Cost-effectiveness analysis of memantine for moderate-to-severe Alzheimer's disease in the Netherlands
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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 memantine, relative to standard care, for the treatment of patients with moderate-to-severe Alzheimer's disease, from a societal perspective. The authors concluded that memantine was more effective and less expensive than usual care, in the Netherlands. The cost-effectiveness framework was valid, key methods were reported, and key areas of uncertainty were investigated. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study assessed the cost-effectiveness of memantine, relative to standard care, for the treatment of patients with moderate-to-severe Alzheimer's disease.

Interventions
Memantine 20mg daily monotherapy was compared with usual care, which included no pharmacological treatment.

Location/setting
Netherlands/secondary care.

Methods
Analytical approach:
The analysis was based on a published Markov model, with a five-year time horizon. The authors stated that a societal perspective was adopted.

Effectiveness data:
Most of the clinical inputs were from the published decision model. Some more recent and relevant data were from Dutch studies. For example, the initial distribution of patients between model health states was from a subsample of 339 patients in a study of disorders associated with dementia in 7,528 residents of a Rotterdam suburb. A key input was the efficacy of memantine over usual care, which was from the pooled analysis of four six-month, double-blind, randomised, placebo-controlled trials. The treatment effect after six months was based on an open-label extension study. Mortality was from Dutch published studies.

Monetary benefit and utility valuations:
The utility values for the level of dependency and residential status were from a UK study of 224 patients with Alzheimer’s disease.

Measure of benefit:
Quality-adjusted life-years (QALYs), time in an independent state, and time in a moderate state were the summary benefit measures. They were discounted at an annual rate of 1.5%.

Cost data:
The economic analysis included the costs of visits, family care, district nursing, hospital admission, regional institutes for mental health, day-care centres (including travel), and informal care. The resource quantities were from Dutch
sources, including official guidelines and a model of the cost of care for patients with dementia. The unit costs were reported and were from official Dutch prices. The costs were in Euros (EUR) and were discounted at an annual rate of 4%. The price year was 2008.

**Analysis of uncertainty:**
A probabilistic sensitivity analysis was carried out using a Monte Carlo simulation, with 10,000 iterations, and using predefined probability distributions for the model inputs. An alternative worst-case scenario assumed that patients received treatment for only two years and its efficacy lasted for only six months. Univariate sensitivity analyses were performed on the odds ratios for the impact of memantine on dependency and severity, on the discount rates, and on the distributions between nursing homes and homes for the elderly.

**Results**
The projected costs were EUR 113,927 with usual care and EUR 110,097 with memantine. The QALYs were 1.207 with usual care and 1.265 with memantine. The time in an independent state was 1.602 years with usual care and 1.751 years with memantine. The time in a moderate state was 2.051 years with usual care and 2.141 years with memantine.

Memantine was dominant as it was more effective and less expensive than usual care.

Results were stable in all sensitivity analyses. Memantine was dominant in 96.8% of simulations. It remained dominant in the worst-case scenario, for 80.7% of simulations.

**Authors’ conclusions**
The authors concluded that memantine was more effective and less expensive than usual care, in the Netherlands.

**CRD commentary**

**Interventions:**
Memantine was appropriately compared with no pharmacological treatment. The authors stated that galantamine was another medical treatment for Alzheimer’s disease, but was not directly comparable.

**Effectiveness/benefits:**
The clinical data appear to have been from appropriate sources. The treatment effect was from a pooled analysis of clinical trials which should have ensured high internal validity. Other data were adjusted for the Netherlands, using a large local database and longitudinal studies. Extensive sensitivity analysis was conducted on all uncertain parameters. QALYs were an appropriate main benefit measure, as Alzheimer’s disease has a strong impact on quality of life. They also allow comparisons with other disease interventions. The utility weights were from a large sample of patients with Alzheimer’s disease and these UK values appear to be transferable to the Dutch context.

**Costs:**
The economic analysis had a broad perspective and included a wide range of costs, including non-medical items, such as informal care, which were relevant for patients with Alzheimer’s disease and their families. The unit costs were extensively presented and were from official Dutch prices. The resource use was from a published Dutch model and was reported for most items. The price year was clearly stated, allowing deflation exercises for other time periods. Conventional discounting was applied and alternative rates were considered. The costs were appropriately varied in the sensitivity analyses.

**Analysis and results:**
The results were clearly presented and an incremental approach was used to compare the two interventions. Incremental cost-utility ratios were not calculated as memantine was dominant. The uncertainty was satisfactorily investigated in deterministic sensitivity analyses and a probabilistic Monte Carlo simulation, and the key results were clearly reported. The authors noted that the conclusions were consistent with those of economic evaluations of memantine in other countries. Therefore, they might be transferable to other similar settings.

**Concluding remarks:**
The cost-effectiveness framework was valid, key methods were reported, and key areas of uncertainty were investigated. The authors’ conclusions appear to be robust.
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