Cost-effectiveness of natalizumab versus fingolimod for the treatment of relapsing multiple sclerosis

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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
The study evaluated the cost-effectiveness of natalizumab in comparison with fingolimod for the treatment of patients with relapsing multiple sclerosis. The authors concluded that their results suggest that natalizumab was less costly and more effective than fingolimod for treatment for relapsing multiple sclerosis. The study was based on valid methods and the data sources and results were reported clearly. The authors’ conclusions appear appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study evaluated the cost-effectiveness of natalizumab in comparison with fingolimod for the treatment of patients with relapsing multiple sclerosis.

Interventions
Natalizumab 300mg by intravenous infusion once every four weeks was compared with fingolimod 0.5mg administered orally once daily.

Location/setting
USA/secondary care

Methods
Analytical approach:
This economic valuation was based on a decision analytic model developed using data from two clinical trials (Polman et al., 2006 and Kappos et al., 2010, see Other Publications of Related Interest). The time horizon was two years. The authors stated that the perspective was that of a USA managed care payer.

Effectiveness data:
The clinical data came from two published randomised controlled trials (RCTs). They were pivotal phase III trials that compared natalizumab (Polman et al., 2006) and fingolimod (Kappos et al., 2010) to placebo. The key clinical outcomes were rate of multiple sclerosis relapses. The authors stated that they used placebo adjusted relapse rates as the comparisons were indirect.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The primary measure of benefit was number of multiple sclerosis relapses avoided.

Cost data:
The direct costs included costs of drug acquisition, administration and monitoring and the costs of managing multiple sclerosis relapses. Unit costs were derived from sources that included wholesale prices, physician fee schedules and published literature. Resource use quantities were based on the published literature and expert opinion. Costs were expressed in 2010 US dollars ($) and were not discounted.
Analysis of uncertainty:
One-way sensitivity analyses were performed to assess the impact of various model inputs that included relapse rate reduction using 95% CIs (confidence intervals) reported in the clinical trials and costs of drug acquisition and drug administration (±10% base-case) and managing multiple sclerosis relapses based on calculated 95% CIs. Probabilistic sensitivity analysis was performed to assess the joint uncertainty of all model parameters simultaneously based on 1,000 Monte Carlo simulations and conventional distributions for model inputs.

Results
Compared to placebo, over two years natalizumab was associated with 0.74 relapses avoided at a cost of $86,461 and fingolimod was associated with 0.59 relapses avoided at a cost of $98,748. The cost per relapse avoided was $117,164 for natalizumab and $168,754 for fingolimod.

Natalizumab dominated fingolimod in that it was less costly and more effective in reducing relapses.

One-way sensitivity analysis showed that results were robust to the range of tested values, which found that natalizumab was more effective and less costly than fingolimod. Probabilistic sensitivity analysis showed that in 95.4% of simulations natalizumab was dominant compared to fingolimod and was cost-effective 95.1% and 96.3% of the time at a willingness to pay threshold of zero and $50,000 per relapse avoided.

Authors' conclusions
The authors concluded that their results suggested that natalizumab was less costly and more effective than fingolimod for treatment for relapsing multiple sclerosis.

CRD commentary
Interventions:
The rationale for selection of the interventions was clear as they were approved alternative treatments in the authors’ setting. These interventions were likely to be relevant clinical options available in other settings.

Effectiveness/benefits:
The primary data sources were two pivotal phased III RCTs and their design should have ensured the validity of the clinical estimates. Selection of data sources was intended to include relevant studies known to the authors but it did not appear that a systematic literature review was carried out. The trials were referenced but not described in detail. Key clinical inputs used were given in a table. The summary benefit measure captured the intermediate impact of treatments on patients’ health (relapse rate). The reader should consider whether the measure of benefit adequately captured the health outcome differences for these treatments. A more comprehensive benefit measure such as quality-adjusted life-years (QALYs) would have been appropriate given the impact of the disease on quality of life and would have enabled cross-disease comparisons.

Costs:
The perspective was clearly defined and it appeared that relevant costs were included. Detailed unit costs and total costs for most items were provided including their data sources. Unit costs were based on conventional USA sources. Details on resource use quantities were given and this aided replication of the analysis in other settings. Costs over one year were not discounted but the time horizon analysed was short (two years). Other details such as discount rate, price year and adjustments of costs were reported.

Analysis and results:
The analytical modelling approach and results were reported satisfactorily. An incremental analysis was applied appropriately to determine the relative cost-effectiveness of the comparators. The one-way and probabilistic sensitivity analyses were appropriate for addressing the issue of uncertainty. The authors discussed the limitations of the study, which included the absence of data from direct head-to-head studies.

Concluding remarks:
The study was based on valid methods. Data sources and results were reported clearly. The authors’ conclusions appear appropriate.
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