Cost effectiveness of etoricoxib versus celecoxib and non-selective NSAIDs in the treatment of ankylosing spondylitis

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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
This study evaluated the cost-effectiveness of etoricoxib compared with celecoxib, diclofenac, and naproxen for patients with ankylosing spondylitis, who required routine non-steroidal anti-inflammatory drug (NSAID) treatment. The authors concluded that their economic evaluation suggested that etoricoxib was the most cost-effective initial treatment for these patients requiring daily NSAIDs. The analyses were comprehensive, but the limitations of the clinical data analysed prohibit the drawing of any firm conclusions.

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

Study objective
This study evaluated the cost-effectiveness of etoricoxib compared with celecoxib, diclofenac, and naproxen for the initial treatment of patients with ankylosing spondylitis, who required routine non-steroidal anti-inflammatory drug (NSAID) treatment.

Interventions
The first-line treatment for ankylosing spondylitis was non-steroidal anti-inflammatory drugs. The interventions were etoricoxib, a cyclooxygenase-2 selective inhibitor, 90mg per day (the anticipated defined daily dose), celecoxib (200 and 400mg per day), diclofenac (150mg per day), and naproxen (1g per day).

Location/setting
UK/primary care.

Methods
Analytical approach:
A comprehensive Bayesian Markov model was developed to determine the costs and benefits of using etoricoxib compared with celecoxib, diclofenac, or naproxen. The parameter distributions were derived directly from the results of a mixed treatment comparison (MTC), which was performed following a systematic review of the literature. The time horizon was 30 years and the authors stated that the perspective was that of the UK NHS.

Effectiveness data:
The effectiveness data were identified by a systematic review of the literature and synthesised using a fixed-effect MTC. The systematic review used keyword searches of MEDLINE articles from 1966 to 2007, EMBASE articles from 1980 to 2007, and EULAR abstracts in 2007. The inclusion criteria were: ankylosing spondylitis patients requiring NSAIDs; at least one of the intervention drugs; outcome measurements of the Bath Ankylosing Spondylitis Functional Index (BASFI), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and discontinuation; randomised controlled trials with a double-blind period; and full published reports in English. The MTC was performed in Winbugs and linked to the decision model, allowing the MTC results to directly propagate the decision model. The clinical outcomes for the MTC were the relative efficacy of etoricoxib compared with the other NSAIDs measured by the changes from baseline in BASFI and BASDAI scores. The probability of discontinuation due to lack of efficacy was also obtained. The main clinical parameters were the BASFI and BASDAI scores; the probability of discontinuation; the probability of experiencing adverse events (including perforation, ulcer or bleeding, and thrombotic cardiovascular events); and the probability of death.
Monetary benefit and utility valuations:
The utility estimates were derived, using a published mapping function to convert the BASFI and BASDAI scores to European Quality of life (EQ-5D) scores (Ara, et al. 2007, see ’Other Publications of Related Interest’ below for bibliographic details). The disutilities associated with adverse events were obtained from the literature.

Measure of benefit:
The measures of benefit were the number of life-years and quality-adjusted life-years (QALYs), which were discounted at an annual rate of 3.5%.

Cost data:
The cost categories included the direct costs of medications, therapy-related adverse events, and disease-specific costs. These costs were from published sources including the British National Formulary (BNF 2007), NHS reference costs (2005), and the Personal Social Services Research Unit (2006), and a formula for the relationship between direct medical costs and the BASDAI score. All costs were in UK pounds sterling (£) and an annual discount rate of 3.5% was applied.

Analysis of uncertainty:
The Markov model was fully probabilistic, with posterior distributions for the effectiveness parameters (the mean change in BASFI and BASDAI scores, probability of discontinuation, and some of the adverse events), which were obtained directly from the MTC. The model averaged the outputs over 100,000 iterations to calculate the incremental cost effectiveness ratios (ICERs) and the incremental net monetary benefit (NMB). Cost-effectiveness acceptability curves (CEACs) were constructed and presented and the expected value of perfect information (EVPI) was evaluated. Alternative scenarios were considered.

Results
The results were presented for two-year, five-year, and 30-year scenarios, and a number of sensitivity analyses.

The 30-year outcomes were £89,990 and 11.56 QALYs for etoricoxib; £103,600 and 11.04 QALYs for celecoxib; £99,950 and 11.09 QALYs for diclofenac; and £99,860 and 11.18 QALYs for naproxen. Etoricoxib dominated all other NSAIDs, as it was less costly and more effective. Etoricoxib was dominant over all time horizons.

The net monetary benefit over 30 years was calculated as £141,200 for etoricoxib, £117,100 for celecoxib, £121,800 for diclofenac, and £123,700 for naproxen. At a willingness to pay (WTP) of zero for a QALY, there was a 78% chance that etoricoxib would be most cost-effective at two years, which increased to over 97% at a WTP of £20,000 per QALY. At five and 30 years, there was over a 99% chance that etoricoxib would be most cost-effective. At a WTP of £20 000 per QALY, the population EVPI indicated that the available evidence was sufficient to make a decision.

Generally, the alternative scenarios did not affect these findings. Excluding the ankylosing spondylitis-specific costs meant that the total costs for etoricoxib were higher than those for other NSAIDs at two years.

Authors' conclusions
The authors concluded that their economic evaluation suggested that, from the NHS perspective, etoricoxib was the most cost-effective initial NSAID for ankylosing spondylitis patients who required daily NSAID treatment. They suggested that including the indirect costs, such as productivity lost and early retirement, could increase the economic benefits.

CRD commentary
Interventions:
The interventions were well described and were relevant for the authors’ setting: the first-line treatment for ankylosing spondylitis was NSAIDs, which included etoricoxib, celecoxib, diclofenac, and naproxen. It was not clear whether there were other relevant NSAIDs that could be used as first-line treatments for ankylosing spondylitis.

Effectiveness/benefits:
The study appropriately derived the effectiveness data using a systematic review, with relevant search strategies and...
inclusion criteria, which were reported. Only four trials met the inclusion criteria and head-to-head comparisons were not available for all interventions, so the authors undertook a MTC to obtain the relative effectiveness of the interventions. Limited details of this MTC were reported. The four trials had different follow-up periods between six and 12 weeks and to facilitate the synthesis it was assumed that this difference in follow-up did not affect the relative treatment effect. It was necessary to combine naproxen and diclofenac as a non-selective NSAID group for the BASDAI score MTC due to a lack of data. Only one trial included etoricoxib and the outcomes were reported at six weeks. The MTC for the BASDAI outcome appears to have relied on two trials. The utilities were derived using a published mapping function to create EQ-5D scores from the trial BASFI and BASDAI outcomes. Relevant studies reporting the adverse event incremental disutilities were identified and in some instances synthesised. QALYs were clearly the most relevant outcome, but it was not clear how the mapping function was derived and whether the data were from the same population of patients receiving first-line treatment for ankylosing spondylitis. Despite comprehensive reporting, the clinical evidence base was poor and the methods could not sufficiently compensate for this.

**Costs:**
The costs were consistent with the study perspective. The cost year appears to have been 2007 and discounting was appropriately applied. No costs were inflated, even though the NHS reference costs were from 2005, and the published sources used to elicit the costs were from other years. This limitation might not have had a big impact on the results. Distributions were applied to all costs, except the drug costs.

**Analysis and results:**
The analytic approach was adequately reported and the model structure was clearly outlined. The methods appear to have been robust, but some were not reported in detail, which might be due to the complicated nature of the analyses and limited reporting space. The results were reported clearly and in full. The uncertainty was fully addressed probabilistically, in scenario analyses, and the expected value of perfect information was calculated. The authors acknowledged some limitations, including the fact that the relative treatment effect was assumed to be the same for six- and 12-week follow-ups; they indicated that these differences in follow-up were not expected to affect the relative treatment effect.

**Concluding remarks:**
The analyses were comprehensive, but the limitations of the clinical data used prohibit the drawing of any firm conclusions.

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