Modeling the cost-effectiveness of a new treatment for MS (natalizumab) compared with current standard practice in Sweden

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 natalizumab in comparison with the current standard therapy using disease-modifying drugs (DMDs), for the treatment of patients with relapsing-remitting multiple sclerosis. Under the model assumptions, natalizumab provided additional health benefits at a similar cost to current DMDs from a societal perspective. The study was based on valid methodology which was well reported and the authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of natalizumab in comparison with the current standard therapy using disease-modifying drugs (DMDs), for the treatment of patients with relapsing-remitting multiple sclerosis (MS).

Interventions
Natalizumab at 13 infusions per year was compared with DMDs which included interferon β-1a, interferon β-1b, and glatiramer acetate.

Location/setting
Sweden/hospital.

Methods
Analytical approach:
This economic evaluation was based on a Markov model developed to simulate the disease progression over a 20-year time frame. The authors stated that the perspectives of both society and the health care system were adopted.

Effectiveness data:
The clinical inputs came from a selection of known, relevant studies. The treatment effect for natalizumab came from a two-year pivotal clinical trial (the Natalizumab Safety and Efficacy in Relapsing Remitting Multiple Sclerosis, AFFIRM, trial) which enrolled 924 patients. The treatment effect for DMDs came from a group of 512 patients from the Swedish MS registry for the Stockholm county. The long-term disease progression came from the Ontario data set of 824 patients with a mean follow-up time of 24.4 years. Data from these sources were selected whenever possible to match the baseline characteristics of patients in the AFFIRM trial. The key clinical endpoint was treatment efficacy, defined as the rate of clinical relapse and rate of sustained progression of disease.

Monetary benefit and utility valuations:
The utility valuations came from a cohort of 1,339 patients, from a recent international survey of MS patients in Europe, who completed the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at 3% per annum.

Cost data:
The economic analysis included the costs of medical services (in-patient and out-patient care, rehabilitation, tests, and drugs), non-medical services (walking aids, wheelchairs, nurse visits, home helps, and personal assistants), patient costs, informal care, and production losses. All costs were based on data from the international survey that supplied the utility valuations, in which costs were related to health status as assessed by the Expanded Disability Status Scale. Costs were presented in Euros (EUR) and were discounted at an annual rate of 3%. The price year was 2005.

Analysis of uncertainty:
A deterministic one-way sensitivity analysis was undertaken to consider the impact of different assumptions for the study perspective, increasing natalizumab costs to account for intensive monitoring, increasing or decreasing natalizumab persistency, decreasing natalizumab treatment efficacy, and varying time horizons and discount rates. These alternative assumptions were either defined by the authors or based on published evidence. A probabilistic sensitivity analysis was also undertaken to generate cost-effectiveness acceptability curves.

Results
In the base-case (20-year time horizon, societal perspective, and AFFIRM estimates for treatment efficacy), the expected QALYs were 8.99 with standard treatment and 9.33 with natalizumab. The expected costs were EUR 613,680 with standard treatment and EUR 609,850 with natalizumab. Thus, natalizumab was the dominant strategy, which means it was both (slightly) less expensive and more effective.

When only health care costs were considered, the incremental cost per QALY gained with natalizumab rose to EUR 38,145.

The sensitivity analysis indicated that, as expected, health benefits were strongly sensitive to variations of the time horizons and treatment efficacy, but the small difference in costs between treatment arms led to wide changes in cost-utility ratios.

The results from the probabilistic analysis showed that natalizumab remained dominant in 55% of simulations and remained below a threshold of EUR 50,000 per QALY in 75% of simulations.

Authors' conclusions
The authors concluded that, under their model assumptions, natalizumab provided additional health benefits at a similar cost to current DMDs from a societal perspective.

CRD commentary
Interventions:
The rationale for the selection of the interventions was clear. The new treatment was compared with a class of drugs representing the current pattern of care in the authors’ setting. These drugs were considered according to their market share as shown in the official registry. The authors noted that an important issue regarding the selection of the comparators was the inconsistency between the clinical trial population and the approved population for natalizumab; in Sweden at the time natalizumab was used in patients who did not adequately respond to their current DMDs. However, the authors demonstrated that, even in comparison with no treatment, natalizumab remained the dominant strategy.

Effectiveness/benefits:
The selection of data sources was based on the authors’ knowledge, and such an approach was intended to ensure the inclusion of the most appropriate evidence. The key characteristics of each source of data (type of source, number of patients involved, etc) were described. In general, these sources were appropriate for deriving the specific sets of data used. For example, the use of a double-blind, randomised, clinical trial to assess the treatment efficacy was a valid choice given the strengths of this study design. The authors attempted to select subgroups of patients with similar characteristics in order to minimise the heterogeneity across the various sources. The statistical approaches used to transform data from primary sources to inputs for the model were described for each set of estimates. The derivation of utility valuations was appropriately described and was based on a validated instrument. QALYs are an appropriate benefit measure, which allow cross-disease comparisons to be made.

Costs:
The analysis of costs was carried out from a very wide perspective and included all the relevant cost categories. A more restricted perspective was also considered in order to make the findings relevant to different decision makers. The source of costs was described and reflected the actual patterns of resource consumption. However, unit costs and resource quantities were not presented separately, given that the cost estimation was linked to disease progression. This approach is quite common in diseases such as MS but might reduce the transparency of the economic analysis. Other details such as the currency conversion, use of discounting, and price year were reported.

Analysis and results:
The findings were clearly presented. The use of an incremental approach to combine the costs and benefits was appropriate. The issue of uncertainty was satisfactorily addressed using two different approaches, which investigated different areas of uncertainty. The results of the sensitivity analysis should be interpreted with caution, as the authors pointed out, because the small difference in costs between treatment arms led to wide changes in cost-utility ratios. The model structure and key parameters were appropriately presented and justified. In general, the analysis was well reported.

Concluding remarks:
The study was based on valid methodology which was very well reported. The authors’ conclusions appear to be robust.

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