states that patiromer is not recommended for treating hyperkalaemia in adults. • There was not an active treatment control group in the clinical studies. • NICE and the SMC both state that the results of clinical trials with patiromer may not be relevant to NHS clinical practice because in the trials most people had a lower level of potassium than would be treated in the NHS. • Some groups of patients were excluded from the OPAL-HK study, who may be required a renin-angiotension-adosterone system inhibitor (e.g. patients with recent cardiovascular events, and severe heart failure). This may reduce the generalisability of the study results to real-life practice. • There is also no evidence to show that patiromer extends life or improves quality of life compared with standard care in people who would have treatment for hyperkalaemia in the NHS. • In the trial twice daily dosing was used but patiromer was licensed for once daily dosing to allow for a three hour window before taking other concomitant medicines to migate the effects of drug interactions/binding. • Limited evidence in severe hyperkalaemia and in patients with end-stage renal disease receiving dialysis. • The current evidence relates to acute use. In the OPAL-HK patients received up to 12 weeks treatment with patiromer. Other studies were up to 1 year duration. Longer-term is needed as partiromer would most likely be used as part of the patient's chronic disease management. • Concerns around cost-effectiveness versus current treatment options based on the current evidence, and the current NHS List price. It is not yet known what level of any discount or any commercial arrangements may be offered by the manufacturer. The group noted that NICE is due to issue a technology appraisal for patiromer in February 2020.
Clinical evidence summary	The OPAL-HK study was a two-part, single blind randomised withdrawal study that evaluated patiromer in patients with hyperkalaemia and chronic kidney disease on stable doses of at least one renin-angiotension-adosterone system inhibitor. The study recruited patients with hyperkalaemia (serum potassium ≥5.1mmol/L and <6.5mmol/L), stage 3 or 4 CKD (eGFR ≥15 to <60mL/min/1.73m^2) and on a stable dose of at least one RAAS inhibitor. The mean age of patients was 64 years (54% aged 65 and over, 17% aged 75 and over), 58% of patients were men, and 98% were Caucasian. Part A of the study included 243 patients treated for 4 weeks. Those with a baseline serum potassium of 5.1 to <5.5 mmol/L were treated with patiromer at a starting dose of

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	8.4g per day for 4 weeks. Those with a baseline serum potassium of 5.5 to <6.5 mmol/L were treated with patiromer at a starting dose of 16.8g per day for 4 weeks. The dose was titrated, as needed, based on the serum potassium level, assessed starting on Day 3 and then at weekly visits to the end of the 4 week treatment period, with the aim of maintaining serum potassium in the target range (3.8 to <5.1 mmol/L). The mean daily doses of patiromer were 13 g and 21 g in patients with serum potassium of 5.1 to <5.5 mmol/L and 5.5 to <6.5 mmol/L, respectively. At the end of 4 weeks 76% (95% CI: 70%, 81%) of patients had a serum potassium in the target range of 3.8 mmol/L to <5.1 mmol/L. In Part B, 107 patients with a Part A baseline serum potassium of 5.5 mmolq/L to <6.5 mmol/L and whose serum potassium was in the target range (3.8 mmol/L to <5.1 mmol/L) at the end of Part A and were still receiving RAAS inhibitor treatment were randomised to continue patiromer or to receive placebo for 8 weeks. In patients randomised to patiromer, the mean daily dose was 21 g at the start of Part B and during Part B. In Part B, serum potassium in patients on placebo increased significantly relative to patients who remained on patiromer (p<0.001). More placebo patients (91% [95% CI: 83%, 99%]) developed a serum potassium ≥5.1 mmol/L at any time during Part B than patiromer patients (43% [95% CI: 30%, 56%]), p<0.001. More placebo patients (60% [95% CI: 47%, 74%]) developed a serum potassium ≥5.5 mmol/L at any time during Part B than patiromer patients (15% [95% CI: 6%, 24%]), p<0.001. The potential of patiromer to enable concomitant RAAS inhibitor treatment was also assessed in part B. 52% of patients receiving placebo discontinued RAAS inhibitor treatment because of recurrent hyperkalaemia compared with 5% of those treated with patiromer.
Safety	The majority of the adverse reactions (ARs) reported from trials were gastrointestinal disorders, with the most frequently reported ARs being constipation (6.2%), diarrhoea (3%), abdominal pain (2.9%), flatulence (1.8%) and hypomagnesaemia (5.3%). Gastrointestinal disorder reactions were generally mild to moderate in nature, did not appear to be dose related, generally resolved spontaneously or with treatment, and none were reported as serious. Hypomagnesaemia was mild to moderate, with no patient developing a serum magnesium level <1 mg/dL (0.4 mmol/L) During the treatment phase of the OPAL-HK study, adverse events were reported in 47% (114/243) of patients, leading to discontinuation of patiromer in 6.2% (15/243) of patients. In the randomised-withdrawal phase, similar proportions of patients reported at least one adverse event, 47% (26/55) and 50% (26/50) of patiromer and placebo patients, respectively.
Patient Perspective	Patiromer is a treatment option for people with high blood serum potassium levels (hyperkalaemia). The company proposes that it would benefit people with stage 3 and 4 chronic kidney disease who are having a renin-angiotensin-aldosterone system inhibitor and who have high levels of serum potassium.
Cost analysis summary	The estimated incidence of hyperkalaemia is 1% to 10% of hospitalised patients, with renal impairment listed as the most common risk factor. The NHS List Price is £300 per 30-sachet pack, each sachet contains 8.4g or 16.8g of patiromer. It is not yet known whether any commercial arrangements will be offered.
Financial impact **PbR: tariff included**	The financial impact of this recommendation is expected to be nil.