Assessment of health economics in Alzheimer's disease (AHEAD): treatment with galantamine 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.

Health technology
Galantamine (Reminyl), a cholinesterase inhibitor that also modulates nicotinic receptors, was evaluated for the treatment of mild to moderate Alzheimer's disease (AD). The dose of galantamine used was 16 mg or 24 mg/day.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients with AD according to the National Institute of Neurologic and Communicative Disorders and Stroke and AD and Related Disorders Association (NINCDS-ADRDA) classification. The inclusion criteria were either Mini-Mental State Examination (MMSE) scores between 11 and 24 with an Alzheimer's Disease Assessment scale (ADAS) score of at least 12, or MMSE scores of 10 to 22 and an ADAS-cog (the cognitive sub-scale of the ADAS scale) score of at least 18.

Setting
The setting was multiple: community, institution, primary care and private care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data were derived from studies published from 1999 to 2001. The resource use data were derived from studies published between 1985 and 1986. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review of published studies and authors' assumptions.

Modelling
The AHEAD (Assessment of Health Economics in Alzheimer's Disease) model was used to evaluate the health and economic consequences of using galantamine (either 16 or 24 mg), compared with placebo, to treat patients with AD. Details of the model were published elsewhere (see Other Publications of Related Interest). The model was based on longitudinal epidemiological data, which were used to predict the time until the patients deteriorated to a level requiring full-time care (FTC), and the time until death. The model was populated with data derived from the literature. The three main health states considered were before patients require FTC, when patients require FTC, and death. The time horizon of the model was 10 years. Two sub-groups of patients were considered. One comprised patients with moderate...
disease only, the other comprised those who responded to treatment. Moderate disease was defined as a baseline MMSE score of less than 18. Response to treatment was defined as having maintained or improved cognition (using the cognitive part of the ADAS-cog) over 6 months.

**Outcomes assessed in the review**
The outcomes assessed from the literature were galantamine efficacy on cognitive deterioration, epidemiological data, and health state utilities.

**Study designs and other criteria for inclusion in the review**
The design of the primary studies was not reported and a formal review of the literature was not performed.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
The model inputs were derived from six primary studies.

**Methods of combining primary studies**
Not stated.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
Galantamine efficacy on cognitive deterioration and epidemiological data were not reported. The values of the health state utilities were 0.60 before and 0.34 after the patients required FTC.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions that were used in the decision model.

**Estimates of effectiveness and key assumptions**
It was assumed that patients discontinuing treatment had changes in cognition and psychotic symptoms equivalent to those of patients who had never received galantamine treatment. It was also assumed that galantamine had no impact on patient survival.

**Measure of benefits used in the economic analysis**
The summary benefit measure used in the economic analysis was the quality-adjusted life-years (QALYs). Both
survival and quality of life data were estimated from the literature. Utility values were derived from carers (paid and unpaid) as proxies for patients' preferences. The mean time to when FTC was needed and survival were also estimated from the model. An annual discount rate of 1.5% was applied to the QALYs.

**Direct costs**
As the time horizon of the model was 10.5 years, the costs were discounted using an annual rate of 6%. The unit costs were not presented separately from the quantities of resources used. The cost categories included in the economic analysis were those derived from patients residing in the community or in an institution, such as inpatient and outpatient care, private care, general practitioner (GP) services, and social services. The perspective of the study was that of the UK NHS. Resource use data were collected from two national surveys conducted by the Office of Population Census Survey during 1985 and 1986 and from national data (Community Care Statistics). Some assumptions were also made. The unit costs were estimated from published sources, including official data. The total expected costs were estimated using modelling. The costs were inflated to 2001 values using the medical component of the consumer price index.

**Statistical analysis of costs**
No statistical analyses of the costs were conducted.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
One-way sensitivity analyses were carried out to investigate the stability of the results. The key model inputs varied were the discount rate, the proportion of patients in institutional care, and the utility values. The ranges used were based on values set by the authors.

**Estimated benefits used in the economic analysis**
Without galantamine, the mean time to when FTC was needed was 3.2 years and mean survival was 5.1 years. When galantamine treatment was started, FTC was required for 12% less time with 16 mg and 15% less time for 24 mg. A mean gain of 0.06 QALYs was predicted.

**Cost results**
The total expected, discounted 10-year per patient costs were 28,134 with no treatment, 28,615 with galantamine 16 mg, and 28,806 with galantamine 24 mg. Compared to placebo, galantamine 16 mg cost an extra 481 and galantamine 24 mg cost an extra 672.

**Synthesis of costs and benefits**
The incremental cost per QALY was 8,693 with galantamine 16 mg relative to placebo. Small savings (228) were predicted in the sub-group of patients with moderate disease, while more substantial savings (1,372) were observed among those responding to galantamine. Similar results were observed with galantamine 24 mg. The most striking results of the sensitivity analysis were related to variations in the proportion of patients needing FTC while they were admitted to an institution. If the proportion of institutionalised patients decreased from 48% to 40% then the net cost per patient was 731 with galantamine 16 mg. However, cost neutrality was observed when 64% of the patients requiring FTC were institutionalised. Variations in the discount rate had negligible effects on the results, while +/- 50% variations in the utility values led to the incremental cost per QALY ranging from 5,810 to 17,431.
Authors' conclusions
Galantamine led to an increase in the costs of care in the first three years of treatment, but the costs were almost completely offset in the long-term due to the delay in the need for full-time care (FTC). Since galantamine was effective in slowing disease progression, the cost per quality-adjusted life-year (QALY) gained was 8,693 in the base-case and cost-savings were predicted for patients with mild disease or those who responded to the therapy.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Placebo was selected because no treatment represented the standard option for the management of patients with AD. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness study used data estimated from the literature. However, a systematic review of the literature was not carried out and details of the primary studies were not given. Aggregated data of the overall study population were provided so that patients with mild to moderate disease could be compared to those with moderate disease only. The methods used to combine the primary estimates were not described and the estimated data were not reported. The authors also made some assumptions, which were not tested in the sensitivity analysis. The validity of the effectiveness data could not be objectively assessed.

Validity of estimate of measure of benefit
The choice of QALYs as the summary benefit measure was appropriate because it measured the impact of the treatment on quality of life. It was assumed that the intervention had no effect on patient survival. The utility values were estimated from a study that used carer values as proxies for patients' preferences. Unfortunately, survival data were not reported. The QALYs were appropriately discounted and the use of a different discount rate was tested in the sensitivity analysis.

Validity of estimate of costs
The perspective of the study was reported and all the relevant categories of costs were included in the analysis. The price year and the sources of data used in the economic evaluation were reported. However, details of the unit costs and resource use were not presented. No statistical tests or sensitivity analyses were carried out on the cost estimates. The authors noted that both the resource use data and unit costs were specific to the UK. The estimates obtained in the analysis were conservative. Thus, even more favourable results should be achievable under real-life conditions.

Other issues
The authors compared their findings with other studies. They did not, however, address the issue of the transferability of the results to other settings. Indeed, they stated that some caution is required when generalising their results because all of their estimates related to the UK setting. Sensitivity analyses were primarily carried out to address the issue of stability of the results rather than variations in data. The authors noted that the main limitation to the validity of their analysis was the use of data derived from short-term trials, which involved a population of patients selected with very strict criteria. It was also noted that the treatment compliance rate might be lower than that observed in the trial. This would result in fewer treated patients, and hence lower treatment costs.

Implications of the study
The main implication of the analysis was that galantamine might be cost-effective for the treatment of AD, and even cost-saving in specific sub-groups of patients. However, this conclusion should be corroborated in further long-term trials.
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Other publications of related interest

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