

Lanthanum carbonate and sevelamer carbonate

for treating hyperphosphataemia in patients with chronic kidney disease

Technology Guidance from the MOH Drug Advisory Committee

Guidance Recommendations

The Ministry of Health's Drug Advisory Committee has recommended:

- ✓ Sevelamer carbonate 800 mg tablet for the treatment of hyperphosphataemia in patients with chronic kidney disease who:
 - have persistent hyperphosphataemia despite optimising treatment with calcium-based phosphate binders; or
 - cannot tolerate calcium-based phosphate binders due to hypercalcaemia.

Subsidy status

Sevelamer carbonate 800 mg tablet is recommended for inclusion on the Medication Assistance Fund (MAF) for the abovementioned indication.

MAF assistance **does not** apply to lanthanum carbonate 500 mg, 750 mg, and 1000 mg tablets.

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Factors considered to inform the recommendations for subsidy

Technology evaluation

- 1.1 The MOH Drug Advisory Committee (“the Committee”) considered the evidence presented for the technology evaluation of lanthanum carbonate and sevelamer carbonate for treating hyperphosphataemia in patients with chronic kidney disease (CKD). The Agency for Care Effectiveness conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for lanthanum carbonate and sevelamer carbonate was considered in line with their registered indications.
- 1.2 The evidence was used to inform the Committee’s deliberations around four core decision-making criteria:
 - Clinical need of patients and nature of the condition
 - Clinical effectiveness and safety of the technology
 - Cost-effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives
 - Estimated annual technology cost and the number of patients likely to benefit from the technology
- 1.3 Additional factors, including social and value judgments, may also inform the Committee’s subsidy considerations.

Clinical need

- 2.1 The Committee noted that local practice was aligned with international clinical guidelines for treating hyperphosphataemia where calcium-based phosphate binders are typically used first-line. Patients are later switched to non-calcium-based phosphate binders in cases of concomitant hypercalcaemia and hyperphosphataemia, severe vascular calcification, or poor phosphate control despite using calcium-based phosphate binders.
- 2.2 The Committee acknowledged that calcium-based phosphate binders are already subsidised on SDL, and there was a clinical need to subsidise a non-calcium-based phosphate binder for second-line hyperphosphataemia treatment to ensure appropriate patient care for those unable to receive calcium-based treatments.

Clinical effectiveness and safety

- 3.1 No randomised controlled trials (RCTs) involving lanthanum or sevelamer use in line with local practice for patients unable to receive calcium-based phosphate binders were identified.
- 3.2 The Committee understood available RCTs showed no significant differences in biochemical efficacy endpoints (such as serum phosphate levels) between sevelamer or lanthanum, and calcium-based phosphate binders among patients with CKD. However, both lanthanum and sevelamer were associated with a lower hypercalcaemia risk compared to calcium-based phosphate binders.
- 3.3 Both lanthanum and sevelamer were also associated with significantly less progression of coronary artery calcification when compared with calcium-based phosphate binders among patients undergoing haemodialysis. However, RCT results showed no consistent risk reduction for cardiovascular mortality with either lanthanum or sevelamer. The Committee also heard that sevelamer resulted in a lower risk of all-cause mortality compared with calcium-based phosphate binders in two small RCTs, but in a larger RCT (around 2,100 patients), mortality benefit was shown only within one subgroup of patients 65 years and older.
- 3.4 Two published head-to-head crossover RCTs comparing lanthanum with sevelamer showed no significant differences in biochemical endpoints between both agents. Results from a published network meta-analysis also showed no significant differences between the agents in terms of all-cause mortality. The most commonly reported adverse events associated with lanthanum and sevelamer were gastrointestinal in nature, such as constipation.
- 3.5 Based on available evidence, the Committee considered lanthanum and sevelamer were clinically comparable for treating hyperphosphataemia.

Cost effectiveness

- 4.1 The Committee considered the cost effectiveness of lanthanum and sevelamer based on published overseas studies in the absence of local economic evaluations studying second-line lanthanum or sevelamer use for treating hyperphosphataemia. The Committee acknowledged that results from a published economic evaluation in the UK showed that for dialysis patients with hypercalcaemia, switching from calcium acetate to sevelamer led to an incremental cost-effectiveness ratio (ICER) of £38,078 per QALY gained, while lanthanum was extendedly dominated. These results were considered marginally cost-effective in the UK context.
- 4.2 The Committee also considered results of a cost-effectiveness study conducted in Singapore comparing sevelamer with calcium carbonate as first-line therapy among patients with CKD, which resulted in an ICER of S\$51,756 per QALY gained. The Committee acknowledged that sevelamer was not positioned as first-line therapy in clinical practice, and results were not relevant for this evaluation.
- 4.3 As part of value-based pricing discussions, the manufacturers of lanthanum and sevelamer offered price discounts contingent on subsidy of their products. The Committee acknowledged that at the price proposed by the manufacturer, cost-effectiveness results for sevelamer in the UK analysis would be improved.
- 4.4 The Committee observed that average doses of lanthanum and sevelamer used in local practice were 2099 mg and 3292 mg respectively, based on data from Singapore General Hospital and the National University Hospital. The dose relativity ratio between both agents was 1.57, falling within the reported range in published dose relativity studies. The Committee considered it appropriate to use these average doses for calculating daily drug costs and budget impact.
- 4.5 Given lanthanum and sevelamer were considered clinically comparable, the Committee concluded that sevelamer carbonate, which had the lower proposed cost, was the more cost-effective option based on a cost-minimisation approach.

Estimated annual technology cost

- 5.1 The Committee estimated around 1100 people with hyperphosphataemia in Singapore would benefit from government assistance for sevelamer carbonate. The annual cost impact was estimated to be \$500,000 to <\$1 million in the first year of listing on the MAF.

Recommendation

- 6.1 Based on available evidence, the Committee recommended sevelamer carbonate 800 mg tablet be listed on the MAF for treating hyperphosphataemia in patients with CKD, given its acceptable clinical and cost effectiveness, and the clinical need for this treatment to ensure appropriate patient care.

About the Agency

The Agency for Care Effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health. It conducts evaluations to inform the subsidy of treatments, and produces guidance on the appropriate use of treatments for public hospitals and institutions in Singapore. When using the guidance, the responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional.

Find out more about ACE at www.ace-hta.gov.sg/about

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