Aprepitant for patients receiving highly emetogenic chemotherapy: an economic analysis for Singapore
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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 assessed the cost-effectiveness of a regimen containing an aprepitant, compared with the usual regimen, for the prevention of chemotherapy-induced nausea and vomiting, in patients receiving highly emetogenic chemotherapy, in Singapore. The authors concluded that the aprepitant-based regimen was cost-effective. There were a few limitations to the effectiveness and utilities data, and the length of the analysis. These limitations should be considered when interpreting the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study assessed the cost-effectiveness of a regimen of drugs including an aprepitant (anti-sickness drug), compared with the usual clinical practice, for the prevention of chemotherapy-induced nausea and vomiting, in patients receiving highly emetogenic chemotherapy.

Interventions
Aprepitant-containing regimens, with ondansetron or granisetron (more commonly used in Singapore) and/or dexamethasone, were compared with standard regimens, without the aprepitant. Three scenarios were reported, each using different randomised controlled trials to inform the model. Chemotherapy consisted of cisplatin, in two scenarios, and anthracycline plus cyclophosphamide, in the third.

Location/setting
Singapore/secondary care.

Methods
Analytical approach:
The analysis was based on a decision-analytic model, with the structure of a published decision tree, that reflected the potential unique combinations of day one (acute phase) and days two to five (delayed phase) chemotherapy-induced nausea and vomiting. The time horizon was five days, which was the length of the trials. The authors stated that the Singapore health care system perspective was adopted.

Effectiveness data:
The effectiveness data came from four published double-blind randomised controlled trials. The main effectiveness measures were the efficacy of the aprepitant versus standard care, in preventing chemotherapy-induced nausea and vomiting. The transition probabilities were calculated from a modified intention to-treat population, based on patients’ diary entries for episodes of vomiting or retching, daily nausea reported on the visual analogue scale, and use of rescue medication. The data from two trials were pooled, for scenario one, due to their similar designs, patient populations, and antiemetic regimens.

Monetary benefit and utility valuations:
None of the trials collected utility data, so the model mapped published utility values, from the literature on chemotherapy-induced nausea and vomiting, to the relevant model health states.
Measure of benefit:
Quality-adjusted life-years (QALYs) were the main benefit measure. Secondary measures included quality-adjusted life-days (QALDs) and emetic events avoided.

Cost data:
The direct costs included those of medications, out-patient physician assessments, diagnostic tests and procedures, emergency department visits, and hospitalisations. The resource use associated with each health state was from the pooled patient-level data from the diaries of patients in the randomised controlled trials. Hospital-related and medical treatment costs were from the Tan Tock Seng Hospital and the National Cancer Centre Singapore. The costs were expressed in Singapore dollars (SGD) and the price year was 2010.

Analysis of uncertainty:
One-way and two-way sensitivity analyses were conducted to determine how changes in the key variables affected the results.

Results
In scenario one, the total costs were SGD 226.41 with aprepitant and ondansetron, SGD 143.27 with ondansetron, or SGD 140.97 with granisetron. The total QALYs were 0.00967 with aprepitant, and 0.00796 without it (with ondansetron or granisetron). The incremental cost per QALY gained with the aprepitant was SGD 48,440 compared with ondansetron alone, or SGD 49,778 compared with granisetron.

In scenario two, the total costs were SGD 223.65 with aprepitant and ondansetron, SGD 168.35 with ondansetron, and SGD 201.39 with granisetron. The total QALYs were 0.00988 with aprepitant, and 0.00894 with ondansetron or granisetron. The incremental cost per QALY gained with the aprepitant was SGD 58,719 compared with ondansetron, or SGD 22,636 compared with granisetron.

In scenario three, the total costs were SGD 124.08 with aprepitant and ondansetron, SGD 97.95 with ondansetron, and SGD 133.29 with granisetron. The total QALYs were 0.0092 with aprepitant and 0.0080 with ondansetron or granisetron. The incremental cost per QALY gained with the aprepitant was SGD 21,421 compared with ondansetron, or it was cost saving compared with granisetron.

The sensitivity analysis showed that the results were robust to changes in the model inputs.

Authors' conclusions
The authors concluded that an aprepitant based-regimen was cost-effective, compared with the usual prevention of chemotherapy-induced nausea and vomiting, for patients treated with highly emetogenic chemotherapy, in Singapore.

CRD commentary
Interventions:
The interventions were clearly defined. The rationale for their selection was clear, as they matched those in the RCTs that supplied the effectiveness data. The alternatives in these trials included the standard regimen, in the authors’ setting.

Effectiveness/benefits:
No systematic review of the literature was reported to identify and select the RCTs, so it is not possible to ascertain if the best available evidence was used. RCTs are generally considered to be valid sources of evidence, due to their design. The authors assumed that the comparators (ondansetron and granisetron) were equally effective and safe, which was supported by a meta-analysis of ondansetron and granisetron in the prevention of acute-phase chemotherapy-induced nausea and vomiting. QALYs were an appropriate outcome measure, as they captured the impact of the intervention on a patient's quality of life, and allow comparisons with other interventions for other diseases. The methods used to assess the quality adjustments, and their sources, were not described in detail. As the time horizon was only five days, no discounting was appropriate.

Costs:
All the cost categories, relevant to the perspective and time horizon, appear to have been included. The cost estimation
methods and the sources were well reported. Given the short time horizon, discounting was not necessary.

**Analysis and results:**
The authors used a simple decision model to evaluate the costs and outcomes of the regimens. No diagram of the model was presented. The five-day time horizon reflected the clinical trials' study period, but it is unclear whether this sufficiently covered all the major outcomes for nausea and vomiting prevention after one cycle of highly emetogenic chemotherapy. Uncertainty was explored in a deterministic sensitivity analysis, but a probabilistic sensitivity analysis could have better captured the overall uncertainty in the model. The reasons for choosing the ranges for the sensitivity analysis were unclear. The authors compared their results with those published elsewhere, which were generally consistent, and they discussed their study limitations.

**Concluding remarks:**
There were a few limitations to the effectiveness and utilities data, and the length of the analysis. These limitations should be considered when interpreting the authors' conclusions.

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