Health outcomes and cost-effectiveness of aprepitant in outpatients receiving antiemetic prophylaxis for highly emetogenic chemotherapy in Germany


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 study estimated the cost-effectiveness of aprepitant with ondansetron plus dexamethasone compared with conventional ondansetron plus dexamethasone in the prevention of chemotherapy-induced nausea and vomiting. The authors concluded that aprepitant was a cost-effective alternative to add to conventional anti-emetic medications. Despite most methods being reported explicitly, limitations were highlighted. The authors’ conclusions should be considered with some caution.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim of the study was to estimate the costs and health benefits of aprepitant, a pharmaceutical agent designed to alleviate chemotherapy-induced nausea and vomiting (CINV), in outpatients undergoing highly emetogenic chemotherapy.

Interventions
Aprepitant was combined with ondansetron and dexamethasone over 4 days following chemotherapy and compared with ondansetron and dexamethasone alone. Ondansetron and dexamethasone were administered 30 minutes prior to chemotherapy and aprepitant 60 minutes prior to chemotherapy. The dosages were reported in the paper.

Location/setting
Germany/outpatient care.

Methods
Analytical approach:
A decision-analytical model (decision tree) was used to synthesise the health care costs and benefit data. The costs and effects were analysed for a 5-day period over a single cycle of chemotherapy. The authors stated the study perspective to be that of the statutory health insurance funds.

Effectiveness data:
Several health outcomes were assessed. However, the main effectiveness measure was "complete response", defined as the percentage of patients who had neither emesis nor rescue therapy over the 5-day cycle and reported nausea <25 mm measured on a 100-mm visual analogue scale (VAS). Evidence for the clinical end points were drawn from two multi-centre, randomised double-blind phase III clinical trials (Hesketh et al. 2003 and Poli-Bigelli et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details). The data were pooled and analyses included 516 and 522 patients in the aprepitant and control groups, respectively. Patients received cisplatin chemotherapy, at least one dose, had at least one post-treatment assessment and had complete health resource use records. Patient demographic, risk-factor and history profiles were balanced across the two groups. A modified intention-to-treat analysis was followed in the original studies.

Monetary benefit and utility valuations:
The utilities were derived from three published studies reporting patient preferences for health states covering CINV. All three studies used VAS techniques to determine the utility scores, while one also used the time trade-off approach.
Following the authors’ consensus opinion, utilities were assigned to the three health states used in the model: “complete protection”, “incomplete response” and “complete response at best”.

Measure of benefit:
The measure of benefit used was the quality-adjusted life years (QALYs). Given the short time horizon of the analysis, "quality-adjusted life-days" were also presented.

Cost data:
Resources included in the evaluation were the three anti-emetic prophylaxis drugs, rescue medications, physician visits and hospitalisations. Individual-level data were collected and the unit costs were presented. German case-mix costs for hospitalisation, average charges for physician visits and pharmaceutical listings for drugs were used to value the resources. The price year was 2004. Prices were reported in euros (EUR).

Analysis of uncertainty:
Uncertainty in the data parameters was investigated through a series of one-way sensitivity analyses, simulation methods and scenario analyses.

Results
The total cost of the aprepitant regimen was EUR 380.04 compared with EUR 330.44 for the control regimen. The corresponding health effects were 0.0097 QALYs for aprepitant and 0.0080 QALYs for the control regimen. The additional health gains from aprepitant were equivalent to 0.63 quality-adjusted life-days or 15 additional hours of perfect health free of nausea and vomiting.

The incremental cost-utility ratio was EUR 28,891 per QALY gained for aprepitant over the 5-day period.

Sensitivity analyses with alternative values for utility values and resource costs revealed incremental cost-utility ratios in the range of EUR 24,653 to EUR 41,880, while simulation-based sensitivity analyses testing variability in the proportions of patients with complete response indicated 95% of simulations resulted in ratios between EUR 16,172 and EUR 52,694.

Authors' conclusions
The authors concluded that aprepitant is a cost-effective option when used in combination with ondansetron plus dexamethasone in highly emetogenic outpatient chemotherapy.

CRD commentary
Interventions:
The two anti-emetic prophylaxis options were described clearly. The profile of the intended patient population, based on those from the clinical trials, was reported.

Effectiveness/benefits:
The effectiveness data were derived from two clinical trials and the selection of these studies was justified. The range of clinical end points used to assess the merits of the two regimens was consistently in favour of aprepitant. The derivation of utilities involved the authors’ opinion, which may introduce biases. In addition, the utilities were based primarily on VAS scores; this valuation approach is less acceptable than other methods as it does not embody choice or preference-based methods. The model structure was illustrated clearly.

Costs:
The types of costs included appear to have been appropriate for the perspective taken and the time horizon. The costing methods were well reported and transparent.

Analysis and results:
The cost and effect analyses were explicit and enable the reader to capture all assumptions and steps taken. It is unclear why the study was conducted over such a short time period and did not capture, at least, a full cycle of cisplatin-chemotherapy. The evaluation was limited by the short timeframe, although it might have been strengthened by
establishing that aprepitant leads to better tolerance and lower toxicity than modern chemotherapy, thereby enhancing its compliance, which might translate to improved survival outcomes. Comparisons of cost per QALY gains over a 5-day period with other studies of longer durations (ranging typically from 1 year to lifetime horizons) are problematic. Significant differences across the two regimens in the proportion of patients experiencing "complete response" have not been demonstrated in two meta-analyses of the efficacy of aprepitant. However, the estimates for this parameter were incorporated into a simulation-based sensitivity analysis and produced wide credible intervals. The results of the sensitivity analyses were well reported. The authors discussed several study limitations and aspects of generalisability.

Concluding remarks:
Despite some limitations with deriving the effectiveness data and the chosen analytical timeframe, the study methods were transparent. The authors’ conclusions should be considered with some caution given the comments above.

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Bibilographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Antiemetics /economics /therapeutic use; Antineoplastic Combined Chemotherapy Protocols /adverse effects; Cisplatin /administration & dosage /adverse effects; Clinical Trials, Phase III as Topic; Cost-Benefit Analysis; Dexamethasone /administration & dosage /adverse effects; Double-Blind Method; Drug Therapy, Combination; Health Resources /economics /utilization; Humans; Morpholines /economics /therapeutic use; Multicenter Studies as Topic; Nausea /chemically induced /economics /prevention & control; Neoplasms /drug therapy /economics; Ondansetron /economics /therapeutic use; Randomized Controlled Trials as Topic; Treatment Outcome; Vomiting /chemically induced /economics /prevention & control

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