INTRODUCTION

• Alzheimer’s disease (AD) is a chronic, progressive neurodegenerative disorder which affects around 465,000 people in the UK.1
• Of the total AD patient population, 31% and 21% of US patients are expected to be in the moderate and severe stages of the disease respectively.2
• The median survival from diagnosis of AD is approximately 6 years (range 1–16 years), with about one-third of the time being spent in the severe stage.3
• An important sub-group of AD patients are those with agitation/aggression or psychotic symptoms (APS). Data from the LASER-AD study in the UK suggest that around 45% of moderate to severe AD patients fall into this category.4
• The total economic burden of dementia in Europe is estimated to be €65–666 billion annually based on 2003 values.5 In the UK alone, the estimated direct cost of AD is between £7.06 billion and £14.93 billion.6
• Postponing or stabilising decline in any of the key symptoms represents a meaningful benefit to both patients and their carers.
• Memantine (MEM) combined with a cholinesterase inhibitor (ChEI) is associated with significant clinical benefits in terms of cognitive function, ability to perform daily activities, mood and behaviour compared to a ChEI alone.7

OBJECTIVES

To assess the cost-effectiveness of memantine in the APS patient subgroup, in the UK setting.

RESULTS

Base-case results
Memantine was associated with:
• Prolongation of time to FTC by 11.2 weeks compared to standard care
• A gain in QALYs of 0.07 over standard care
• A decrease in costs of £4,970 (£5,930) compared to standard care.

Memantine is a dominant treatment strategy compared to standard care.

Table II: Base–case cost-effectiveness, MEM + standard care vs. standard care

<table>
<thead>
<tr>
<th>Memantine + standard care</th>
<th>Cost</th>
<th>QALYs</th>
<th>Time in pre-FTC (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard care</td>
<td>£93,485</td>
<td>1.563</td>
<td>1.731</td>
</tr>
<tr>
<td>Incremental</td>
<td>£98,816</td>
<td>1.493</td>
<td>1.516</td>
</tr>
<tr>
<td></td>
<td>-4,971</td>
<td>0.069</td>
<td>0.215</td>
</tr>
</tbody>
</table>

Sensitivity Analyses Results
Results of the sensitivity analyses confirm the robustness of the base-case analysis results. The probabilities of the memantine strategy being superior to the standard care strategy in all probabilistic sensitivity analyses are summarised in Table 3 below.

Table III: Summarised results of the probabilistic sensitivity analysis

<table>
<thead>
<tr>
<th>Memantine better than standard care</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less costly</td>
<td>99.98%</td>
</tr>
<tr>
<td>More effective</td>
<td>100.00%</td>
</tr>
<tr>
<td>Dominant (less costly and more effective)</td>
<td>99.98%</td>
</tr>
<tr>
<td>Cost-effective at £20,000 per QALY</td>
<td>100.00%</td>
</tr>
<tr>
<td>Cost-effective at £30,000 per QALY</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

Memantine was the dominant treatment strategy in all one-way deterministic sensitivity analyses, except when costs and utilities were derived from Green et al. (2005).11 In this case, memantine was still associated with higher QALYs and longer time in the pre-FTC state.

METHODS

Study design: Cost-utility analysis based on a 5-year Markov cohort model
Population: Pre-FTC (Full Time Care) moderate to severe AD patients presenting with APS
Comparators: MEM + standard care vs. standard care (background ChEI or no pharmacotherapy)
Perspectives: UK National Health Service and the Personal Social Services
Discounting: 3.5%, half-cycle correction was applied to both costs and health benefits
Time horizon: 5 years

Structure of the Markov model
• The Markov model incorporated three health states: pre-FTC, FTC and death.
• Each Markov cycle was 1 month, yielding 60 cycles over the 5 year period.
• Effectiveness estimates came from a meta-analysis of six randomised clinical trials.8
• Transition probabilities, baseline characteristics, resource utilisation, health utility weights and mortality rates were derived from the LASER-AD study.9,10
• The clinical benefits of memantine have been found to be greater in the APS sub-population of AD patients.10 This has therefore been reflected in the ‘memantine effect’ input values for the model.
• Utility values were derived from mapping of healthcare questionnaire results to the EQ-5D dimensions. This allowed researchers to calculate the utility values for the three health states of the model.

Costs
• Costs included: routine patient management, hospitalisation, social community services, institutionalisation and medications (see Table 1).
• Treatment costs for memantine were £64.80 per cycle + £126.36 for initial consultation and £35 every 6 cycles for subsequent GP monitoring visits.
• The drug acquisition cost of ChEIs were not taken into account as it was assumed that patients in both groups would have the same level of ChEI usage.

Sensitivity analysis
• The model underwent extensive stochastic and one-way deterministic analyses across clinical inputs, discount rates (0% and 6%), costs (+30%) and utilities.

REFERENCES
1 Alzheimer’s Society (UK) Factsheet 401 – ‘What is Alzheimer’s Disease?’ Available at: http://www.alzheimers.org.uk/factsheet/401
10 Lundbeck data on file.

CONCLUSIONS
• Memantine represents an effective treatment for AD patients with APS in the UK and is an efficient use of NHS resources.
• The model demonstrates that memantine yields higher health benefits at no additional costs relative to standard care.
• The estimated benefits and cost savings are almost twice higher than those previously estimated in the general population of moderate/severe AD patients.
• The sensitivity analyses confirm the robustness of the base-case results, with memantine dominant in 99.98% of all probabilistic simulations.

ACKNOWLEDGEMENTS
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