



VERDICT & SUMMARY

Lanthanum carbonate

(Fosrenol[®]▼)

For the treatment of hyperphosphataemia in chronic renal failure

Committee's Verdict: **CATEGORY B (Q3)**

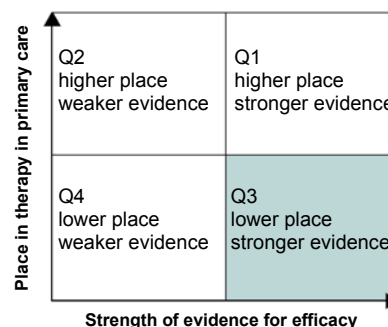
BNF: 9.5.2.2

Lanthanum carbonate is suitable for prescribing in primary care with the guidance of an ESCA, once it has been initiated and the dose stabilised in secondary care. However, because many patients on dialysis are seen and monitored frequently in secondary care, it may be more practical for all their related prescribing needs to be met in secondary care.

Category B: suitable for restricted prescribing under defined conditions

Q rating: The evidence for the efficacy of lanthanum carbonate was considered to be relatively strong, based on randomised controlled trials that have shown that lanthanum reduces serum phosphorus concentrations to a greater extent than placebo. One open-label study compared it with calcium carbonate and found no difference in efficacy. Any advantage of lanthanum carbonate over sevelamer has yet to be established and this gives it a relatively low place in therapy in primary care.

The Q rating relates to the drug's position on the effectiveness indicator grid. The strength of the evidence is determined by the quality and quantity of studies that show significant efficacy of the drug compared with placebo or alternative therapy. Its place in therapy in primary care takes into account safety and practical aspects of using the drug in primary care, alternative options, relevant NICE guidance, and the need for secondary care input.



MTRAC reviewed lanthanum because it is a new product with potential for prescribing in primary care.

Licensed indication

Lanthanum carbonate is indicated as a phosphate binding agent for use in the control of hyperphosphataemia in chronic renal failure patients on haemodialysis or continuous ambulatory peritoneal dialysis (CAPD).¹

Background information

Chronic renal failure is usually the result either of primary renal disease (e.g. glomerulosclerosis) or of renal damage in a multi-system disorder (e.g. diabetes mellitus and hypertension).² End-stage renal disease is defined as an irreversible decline in kidney function that is fatal in the absence of dialysis.³ The reduced kidney function leads to protein energy malnutrition, fluid retention (contributing to hypertension and cardiovascular events), anaemia, dyslipidaemia, and disturbances in bone and mineral metabolism (such as hyperphosphataemia, hypo- or hypercalcaemia). Hyperphosphataemia, together with reduced production of vitamin D₃, leads to the development of secondary hyperparathyroidism.

In 2001, the number of patients receiving renal replacement therapy (dialysis or transplantation) in

England was 547 patients per million population.² About half of these were on dialysis.

Current treatment options for controlling hyperphosphataemia in patients on haemodialysis include control of dietary phosphate intake (mainly protein) and the concomitant use of oral phosphate binders such as calcium carbonate, calcium acetate, aluminium hydroxide, sevelamer and lanthanum carbonate.

Clinical efficacy

All clinical trials were done in adult patients with end-stage renal failure (ESRF) on haemodialysis or CAPD, with serum phosphorus ≥ 1.8 mmol/L after wash-out of previous treatment with phosphate binder. Numbers of patients given below refer to the numbers in double-blind comparative phases in the trials. Four randomised controlled trials (RCTs) comparing the efficacy of lanthanum with placebo in patients with ESRF included a double-blind phase (total n = 335).⁴⁻⁷ The trials included a wash-out phase, an open-label dose-titration phase (three trials only) in which all patients received lanthanum, and a double-blind placebo-controlled phase lasting four or six weeks. Doses of lanthanum were fixed in this phase and

ranged from 225 to 3,000 mg daily. In one trial, only responders in the prior titration phase (phosphorus concentrations \leq 1.8 mmol/L) were included in the comparative phase.⁶ The primary outcome was serum phosphorus control, reported either as the mean reduction in concentration or the percentage of patients with concentrations \leq 1.8 mmol/L.

The mean serum phosphorus concentrations were significantly lower in lanthanum-treated groups (1.6 to 1.9 mmol/L where values were reported) than in placebo-treated groups (2.3 to 2.5 mmol/L; $p < 0.001$). The reduction with lanthanum 225 or 675 mg daily was not significant. Serum phosphorus was controlled in a higher percentage of patients taking lanthanum (65% in the study in which this was a primary outcome) than placebo (21%; $p < 0.01$).⁶

One open-label study ($n = 443$; duration 25 weeks) compared lanthanum carbonate with calcium carbonate, using doses adjusted monthly to control serum phosphorus.⁸ No difference in efficacy was found between the treatments. Phosphorus was controlled in 66% of patients with lanthanum and in 64% with calcium.

Adverse effects

One two-year open-label study ($n = 1,359$; study completed by 517 patients) assessed safety as the primary outcome in patients treated either with lanthanum or with other phosphate binders.⁹ The percentage of patients withdrawing was greater with lanthanum (71%) than with other treatment (53%). The most common reasons for withdrawal were adverse events (lanthanum patients 14% vs. control group 4%) and death (6% vs. 14%). The groups were not comparable in duration of exposure to treatment (lanthanum: mean 370 days, comparator: 501 days).

The most common adverse events reported in the trials were gastrointestinal, including nausea, vomiting and diarrhoea, which were reported in up to 37% of lanthanum-treated patients.⁹ Lanthanum treatment was not associated with changes in serum calcium concentrations. In the trial comparing lanthanum with calcium carbonate, the incidence of clinically significant hypercalcaemic events was greater in the calcium-treated group.⁸

Lanthanum plasma concentrations were higher in patients treated with lanthanum than with placebo or calcium, but they remained low (mean values of about 5 nmol/L compared with 1 nmol/L with placebo) and did not appear to increase over time.

For additional information on adverse events, refer to the Summary of Product Characteristics.¹

Additional information

- Doses of lanthanum carbonate are titrated from 750 to 3,750 mg daily according to response.¹
- At current prices, the cost of one year's treatment with lanthanum carbonate 1,500 to 3,000 mg daily is £1,388 to £1,963, and with sevelamer 7,200 mg daily it is £2,240.

References

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4. Joy MS, Finn WF. Randomized, double-blind, placebo-controlled, dose-titration, phase III study assessing the efficacy and tolerability of lanthanum carbonate: a new phosphate binder for the treatment of hyperphosphatemia. *Am J Kidney Dis* 2003;**42**:96-107.
5. Finn WF, Joy MS, Hladik G. Efficacy and safety of lanthanum carbonate for reduction of serum phosphorus in patients with chronic renal failure receiving hemodialysis. *Clin Nephrol* 2004;**62**:193-201.
6. Al-Baaj F, Speake M, Hutchison AJ. Control of serum phosphate by oral lanthanum carbonate in patients undergoing haemodialysis and continuous ambulatory peritoneal dialysis in a short-term, placebo-controlled study. *Nephrol Dial Transplant* 2005;**20**:775-782.
7. Chiang SS, Chen JB, Yang WC. Lanthanum carbonate (Fosrenol) efficacy and tolerability in the treatment of hyperphosphatemic patients with end-stage renal disease. *Clin Nephrol* 2005;**63**:461-470.
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9. Finn WF. Lanthanum carbonate versus standard therapy for the treatment of hyperphosphatemia: safety and efficacy in chronic maintenance hemodialysis patients. *Clin Nephrol* 2006;**65**:191-202.

Launch date: September 2006

Manufacturer: Shire

PL 08081/0041 - 0044

WARNING: This sheet should be read in conjunction with the Summary of Product Characteristics
This guidance is based upon the published information available in English at the time the drug was considered. It remains open to review in the event of significant new evidence emerging.

MTRAC can be contacted at the Dept. of Medicines Management, Keele University, Keele, Staffs ST5 5BG
Tel: 01782 584131 Fax: 01782 713586 Email: mtrac@keele.ac.uk Web: www.mtrac.co.uk

RELEVANT NICE GUIDANCE WAS NOT AVAILABLE AT THE TIME OF ISSUE OF THIS VERDICT

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