Cost effectiveness of memantine in Alzheimer's disease in the UK

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 objective was to assess the cost-effectiveness of memantine for treatment of moderate to severe Alzheimer’s disease. The authors concluded that memantine could be regarded as a cost-effective treatment. The study methodology was good and the methods and results were reported adequately. Given the scope of the study, the authors’ conclusions appear valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of memantine for treatment of moderate to severe Alzheimer’s disease.

Interventions
Two interventions were compared: memantine; and established clinical practice of either no pharmacological treatment or background therapy with acetylcholinesterase inhibitors (AChEIs).

Location/setting
UK/Outpatient secondary care.

Methods
Analytical approach:
A decision analytic Markov model was used to assess costs and outcomes associated with the two interventions. The mode comprised three health states: pre-full time care, full time care and death. The time horizon was five years. The authors reported that the perspective was that of the UK National Health Service (NHS) and Personal Social Services (PSS).

Effectiveness data:
Clinical and effectiveness data were obtained from previously published studies that included randomised controlled trials and a UK epidemiology study. The main effectiveness estimates used in the model were the effectiveness of the interventions on cognition, functioning and behaviour. These estimates were obtained from a previously published meta-analysis of six large multicentre randomised controlled studies (see Other Publications of Related Interest for more bibliographic details). Transitions probabilities between the three health states were derived using a new published predictive equation of time to full time care. The predictive equation was derived using the London and South East Region (LASER-AD) UK epidemiological study.

Monetary benefit and utility valuations:
EQ-5D utility estimates were obtained by mapping relevant components of the 12-item Health Status Questionnaire, Ferm’s D-test and the quality of life scale in Alzheimer’s disease into each of the five domains of the EQ-5D.

Measure of benefit:
The measure of health benefit was quality-adjusted life-years (QALYs) gained. Benefits could be generated over the lifetime of the patient and future benefits were discounted using an annual rate of 3.5%.

Cost data:
The direct costs included in the study related to routine patient management, medications, hospitalisation, social community services and institutionalisation. These costs were obtained from the LASER-AD study. In this study the Client Service Receipt Inventory (CSRI) was adapted for use with elderly patients and used to record all healthcare and social care resource use. All resource use was then valued using UK published sources. The price year was 2009. Costs could be incurred over a five-year time horizon and future costs were discounted using an annual rate of 3.5%. All costs were reported in UK pounds sterling (£).

Analysis of uncertainty:
A series of one-way sensitivity analyses varied each model parameter to determine the key drivers of uncertainty in the model. A probabilistic sensitivity analysis was undertaken by fitting probability values alongside the model parameters. This analysis was run with 10,000 Monte Carlo simulations.

Results
The average QALYs gained over five years were 1.502 with standard care and 1.533 with memantine (+0.031).

The average five-year cost per patient was £94,787 with standard care and £93,076 with memantine (+£1,711).

Costs and benefits were not combined as memantine was found to be dominant over standard care (less costly and more effective).

Results of the probabilistic sensitivity analysis showed that at a willingness to pay threshold of £20,000 the probability that memantine was cost-effective was 98.1% and at a willingness to pay threshold of £30,000 was 98.5%.

Authors' conclusions
The authors concluded that memantine could be regarded as a cost-effective treatment in the management of moderate and severe Alzheimer's disease.

CRD commentary
Interventions:
The interventions under study were reported adequately. There was no discussion regarding other potential comparators. Due to the comparative nature of economic evaluations the existence of any other relevant comparators would impact the results.

Effectiveness/benefits:
The methods underpinning the derivation of the predictive equation and its use were fairly well reported and seemed appropriate. The main measure of effectiveness was derived from a published systematic review and meta-analysis of randomised controlled trials. These trials were likely to represent all relevant treatment effectiveness information. Simplifying assumptions included the assumption that immediate benefits from treatment modified patients' time-related risk of progression from pre-full-time care to the full-time care health state were obtained and maintained for a five year period. These assumptions were in line with those made in previous analysis but their validity should be considered carefully. Use of mapping methodology was an appropriate means of obtaining utility outcomes for the health states; whether these methods were as robust as direct elicitation was not clear. It was unclear why this method was preferred over estimates in the literature that were used in sensitivity analysis.

Costs:
The perspective adopted in the economic analysis was reported explicitly to be that of the NHS and PSS. It appeared that all relevant major categories of costs and costs for this perspective were included in the model. Sources of costs and resource use were reported adequately. The time horizon, discount rate and price year were all stated clearly.

Analysis and results:
A decision Markov model was used to synthesise cost and outcome information. Appropriate details of the model structure were provided and included a graphical depiction. The impact of uncertainty on the model's results was tested exhaustively with a series of one-way and probabilistic sensitivity analysis. The authors reported that they had to assume that benefits of treatment at six months (the maximum follow-up in the trials included in the study) were sustained over time.
Concluding remarks:
Study methodology was good and the methods and results reported adequately. There was uncertainty surrounding the utility outcomes and long-term effectiveness of the treatment. However, the authors conclusions are appropriate.

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