Economic evaluation of clodronate and zoledronate in patients diagnosed with metastatic bone disease from the perspective of public and third party payors in Brazil

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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 examined the cost-effectiveness of zoledronate or clodronate, for the prevention and treatment of skeletal events, in patients with metastatic bone disease. The authors concluded that clodronate led to better clinical outcomes and saved costs, compared with zoledronate, from the perspectives of the public and private payers. The methods were valid and the costs were extensively reported. The authors’ conclusions appear to be robust.

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

Study objective
This study examined the cost-effectiveness of zoledronate or clodronate, for the prevention and treatment of skeletal events, in patients with metastatic bone disease.

Interventions
Oral clodronate (1,600mg per day) was compared with intravenous zoledronate (4mg every four weeks). Treatment was assumed to continue over the patients’ lifetime.

Location/setting
Brazil/secondary care and out-patient.

Methods
Analytical approach:
The analysis was based on a Markov model, with three time horizons: one year, five years, and 10 years. The authors stated that it was carried out from two perspectives: the public Ministry of Health, and the private supplementary medicine system.

Effectiveness data:
Most of the data were from a published meta-analysis of randomised trials comparing the two treatments. The risk of osteonecrosis was from published studies. The incidence of skeletal events was a key input for the model and was from the published meta-analysis.

Monetary benefit and utility valuations:
The utility values were from a published economic evaluation.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years without skeletal events were the summary benefit measures.

Cost data:
The five main categories of costs were: drugs, physician visits, hospitalisations, surgical and medical care, and laboratory tests. The unit costs for the public and private payers were from official databases that reported medical service claims and the actual resources paid by each system. The drug costs were calculated from their wholesaler list prices for branded and generic drugs, in Brazil, with equal weight between products. The unit costs and resource quantities were reported in detail, with costs in Brazilian reais (BRL). The price year was 2008.
Analysis of uncertainty:
One-way and multi-way sensitivity analyses were carried out to identify the most influential inputs. A Monte Carlo simulation was performed, using conventional probability distributions for all the model inputs.

Results
Over five years, from the public perspective, the expected costs were BRL 46,313 with clodronate and BRL 50,318 with zoledronate. The largest component was the drug costs. The expected life-years free of skeletal events were 1.81 with clodronate and 1.76 with zoledronate. The QALYs were 2.00 with clodronate and 1.90 with zoledronate.

Clodronate was dominant, as it was more effective and less expensive than zoledronate. Similar results were observed from the perspective of the private payer, and with the other time horizons; clodronate remained dominant in all cases.

The most sensitive parameter was the probability of osteonecrosis. When equal incidence was assumed for the two treatments (in the base case it was zero for clodronate and 7% for zoledronate), zoledronate became dominant. The probabilistic sensitivity analysis showed that clodronate was the preferred option in over 60% of cases from the public perspective.

Authors’ conclusions
The authors concluded that clodronate led to better clinical outcomes and saved costs, compared with zoledronate, from the perspectives of the public and private payers.

CRD commentary
Interventions:
The authors justified their selection of the comparators, on the grounds that zoledronate and clodronate were the two bisphosphonates approved for the treatment and prevention of skeletal events in patients with metastatic bone disease, in Brazil.

Effectiveness/benefits:
Most of the clinical data were from the meta-analysis of randomised trials, which was not described, but should have had high internal validity. Other data were from studies that were not described. The authors acknowledged that compliance and adherence to treatment as well as adverse drug reactions were not considered and their inclusion might have had an impact on the results, but adverse reactions were likely to be similar between the two drugs. Life-years and QALYs appear to have been valid benefit measures. QALYs include an assessment of deterioration in health-related quality of life. The utility weights were from published studies; the population studied and the instrument used were not reported.

Costs:
Two perspectives were taken, with different estimates for the unit costs, depending on the viewpoint. National databases were appropriately used to derive these costs and they were described. The unit costs and resource quantities were provided in detail, allowing replication of the analysis. The price year was reported, and reflation exercises should be possible. The impact of variations in each cost category on the total costs was investigated.

Analysis and results:
The results were clearly presented. An incremental approach was used to identify the best treatment. Appropriate instruments were used to assess uncertainty and the results were extensively presented and discussed. It was unclear whether discounting was applied and it would have been relevant for the five- and 10-year time horizons. The authors compared their results with those of other published studies; these generally used different sources for the clinical inputs and had different findings. They stated that caution was required in transferring their results to other settings.

Concluding remarks:
The methods were valid and the costs were extensively reported. The authors’ conclusions appear to be robust.

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