Estimating the health benefits and costs associated with ezetimibe coadministered with statin therapy compared with higher dose statin monotherapy in patients with established cardiovascular disease: results of a Markov model for UK costs using data registries

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 benefits and costs associated with ezetimibe co-administered with statin therapy in patients with a history of cardiovascular disease. The authors concluded that, in some instances, ezetimibe co-administered with statin therapy compared with statin monotherapy might be cost-effective. However, they acknowledged that further research was required to establish the long-term benefits of ezetimibe. The methodology appears to have been appropriate and was clearly reported. The conclusions reached by the authors seem accurate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the benefits and costs associated with ezetimibe co-administered with statin therapy in a cohort of 1,000 hypothetical male patients aged 55 years, with a history of cardiovascular disease, whose cholesterol levels were not appropriately controlled with a statin alone.

Interventions
Ezetimibe (10mg per day), co-administered with statin therapy, was compared with statin monotherapy (simvastatin 20mg per day or atorvastatin 40mg per day), titrated by one dose increments.

Location/setting
UK/primary care.

Methods
Analytical approach:
A Markov model was used to assess the benefits and costs associated with the two treatment strategies. A lifetime horizon was used. The authors stated that the study perspective was that of the UK Department of Health.

Effectiveness data:
The effectiveness data were derived from a systematic review of the literature. A meta-analysis was performed on a number of published randomised controlled trials (RCTs) comparing ezetimibe (co-administered with a statin) with statin monotherapy. RCTs of fixed dose treatment regimens, with a minimum treatment duration of 12 weeks, in individuals aged 18 and over, were included. An adjustment was made to model second-line lipid-lowering benefits. The transition probabilities between health states, including the probability of myocardial infarction, stroke and cardiovascular death, were obtained from UK registries. The main clinical parameter was the reduction in low-density lipoprotein cholesterol.

Monetary benefit and utility valuations:
Quality of life utility values were derived from published studies, using the European Quality of life (EQ-5D) questionnaire. Where possible, data collected on individuals in the UK were used. No utility estimates were available for some events, so assumptions were made by the authors.

Measure of benefit:
The measure of benefit was the number of quality-adjusted life-years (QALYs).

Cost data:
The cost category was drug costs. The cost data were obtained from the British National Formulary (a publication from the British Medical Association and Royal Pharmaceutical Society of Great Britain), while the resource use data were derived from a National Health Service publication. The price year was 2006. The costs were expressed in UK pounds sterling and discounted at an annual rate of 3.5%.

Analysis of uncertainty:
Uncertainty was assessed using one-way and probabilistic sensitivity analyses. The one-way sensitivity analysis included all the key parameters. The probabilistic sensitivity analysis involved 10,000 Monte Carlo simulations, with the results presented as confidence ellipses within the cost-effectiveness plane.

Results
Using a lifetime horizon, the base-case analysis showed that ezetimibe co-administered with current statin therapy was estimated to provide a mean of 134 additional quality-adjusted life-years (QALYs) at a mean incremental cost of £3,693,000, giving a cost per QALY of £27,475 (95% CI: 27,331 to 27,620).

The sensitivity analyses showed that changes to the effectiveness of the second line treatment had the largest impact on the model results, with incremental cost-effectiveness ratios (ICERs) ranging from £22,500 to £43,000 per QALY.

Other results were presented in the paper.

Authors' conclusions
The authors concluded that, in some instances, ezetimibe co-administered with statin therapy compared with statin monotherapy might be cost-effective. However, they acknowledged that further research was required to establish the long-term benefits of ezetimibe.

CRD commentary
Interventions:
The interventions were clearly described and were appropriately selected as they represented current practice in the authors' setting.

Effectiveness/benefits:
The main effectiveness estimates were derived from RCTs, which were combined using meta-analysis, which should ensure a high degree of internal validity. Full details of the review methodology were not presented in this paper, so an assessment of the quality was not possible. The use of UK registries, for estimates of the transition probabilities between various health states, was appropriate, but limits the generalisability of the results. Overall, the effectiveness data were well reported.

Costs:
Although only drug costs were included in the analysis, this was appropriate as other relevant costs were assumed to be identical across the two interventions. The sources of the cost and resource use data were clearly described, as were the actual cost estimates. Adjustments, including the price year and discounting, were reported. Uncertainty in the cost estimates was evaluated in the univariate sensitivity analysis, but distributions were not applied.

Analysis and results:
The authors conducted an appropriate incremental analysis and full results were reported. The issue of uncertainty was addressed through univariate and probabilistic sensitivity analyses, increasing the generalisability of the study results. The methods used throughout the study were well reported, including a diagram of the model. The authors reported some limitations of their analysis, including the limited availability of clinical evidence on the effectiveness of ezetimibe.

Concluding remarks:
The methodology appears to have been appropriate and was clearly reported. The conclusions reached by the authors seem accurate.

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