Cost-effectiveness of posaconazole versus fluconazole or itraconazole in the prevention of invasive fungal infections among neutropenic patients in the United States


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 posaconazole compared with fluconazole or itraconazole, for the prevention of invasive fungal infections in patients with acute myelogenous leukaemia or myelodysplastic syndrome, who were neutropenic following chemotherapy. Posaconazole was very likely to be not only cost-effective compared with standard treatment, but also cost saving. The study appears to have been satisfactorily carried out and was well reported, enhancing the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of posaconazole compared with fluconazole or itraconazole for the prevention of invasive fungal infections in patients with acute myelogenous leukaemia or myelodysplastic syndromes, who were neutropenic following chemotherapy.

Interventions
The three treatments were posaconazole at 600mg per day, fluconazole at 400mg per day, or itraconazole at 200mg per day. These treatments lasted for up to 84 days.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a decision-analytic model, with a 100-day time horizon, followed by a Markov model that estimated the costs and benefits over a patient’s lifetime. The authors stated that the analysis was carried out from the perspective of the payer.

Effectiveness data:
The clinical data were from a selection of relevant studies. The prophylaxis efficacy over 100 days and the baseline patients’ characteristics were from a multinational randomised controlled trial (Cornely, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details) that compared the three treatments. There were 304 patients in the posaconazole group, 240 patients in the fluconazole group, and 58 patients in the itraconazole group. The long-term progression data for patients with either myelodysplastic syndrome or acute myelogenous leukaemia were from the US National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) database and other sources. Some assumptions were also needed, such as the equal mortality due to invasive fungal infections, for all treatments. The efficacy of prophylaxis was the key input.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years (LYs) and cases of invasive fungal infection were the summary benefit measures. A 3% annual discount rate
was applied.

Cost data:
The economic analysis included the costs of treating an invasive fungal infection in hospital and the costs of antifungal prophylaxis. In-hospital data were from the Healthcare Cost and Utilization Project - Nationwide Inpatient Sample (HCUP-NIS). These charges were converted into costs, using a hospital-specific cost-to-charge ratio. The drug costs were based on their official prices for fluconazole and itraconazole and obtained from the manufacturer for posaconazole. They were in US dollars ($), for the price year 2006, and they were discounted at an annual rate of 3%.

Analysis of uncertainty:
In an alternative scenario, the treatment-specific mortality from cases of invasive fungal infection was used and these data were from the clinical trial. A series of one-way sensitivity analyses were carried out on the model inputs, such as drug efficacy, costs, and long-term survival. Published ranges of values (confidence intervals or standard deviations) were mainly used. A second-order Monte Carlo simulation was carried out, by running 1,000 iterations of posaconazole versus fluconazole or itraconazole and cost-effectiveness acceptability curves were generated.

Results
The expected total costs were $3,900 with posaconazole and $4,500 with fluconazole or itraconazole. The number of cases of invasive fungal infection was 0.05 with posaconazole and 0.11 with fluconazole or itraconazole. The LYs gained were 2.50 with posaconazole and 2.43 with fluconazole or itraconazole. Posaconazole was dominant as it was less expensive and more effective, using either benefit measure.

These results were generally stable. Only when the most unfavourable estimate for the risk of invasive fungal infection with posaconazole was used, did the incremental cost per LY gained rise to $48,600.

There was a 73% probability of posaconazole being dominant and a 96% probability of it being cost-effective, at a threshold of $50,000 per LY gained.

Authors' conclusions
The authors concluded that posaconazole was very likely to be not only cost-effective, compared with either fluconazole or itraconazole, but also cost-saving, from the perspective of the US payer.

CRD commentary
Interventions:
The authors stated that fluconazole and itraconazole were the standard antifungal agents for the prevention of invasive fungal infections in the patient population studied. Market shares were used to consider fluconazole and itraconazole, in the US setting. Posaconazole was the new broad-spectrum antifungal agent, and was recommended by the National Comprehensive Cancer Network (NCCN).

Effectiveness/benefits:
The approach used to identify the data sources aimed to include the most appropriate data that were already known to the authors. A systematic search for data is generally considered to be more appropriate, but the sources appear to have been valid, although they were not fully described. The treatment effect was from a multinational head-to-head clinical trial, which should have had a high internal validity. The remaining epidemiological inputs were from country-specific databases, which included a large number of patients, who were representative of those requiring antifungal therapy. The authors did not investigate any issues around the use of data from different sources, which might not be homogeneous, but they did investigate the uncertainty in these clinical inputs in the sensitivity analysis. The benefit measures were appropriately selected and might be interesting to different stakeholders. LYs are also comparable with the benefits of other health care interventions.

Costs:
The economic analysis included those costs relevant to the perspective adopted. A list of cost items was not provided and the in-patient costs were presented as a total category. The data sources were reported and reflected the US health care system. Other details, such as the price year and the use of discounting, were reported. The cost estimates were
varied in the sensitivity analysis.

**Analysis and results:**
The outcomes of the model were clearly reported and an incremental approach was used to synthesise the expected costs and benefits of the two strategies. The issue of uncertainty was satisfactorily investigated, using various approaches, and the methods and results were clearly reported and discussed. The key details of the model were reported and the two time horizons were appropriate. Some potential limitations were noted by the authors, such as the comparison with itraconazole or fluconazole pooled together and not analysed separately. Another limitation was the use of a single source for the treatment efficacy.

**Concluding remarks:**
The study appears to have been satisfactorily carried out and was well reported, enhancing the validity of the authors’ conclusions.

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