Cost-effectiveness of zoledronic acid vs clodronic acid for newly-diagnosed multiple myeloma from the United Kingdom healthcare system perspective
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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 of the study was to assess the cost-effectiveness of zoledronic acid versus clodronic acid in patients with newly diagnosed multiple myeloma. The authors concluded that zoledronic acid was a cost-effective treatment in patients with multiple myeloma. The quality of the study methodology was good. Methodology and results were reported adequately. Given the scope of the study, the authors’ conclusions appear appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective of the study was to assess the cost-effectiveness of zoledronic acid versus clodronic acid in patients with newly diagnosed multiple myeloma.

Interventions
The study compared zoledronic acid 4mg IV every three to four weeks with clodronic acid 1,600mg daily.

Location/setting
UK/Outpatient secondary care.

Methods
Analytical approach:
The authors reported that a partitioned survival analysis was developed to estimate outcomes and costs. The time horizon of the study was 20 years (which the authors reported would equate to the lifetime of the patient). The authors stated that the perspective was that of the UK publicly funded healthcare system.

Effectiveness data:
Clinical and effectiveness data were derived from previously published studies. The main measures of effectiveness were overall survival, progression-free survival, incidence of skeletal-related events and adverse events. These measures were obtained from a randomised placebo-controlled trial with a two-by-two factorial design (Medical Research Council Myeloma IX study). The study included 1,270 randomised patients from 120 UK centres and a median follow-up of 3.7 years (see Other Publications of Related Interest). The authors reported that all other data came from secondary sources identified by reviews of the literature.

Monetary benefit and utility valuations:
Utility estimates were obtained from EQ-5D assessments collected in the Medical Research Council trial. EQ-5D responses were converted into utilities using UK community preference weights.

Measure of benefit:
Quality-adjusted life-years (QALYs) gained. Future benefits were discounted using an annual rate of 3.5%.

Cost data:
Direct costs included those for bisphosphonate treatment, zoledronic acid (including administration), clodronic acid, thalidomide, treatment of adverse events, treatment of skeletal-related events (including fractures, surgery to bone...
lesions and spinal cord compression) and follow-up costs. Resource use associated with treatment of skeletal-related events was derived from a published study conducted in UK, Germany and France. Unit costs were derived from UK reference costs. Drug costs were derived from the manufacturers of zoledronic acid and British National Formulary. All costs were reported in UK pounds sterling (£). The price year was not reported. Future costs were discounted using an annual rate of 3.5%.

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken by simultaneously sampling 1,000 times from probability distributions of model parameters. Results of this analysis were presented in a cost-effectiveness acceptability curve. A series of one-way sensitivity analyses assessed the impact of varying model parameters.

Results
Average QALYs gained per patient was 2.99 with zoledronic acid and 2.68 with clodronic acid.

Average costs per patient were £9,829 with zoledronic acid and £8,176 with clodronic acid.

Costs and benefits were combined using an incremental cost-utility ratio (additional cost per QALY gained). When zoledronic acid was compared to clodronic acid the incremental cost-utility ratio was £5,443 per QALY gained.

Results of the probabilistic sensitivity analysis showed that the probability that zoledronic acid was cost-effective when compared to clodronic acid was 90% at a willingness to pay threshold of £20,000 per QALY gained and 94% at a threshold of £30,000 per QALY gained.

Authors’ conclusions
The authors concluded that zoledronic acid was a cost-effective treatment in patients with multiple myeloma.

CRD commentary
Interventions:
The interventions under study were reported adequately. The selected comparators appeared appropriate as the two regimens (dosages and administration patterns) were based on the chemotherapy options investigated in the Medical Research Council trial.

Effectiveness/benefits:
Most of the effectiveness data were derived from a large UK multicentre randomised controlled trial. It was likely that the main estimates of effectiveness were internally valid and reliable and the sample was likely to have been representative of UK patients. Details of the trial methods were reported sufficiently and full references were provided. The authors reported that other clinical estimates used in the model were derived from reviews of the literature. They did not report whether the literature reviews were systematic in nature so it was not possible to determine whether all the relevant literature was included. QALYs made an appropriate outcome measure as they captured the impact of the intervention on the quality and length of life and enabled comparisons to be made across various health care interventions. Details on how the utilities were elicited were provided and appeared relevant to the study setting and population.

Costs:
The perspective adopted in the economic analysis was explicitly reported to be that of the healthcare system. It appeared that all major relevant costs for the perspective were included in the analysis. The sources for resource use and unit costs were reported adequately. Time horizon, discount rate and currency details were all reported. The authors did not report the price year and this would hamper any inflationary exercises.

Analysis and results:
A partitioned survival analysis model was used to synthesise cost and outcome information. The authors reported that this approach was commonly used for studies that evaluated oncology therapies, especially for advanced or metastatic cancers. Appropriate details of the methods were reported but there was no graphical depiction. The impact of uncertainty in the model was tested appropriately using a series of one-way and probabilistic sensitivity analyses. The authors reported that a main limitation to the study was limited data on the long-term effectiveness of zoledronic acid.
Concluding remarks:
Overall, the quality of the study methodology was good. Methodology and results were reported adequately. Given the scope of the study, the authors' conclusions appear appropriate.

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