The cost effectiveness of zoledronic acid 5mg for the management of postmenopausal osteoporosis in women with prior fractures: evidence from Finland, Norway and the Netherlands


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 assessed the cost-effectiveness of zoledronic acid 5mg once yearly infusion as a first-line treatment for the secondary prevention of fragility fractures in women with postmenopausal osteoporosis. The authors concluded that their analysis suggested that zoledronic acid was a cost-effective first-line option. The study methodology was adequate, but limited reporting on key evidence means that it is unclear if the authors' conclusions are appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The study assessed the cost-effectiveness of zoledronic acid 5mg as a first-line treatment for the secondary prevention of fragility fractures in women with postmenopausal osteoporosis in Finland, Norway and The Netherlands.

Interventions
The interventions investigated were: zoledronic acid 5mg once-yearly infusion; branded alendronate 70mg orally once weekly; generic alendronate 70mg orally once weekly; branded risedronate 35mg orally once weekly; branded ibandronate 150mg orally once monthly and 3mg injection once quarterly; and basic treatment (placebo, calcium plus vitamin D).

Location/setting
Finland, Norway and The Netherlands/primary care.

Methods
Analytical approach:
A discrete event individual-patient simulation based on the model inputs used in a previous modelling analysis (undertaken in the UK for NICE) was used and locally adapted for each country (Stevenson, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details). A lifetime time horizon was used in the model. The authors reported that the perspective adopted in the economic analysis was that of the healthcare system of the three countries studied.

Effectiveness data:
Clinical and effectiveness studies came from those identified for the UK model (Stevenson, et al. 2005) and other published studies. The main measure of effectiveness used in the model was the risk reduction of site-specific fractures. This estimate was from published randomised controlled trials.

Monetary benefit and utility valuations:
Baseline quality of life estimates came from age-specific utility values observed in a sample drawn from the UK population. Other utility estimates were obtained from sources identified in the UK model (Stevenson, et al. 2005) and other published studies.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained. As benefits could be generated over the
lifetime of the patient, future benefits were discounted using an annual rate of 5.0% for Finland, 4.0% for Norway and 1.5% for The Netherlands.

Cost data:
The direct costs included in the model were those associated with hip fracture costs, nursing home, vertebrae fracture, proximal humerus fracture, death, drug costs, and visits to doctors. Only costs directly attributable to a fracture event and its direct treatment were included. Costs came from previously published studies and national drugs agencies. When local costs were not available, costs were adjusted for inflation and exchange rates applied. For The Netherlands and Finland, costs were reported in Euros (EUR). For Norway, costs were reported in Norwegian Krona (NOK). As costs could be incurred over the lifetime of the patient, future costs were discounted using an annual rate of 5.0% for Finland, 4.0% for Norway and 4.0% for The Netherlands.

Analysis of uncertainty:
Sensitivity analyses were performed comparing zoledronic acid with branded alendronate. These included one-way sensitivity analyses and a probabilistic sensitivity analysis. The probabilistic analysis was carried out using 1,000 Monte Carlo simulations sampling from probability distributions in each parameter.

Results
The authors did not report the disaggregated costs and benefits for each intervention.

Costs and benefits were combined using an incremental cost-utility ratio (the additional cost per QALY gained). When compared with branded alendronate, the incremental cost-utility ratio of zoledronic acid 5mg once yearly infusion was EUR 25,287 in Finland, EUR 873 in The Netherlands and dominant in Norway (zoledronic acid was both more effective and less costly).

Results of the probabilistic sensitivity analysis showed that at a cost-effectiveness threshold of EUR 30,000, the probability of zoledronic acid 5mg being cost-effective in Finland was 57% and 79% in The Netherlands, and at a cost-effectiveness threshold of NOK 200,000 in Norway, the probability of zoledronic acid 5mg being cost-effective was 87%.

For other drug comparisons, zoledronic acid 5mg had a lower incremental cost-utility ratio when compared with basic treatment, than all other branded bisphosphonates in Finland. Zoledronic acid 5mg, risedronate and alendronate (branded and generic) dominated over basic treatment in Norway. Zoledronic acid 5mg had lower incremental cost-utility ratios than branded risedronate and ibandronate when compared with basic treatment in The Netherlands.

Authors' conclusions
The authors concluded that their analysis suggested that zoledronic acid 5mg once yearly infusion was a cost-effective first-line option for osteoporosis in postmenopausal women.

CRD commentary
Interventions:
The interventions under study were reported adequately and appropriate details were given. Commonly prescribed treatment appropriately appeared to be included as a comparator.

Effectiveness/benefits:
Clinical and effectiveness estimates were from previously published studies. Many of the estimates came from sources identified in a published UK model (Stevenson, et al. 2005). Sources were updated using published studies. The main measure of effectiveness came from published randomised controlled trials, which were likely to be reliable. However, the methods used to identify published studies were not reported, so it was not possible to determine if all relevant information was included in the model. In particular, it was not clear if there were other relevant randomised control trials investigating zoledronic acid that could have been included in the analysis.

Costs:
The authors explicitly reported the perspective of the study as that of the healthcare system. For this perspective all relevant major costs appeared to have been included in the analysis. The sources from which costs came were
adequately reported for each of the three countries under study. The discount rate, time horizon and currency details were reported, but the price year was not.

Analysis and results:
A discrete event simulation model was used to synthesise cost and outcome information, which was a reasonable approach similar to that used in a peer-reviewed publication. The authors undertook a comprehensive sensitivity analysis, including one-way and probabilistic sensitivity analyses. However, these analyses were undertaken for the comparisons of zoledronic acid 5mg once yearly infusion and basic treatment. As a result, the sensitivity of the results to variation in certain parameters was not investigated for other interventions. In addition, the costs and outcomes disaggregated for each intervention and country were not reported. As a main limitation to their study, the authors reported that treatment-associated adverse events were not included in the model.

Concluding remarks:
The study methodology was adequate, but limited reporting on key evidence means that it is unclear if the authors' conclusions are appropriate.

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