INAHTA Briefs

Issue 2001/04

Title **Guidance on the use of donepezil, rivastigmine, and galantamine for the treatment of Alzheimer's disease**

Agency **NICE, National Institute for Clinical Excellence**
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Reference **Technology Appraisal Guidance No19, ISBN 1-84275-061-7**
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Aim

To review and consider the available evidence on the clinical and cost-effectiveness of donepezil, rivastigmine, and galantamine for the treatment of Alzheimer's disease, and to issue guidance on their use to the National Health Service in England and Wales.

Conclusions and results

- A systematic review identified 5 randomized controlled trails for donepezil, 5 for rivastigmine, and 3 for galantamine. It also identified 3 systematic reviews for donepezil, 3 for rivastigmine, and one for galantamine.
- RCT evidence demonstrates that all 3 drugs to have some effect on global outcome measures. All 3 drugs also show statistically significant improvement in cognitive function with average improvements of 1-2 points (out of 30) in mini-mental state examination (MMSE) over 6 months compared to placebo (N.B. there is an average decline of 4-5 points over the same period in placebo-treated patients).
- Not all patients benefit from using these drugs. It is also difficult to predict before treatment commences who will benefit the most.
- Evidence that quality of life has been improved by treatment with these drugs is mixed.
- A systematic review of health economic evidence identified nine published studies, 5 for donepezil and 4 for galantamine.
- The main economic benefit of these drugs is the cost saving from delayed progression to the requirements for nursing home care. This cannot be estimated reliably from existing trial evidence.
- Many of the published economic studies were conducted in settings outside the United Kingdom. About half of the studies suggested that the drugs are cost saving. Other studies show a cost per QALY gained ranging from zero to approximately £30,000.
- The three manufacturer submissions present a cost per QALY gained ranging from cost saving up to approximately £10,000.
- Mini-mental state examination scores of above 12 are necessary to demonstrate cost effective use of these drugs.

Recommendations

The 3 drugs should be made available in the National Health Service for England and Wales as one component in the management of people with mild and moderate Alzheimer's disease whose mini-mental state examination score is above 12 points. This is subject to a number of conditions including specialist assessment before therapy is initiated, and a further assessment, which will usually be 2 to 4 months after the patient has reached the maintenance dose. Patients should be reviewed using the MMSE score every 6 months and therapy maintained only while their score remains above 12 points. *(continued on page 2)*

Written by Dr. Carole Longson, NICE, United Kingdom

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Methods

A comprehensive systematic literature review was undertaken by the Wessex Institute for Health Research and Development at the University of Southampton and submitted to the Institute as an Assessment report (the full Assessment Report is available on our website. The Appraisal Committee of the Institute considered the Assessment Report together with submissions from manufacturers, and patient and professional organizations. Expert clinicians and patient advocates provided personal representation at the Appraisal Committee meeting.

Further research/reviews required

Research should identify whether these drugs are of similar effectiveness, their place in the treatment of severe dementia, and whether they are of benefit in the treatment of other forms of dementia. The effect of these drugs on the delay in progressing to institutionalised care is not well established. Health economic studies should be carried out which allow more precise estimates of the magnitude of this effect to be made.

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