Cost-effectiveness of oral clodronate compared with oral ibandronate, intravenous zoledronate or intravenous pamidronate in breast cancer patients

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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 compared the clinical and economic impact of four bisphosphonates, which were oral clodronate, oral ibandronate, intravenous zoledronate, and intravenous pamidronate, for the management of the risk of osteoporosis and skeletal-related events, in women with metastatic breast cancer. Oral clodronate was the cheapest treatment for metastatic breast cancer, in both Germany and the UK. There were some methodological limitations, which might affect the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to compare the clinical and economic impact of four bisphosphonates, which were oral clodronate (CLO), oral ibandronate (IBA), intravenous zoledronate (ZOL), and intravenous pamidronate (PAM), for the management of the risk of osteoporosis and skeletal fractures, in women with metastatic breast cancer (BC).

Interventions
The four therapies were oral CLO (1600mg per day), oral IBA (50mg per day), intravenous ZOL (4mg every three to four weeks), and intravenous PAM (90mg every three to four weeks). All patients also received IV chemotherapy.

Location/setting
Germany and UK/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a cost-minimisation analysis because the efficacy profiles of the four treatments were assumed to be similar. The time horizon was 14.3 months, which corresponded to the mean average survival of patients with metastatic BC. The authors did not state explicitly the perspective adopted.

Effectiveness data:
A systematic literature review was undertaken to identify the relevant sources of data on the treatment effectiveness. Databases such as PubMed and the Cochrane Controlled Trials Register up to November 2006 were searched, together with the relevant references in reviews published by peer-reviewed journals. The efficacy estimate, which was assumed to be similar for the four treatments, was derived by pooling the findings from eight placebo-controlled clinical trials. A heterogeneity test showed that these studies were comparable. The key clinical input was the reduction in skeletal-related events associated with the use of bisphosphonates.

Monetary benefit and utility valuations:
The authors assumed that the use of bisphosphonates improved the patients’ quality of life (QoL) by 29% in comparison with placebo.

Measure of benefit:
No summary benefit measure was used.
Cost data:
The analysis included the costs of drugs, skeletal-related event care for pathological fractures, personnel, supplies, other medications, treatment of adverse events related to the four drugs, such as renal failure or osteonecrosis of the jaw, transportation to hospital, and patient time, which was counted in one hour absences from work. The resource use data appears to have been based on previous publications and authors' assumptions. The costs came from national official prices and published studies. The economic value of patient time was based on average wages. All costs were reported in Euros (EUR) for both countries and UK costs were converted at the exchange rate for November 2006. The price year was not explicitly reported.

Analysis of uncertainty:
A deterministic univariate sensitivity analysis was undertaken to investigate the impact of changes in the incidence of osteonecrosis of the jaw and renal impairment on the expected costs.

Results
The efficacy of all bisphosphonates in reducing skeletal-related events was 29%.

In Germany, the expected cost per patient was EUR 8,661.52 with CLO, EUR 9,753.90 with IBA, EUR 11,161.81 with ZOL, and EUR 11,021.92 with PAM.

In the UK, the expected cost per patient was EUR 6,916.39 with CLO, EUR 7,758.18 with IBA, EUR 10,585.58 with ZOL, and EUR 9,906.38 with PAM.

Changes in the incidence of osteonecrosis of the jaw and renal impairment did not affect these findings.

Authors' conclusions
The authors concluded that oral CLO was the cheapest treatment for managing the risk of skeletal events in patients with metastatic BC in both Germany and the UK.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear in that the four drugs were the most effective bisphosphonates for BC patients.

Effectiveness/benefits:
The systematic search of commonly used databases to identify the relevant sources of data was appropriate. The authors provided some information on the primary studies. In general, the use of clinical trials should have ensured the validity of the clinical estimates. Furthermore, the authors demonstrated the homogeneity among the primary studies and used a statistical approach to pool the primary data. However, the authors made a key assumption on the equal efficacy of the four treatments, which was justified on the grounds of the inconclusive evidence on the superior profile of one bisphosphonate over any other. Moreover, no head-to-head studies were found, and indirect comparisons were needed. The authors provided an estimate of the impact of the bisphosphonates on patients' QoL, but this estimate was not used in the economic analysis.

Costs:
The viewpoint was not explicitly stated, but the categories of costs appear to have reflected a societal perspective. A breakdown of the cost items was provided for most categories, although some of them were reported as macro-categories, especially those derived from published studies. Statistical analyses of the costs were carried out. Reflation exercises will be difficult as the price year was not explicitly reported.

Analysis and results:
The analysis was based on a cost-minimisation approach, which precludes the synthesis of costs and benefits. The issue of uncertainty was only partially addressed, and only a few sensitivity analyses were carried out. The findings were reported in detail.
Concluding remarks:
This study has some methodological limitations due to the use of a cost-minimisation analysis and a lack of an analysis of uncertainty. Thus, the authors’ conclusions should be treated with some caution.

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