Cost-effectiveness of lanthanum carbonate versus sevelamer hydrochloride for the treatment of hyperphosphatemia in patients with end-stage renal disease: a US payer perspective


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study investigated the cost-effectiveness of lanthanum carbonate compared with sevelamer hydrochloride in adults with hyperphosphataemia with end-stage renal stage. The authors concluded that lanthanum carbonate was therapeutically effective and a cost-effective treatment relative to sevelamer hydrochloride. There was insufficient detail on the costing and available clinical evidence and considerable uncertainty presented in the results to be confident that the authors' conclusions were appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
To examine the costs and health benefits of lanthanum carbonate for the treatment of hyperphosphataemia in patients with end-stage renal disease, previously treated on a calcium-based binder and with serum phosphorus exceeding ≥6.0mg/dL and calcium values exceeding ≥8.4mg/dL.

Interventions
Lanthanum carbonate compared with sevelamer hydrochloride. Patients were assumed to receive either lanthanum carbonate at 2,250mg/day for the first week and 3,000mg/day thereafter or sevelamer hydrochloride at 4,800mg/day for the first week and 6,400mg/day thereafter. Patients had previously used a calcium-based binder agent.

Location/setting
Texas USA, community care

Methods
Analytical approach:
A health state transition Markov model was used to model the ongoing risk of cardiovascular disease and mortality. Evidence was synthesised from published studies, epidemiological data and one key clinical trial (Sprague SM et al. 2009, see Other Publications of Related Interest). The analysis time horizon was 10 years. The authors stated the study perspective was from the USA payer perspective.

Effectiveness data:
The key clinical outcome was reduction in serum phosphate levels measured in mg/dL and subsequently linked to risk of cardiovascular disease (CVD) events and mortality and cardiovascular events. The key study was a randomised head-to-head cross-over trial where the outcome was reduction in serum phosphate levels. A modified intention-to-treat analysis approach was taken with those receiving at least one dose of either lanthanum carbonate or sevelamer hydrochloride. The last observation carried forward was used for addressing missing data. The sample size was 188. The relative risk of CVD according to phosphate levels was derived from Block GA et al. 2004 (see Other Publications of Related Interest) and the relative risk of CVD mortality by phosphate levels was derived from Tentori F et al. 2008 (see Other Publications of Related Interest).

Monetary benefit and utility valuations:
Utility estimates were derived from published studies. A weighted average of the five CVD events were combined into one utility score for occurrence of CVD events for the first year and increased by 5% each year thereafter.
Measure of benefit:
The measures of benefit used were life years saved and quality-adjusted life-years (QALYs) discounted annually at 5%.

Cost data:
Direct medical costs included pharmaceuticals, costs of treating CVD events, CVD maintenance costs and mortality costs for CVD. Renal dialysis costs were omitted as these were assumed to occur equally in both arms. Drug quantities were extracted from the trial and published literature was relied on for the CVD event costs which were weighted by the proportions of CVD event occurrences. Pharmaceutical costs were USA average wholesale prices. Costs were presented in US $2009.

Analysis of uncertainty:
The model parameters were examined with one-way and probabilistic sensitivity analyses. One-way analyses were performed using most data parameters and when 95% confidence intervals were not available, values were tested ±20%. For probabilistic sensitivity analysis, 1,000 simulations were run using beta, gamma and log-normal distributions for model inputs. Sensitivity analysis results were illustrated using cost-effectiveness acceptability curves and cost-effectiveness planes.

Results
Over 10 years, for adults with end-stage renal disease who were previously treated with a calcium-binder, total costs for lanthanum carbonate were $48,575 compared with $47,959 for sevelamer hydrochloride. The corresponding QALYs were 3.078 for lanthanum carbonate compared with 3.053 for sevelamer hydrochloride. The incremental cost per QALY was $24,724. The incremental cost per life year saved was $15,053.

The results of the one-way sensitivity analyses showed the base findings were highly sensitive to changes in the price of lanthanum carbonate (an increase in lanthanum carbonate cost by 10% produced $111,898 per QALY gained) but stable to variations in other input values. From the probabilistic sensitivity analyses, the authors stated there was a 62% probability that lanthanum carbonate would be cost-effective at a threshold of $50,000 per QALY gained.

Authors' conclusions
The authors concluded that lanthanum carbonate was a cost-effective strategy compared with sevelamer hydrochloride for patients with hyperphosphataemia and end-stage renal disease. They stated that the cost-effectiveness results were robust in the sensitivity analyses.

CRD commentary
Interventions:
The therapeutic agents compared were well described. Readers should decide whether lanthanum carbonate was indicated for second-line therapy in their own setting and consult the trial report to assess exact details of treatment and baseline characteristics within the two groups and whether these were applicable in their own setting.

Effectiveness/benefits:
The clinical effectiveness of the agents was based on a head-to-head randomised controlled trial. The authors did not make it clear that this was the only trial making this comparison. The authors stated that economic evaluations for both lanthanum carbonate and sevelamer hydrochloride were conducted with similar comparators, so there may have been indirect clinical evidence available. The authors stated as a limitation that the effectiveness data was based on a relatively short follow-up. The clinical data that linked phosphate levels to CVD events and mortality were appropriately USA patient data. The authors stated that side-effects were not included as there was no significant difference shown in the trial. The actual results were not reported. Some things were unclear without specialist knowledge (such as why the baseline probability of a CVD event should be a weighted average of five CVD events rather than the probability of having any one of these events). Utility values were derived from literature that reported utilities for patients with end-stage renal disease and CVD disease. It was unclear whether the CVD utility decrement was applicable to the utilities with which it was multiplied.

Costs:
The resource quantities and unit costs were summarised briefly in the report. It was unclear whether the measurement...
and valuation of these resources would appear comprehensive and reasonable without reading the original sources. It may have been reasonable to include a cost for CVD mortality but the costs involved were not described. Costs were omitted for side-effects of treatment, concurrent CVDs, hypercalcaemia and dialysis and it was not known what impact these omissions would have on the results.

Analysis and results:
An incremental cost-effectiveness analysis was appropriately conducted and the results were well reported. Uncertainty around the results was appropriately presented given the sensitivity analyses conducted. The authors referred to other economic evaluations that compared each of the comparators in this study to calcium-based binders but the results for these were not reported. Limitations also acknowledged in the report included the various data sources used, multiple assumptions necessary and the extrapolation of 10-week trial data into the longer term.

Concluding remarks:
There was insufficient detail on the costing and available clinical evidence and considerable uncertainty presented in the results to be confident that the authors' conclusions were appropriate.

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