A modeled economic evaluation of sevelamer for treatment of hyperphosphatemia associated with chronic kidney disease among patients on dialysis in the United Kingdom

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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 objective was to assess the cost-effectiveness of sevelamer for the treatment of hyperphosphatemia, associated with chronic kidney disease, in patients receiving dialysis. The authors concluded that sevelamer offered good value, compared with calcium-based binders. The reporting was good and the methods were adequate, but several uncertainties remain, limiting the evaluation. These limitations should be considered fully when interpreting the results.

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

Study objective
The objective was to assess the cost-effectiveness of sevelamer for the treatment of hyperphosphatemia, associated with chronic kidney disease, in patients who had been receiving dialysis for an average of 38.2 months.

Interventions
The intervention was sevelamer carbonate (6.9g/day) for the initial treatment of hyperphosphatemia. The comparator was calcium-based phosphate binders, which were those most commonly used in the UK; it was assumed that 70% of patients received calcium acetate (5.3g/day) and 30% received calcium carbonate (4.9g/day).

Location/setting
UK/secondary care.

Methods
Analytical approach:
A Markov model was developed to estimate the cost-effectiveness of sevelamer, over a lifetime. The authors stated that they adopted a UK NHS perspective.

Effectiveness data:
The key effectiveness estimate was the comparative overall survival rate. Treatment-specific overall survival, up to 44 months, was from the Dialysis Clinical Outcomes Revisited (DCOR) study, a multicentre, randomised, open-label trial, of 2,103 patients, in the USA. Survival was extrapolated to a lifetime, using Weibull regression. The effectiveness of sevelamer in reducing hospitalisations was from the DCOR study. It was assumed that the reduction in hospitalisations was maintained over the patient's lifetime.

Monetary benefit and utility valuations:
The utility score for patients on dialysis (0.61) was from a published systematic review of the published literature for utility measures, associated with chronic kidney disease. The five included studies used either the EQ-5D or time trade-off techniques, and were conducted in the USA, the Netherlands, Canada or Sweden.

Measure of benefit:
The health benefit was measured in quality-adjusted life-years (QALYs). Future QALYs were discounted at an annual rate of 3.5%.

Cost data:
The drug and hospital costs incurred by the NHS were analysed. Hospitalisations and resource use were from the DCOR study, and were combined with unit costs, from UK sources. The drug costs for calcium acetate and calcium carbonate were from the 2009 British National Formulary. The cost of sevelamer was based on the 2009 manufacturer's price for sevelamer hydrochloride. The cost per patient bed-day for each hospitalisation was from NHS Reference costs for 2007 to 2008. The cost of dialysis was excluded. Where necessary, the costs were inflated to 2009 values, using the most recent UK consumer price index. Future costs were discounted at an annual rate of 3.5%. All costs were reported in UK £.

Analysis of uncertainty:
One-way sensitivity analysis was conducted to assess the impact of model assumptions and parameter uncertainty, on the results. Subgroup analyses were conducted to assess the effects of restricting the analysis to various age groups.

**Results**
Over a lifetime, the calcium-based binders cost £29,856 per patient and produced 4.6476 life-years or 2.8164 QALYs; sevelamer cost £39,701 and produced 5.3808 life-years or 3.2608 QALYs. Sevelamer had an incremental cost of £9,845 and produced an additional 0.7332 life-years or 0.4443 QALYs.

The incremental cost-effectiveness ratio (ICER) for sevelamer over calcium-based binders was £13,427 per life-year gained or £22,157 per QALY gained.

The results were sensitive to variations in overall survival (HR 0.93) and the inclusion of dialysis costs. Using the lower and upper 95% confidence limits for the hazard ratio for overall survival (0.79 to 1.10), the ICER ranged from £20,019 per QALY gained to sevelamer being dominated by calcium-based binders (sevelamer producing fewer QALYs at a higher cost). When the annual cost of dialysis was included the ICER increased to £84,269 per QALY gained. In the subgroups, the ICER reduced to £15,864 per QALY gained for patients aged 45 years or older, or £13,296 for patients aged 65 years or older.

**Authors' conclusions**
The authors concluded that sevelamer was good value, compared with calcium-based binders.

**CRD commentary**
**Interventions:**
The intervention was clearly stated. An appropriate comparator, standard care, was used. The authors did not mention any relevant alternatives that were excluded from the analysis.

**Effectiveness/benefits:**
The effectiveness data were clearly reported. They were from a large randomised controlled trial, which is the gold standard design. The authors highlighted a limitation of their analysis that was the use of US data. They stated that UK population data were not available, so it was assumed that the US data were generalisable to the UK. It was assumed that the reduction in hospitalisation achieved with sevelamer over calcium-based binders was maintained over the lifetime of the patient. A clear justification was provided for this assumption, but reliable evidence was lacking. The authors acknowledged that the quality of life impact of hospitalisation was not included, but they suggested that this should have minimal effect of the outcomes. The utility estimate informing the QALYs was based on non-UK data, it was unclear if there were any issues with generalisability. The utilities were derived using valid methods.

**Costs:**
The costs were clearly reported, and appropriate sources and adjustment methods were used. A key assumption was the exclusion of the cost of dialysis. A solid rationale was provided, with a full discussion of the issues of including treatments, such as dialysis, when evaluating drugs which extend life, but do not reduce the need for such treatments. The authors argued that including dialysis would result in any new, life-extending drug being deemed not cost-effective due to the high cost of dialysis. This seems plausible, but controversial, with other published evaluations choosing to include these dialysis costs. Including the cost of dialysis, the ICER significantly increased to £84,269 per QALY gained, making the intervention not cost-effective.

**Analysis and results:**
The model was clearly described, with a diagram. Appropriately, an incremental analysis was conducted. For the sensitivity analysis, the range of values for each parameter was reported, but not always clearly justified. Multiway sensitivity analysis or probabilistic sensitivity analysis could have more comprehensively assessed the uncertainty. The authors implied that the upper confidence limit of the hazard ratio for mortality was not reliable, since the DCOR study lacked the power to detect a statistically significant difference in survival. This highlighted the significant uncertainty in the survival estimate. The authors proposed that an adequately powered, long-term prospective, randomised trial should be conducted to produce a reliable estimate.

Concluding remarks:
The reporting was good and the methods were adequate, but several uncertainties remain, limiting the evaluation. These limitations should be considered fully when interpreting the results.

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