Cost-effectiveness of memantine in moderate-to-severe Alzheimer's disease patients receiving donepezil


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 aim was to assess the cost-effectiveness of adjuvant memantine in patients with moderate-to-severe Alzheimer’s disease, who were receiving stable doses of donepezil. The authors concluded that memantine plus donepezil improved the clinical outcomes and reduced the total costs of care in comparison with donepezil alone. The study appears to have been based on valid methodology and uncertain areas were satisfactorily investigated. The authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to assess the cost-effectiveness of adjuvant memantine in patients with moderate-to-severe Alzheimer’s disease (AD), who were receiving stable doses of donepezil.

Interventions
The two strategies were one year of combination treatment of memantine plus donepezil compared with one year of donepezil alone.

Location/setting
USA/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a micro-simulation decision model which determined changes in cognitive function over time. A lifetime horizon was considered. The authors stated that the perspective adopted was that of society.

Effectiveness data:
The clinical data were derived from published studies which were selected and justified by the authors. The key characteristics of the sources used were reported. For example, the data on disease progression came from an observational study of 180 patients with AD. The data on treatment effect for memantine plus donepezil compared with donepezil alone were derived from a recently published phase III randomised controlled trial (RCT) with a 12-month follow-up. The donepezil treatment effect was taken from a placebo-controlled clinical trial and superimposed on the natural history of AD. Some assumptions were also made, mainly on the long-term impact of the two treatments. The key clinical outcome was the impact of treatment on cognitive function, assessed by the Severe Impairment Battery (SIB).

Monetary benefit and utility valuations:
The utility valuations were derived from published data on the relationship between the Health utilities Index Mark 3 (HUI3) and the disease severity. These data came from a cross-sectional study in which the HUI3 was administered to caregivers of 679 patients with AD, dwelling in the community and in institutions.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure and a 3% annual discount rate was applied. Changes in SIB score were also reported, but were not combined with costs.

Cost data:
The analysis considered both expenditures on formal health care services (inpatient, outpatient, home health, pharmacy, and long-term care) and informal services (unpaid caregiver time) to reflect the societal perspective. The costs and quantities were presented as macro-categories related to the severity of disease. These costs were derived from published sources. Drug dosages were based on consumption patterns in the RCT and costed using average wholesale prices. The costs were in US dollars ($) and the price year was 2005. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A deterministic univariate sensitivity analysis was undertaken by varying the model inputs by plus 10% or minus 10% of their baseline values, except for the baseline score for mental impairment which was varied using the published range. The best and worst case scenarios were considered.

Results
Over a lifetime, the combination therapy was a dominant strategy since it led to additional benefits at lower costs. The loss in QALYs was 0.5273 with combination therapy and 0.5545 with donepezil alone. The total costs were $248,393 with combination therapy and $248,635 with donepezil alone. Specifically, the increased drug costs for combination therapy ($1,250) were more than offset by the reduction in other formal and informal costs ($1,492).

When the time horizon was one year or shorter, the combination therapy was no longer dominant, but the incremental cost per QALY gained did not exceed $3,475 even after only six months of treatment.

The sensitivity analysis corroborated these base-case findings and even more favourable results were achieved among patients with more advanced AD at the initiation of therapy. In the worst case scenario, the incremental cost per QALY gained with memantine plus donepezil compared with donepezil was $7,867.

Authors' conclusions
The authors concluded that memantine plus donepezil for the treatment of moderate-to-severe AD improved clinical outcomes and reduced total costs of care in comparison with donepezil alone.

CRD commentary
Interventions:
The selection of the comparators was justified. The authors used the results from a recent RCT, which compared donepezil alone with combination treatment.

Effectiveness/benefits:
A selective review of clinical studies was used to identify relevant sources for the clinical inputs. The authors provided some key details on these published studies, and it appears that valid sources were used. A RCT was used to derive the data on treatment effect of combination therapy compared with donepezil alone and this represents a strong source given its robust design. The authors justified their decision to take the treatment effect for donepezil alone from a placebo-controlled trial instead of from the head-to-head trial, by stating that the benefits of donepezil in the head-to-head trial were likely to be an artefact of that trial given the patient characteristics. Other sources of data such as life tables and observational studies were also partially described and appear to have been appropriate. The derivation of the benefit measure was clearly described and the methods used to associate the utility values with the model health states were extensively described.

Costs:
The perspective was that of society and the costs relevant to the health care payer and the patient were included. These costs were presented as macro-categories and were not broken down into individual cost items. Furthermore, the costs and quantities were not presented separately. This might reduce the transparency of the analysis as well as the possibility of replicating the analysis in other settings. The sources used to derive these costs were not described. The
price year and the use of discounting were reported.

Analysis and results:
The synthesis of costs and benefits was appropriate. The issue of uncertainty was addressed in the sensitivity analysis, the key findings of which were presented. The authors did not perform a probabilistic sensitivity analysis due to the lack of data on the distributions of many of the key model parameters. The authors noted some limitations to their analysis. For example, the period of efficacy (12 months) was twice the length of the follow-up in the RCT. Furthermore, some assumptions on the use of specific measures of disease severity were made, although these were generally conservative assumptions.

Concluding remarks:
The study appears to have been based on valid methodology and uncertain areas were satisfactorily investigated. The authors' conclusions appear to be valid.

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