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NHS
National Institute for Health and Clinical Excellence

Quick reference guide

Donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease (amended)

Following the outcome of a judicial review in August 2007, NICE has amended and reissued this guidance.

This guidance constitutes a review of 'NICE technology appraisal guidance 19' on the use of donepezil, galantamine and rivastigmine for the treatment of mild to moderately severe Alzheimer's disease, published in 2001, and a new appraisal of the clinical and cost effectiveness of memantine for moderately severe to severe Alzheimer's disease.

1 Guidance

This guidance applies to donepezil, galantamine, rivastigmine and memantine within the marketing authorisations held for each drug at the time of this appraisal; that is:

- donepezil, galantamine, rivastigmine for mild to moderately severe Alzheimer's disease
- memantine for moderately severe to severe Alzheimer's disease.

The benefits of these drugs for patients with other forms of dementia (for example, vascular dementia or dementia with Lewy bodies) have not been assessed in this guidance.

1.1 The three acetylcholinesterase inhibitors donepezil, galantamine and rivastigmine are recommended as options in the management of patients with Alzheimer's disease of moderate severity only (that is, subject to section 1.2 below, those with a Mini Mental State Examination [MMSE] score of between 10 and 20 points), and under the following conditions.

- Only specialists in the care of patients with dementia (that is, psychiatrists including those specialising in learning disability, neurologists, and physicians specialising in the care of the elderly) should initiate treatment. Carers' views on the patient's condition at baseline should be sought.
- Patients who continue on the drug should be reviewed every 6 months by MMSE score and global, functional and behavioural assessment. Carers' views on the patient's condition at follow-up should be sought. The drug should only be continued while the patient's MMSE score remains at or above 10 points (subject to section 1.2 below) and their global, functional and behavioural condition remains at a level where the drug is considered to be having a worthwhile effect. Any review involving MMSE assessment should be undertaken by an appropriate specialist team, unless there are locally agreed protocols for shared care.

When using the MMSE to diagnose moderate Alzheimer's disease, clinicians should be mindful of the need to secure equality of access to treatment for patients from different ethnic groups (in particular those from different cultural backgrounds) and patients with disabilities.

NICE technology appraisal guidance 111 (amended September 2007)

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

1.2 In determining whether a patient has Alzheimer's disease of moderate severity for the purposes of section 1.1 above, healthcare professionals should not rely, or rely solely, upon the patient's MMSE score in circumstances where it would be inappropriate to do so. These are:

- where the MMSE is not, or is not by itself, a clinically appropriate tool for assessing the severity of that patient's dementia because of the patient's learning or other disabilities (for example, sensory impairments) or linguistic or other communication difficulties

or

- where it is not possible to apply the MMSE in a language in which the patient is sufficiently fluent for it to be an appropriate tool for assessing the severity of dementia, or there are similarly exceptional reasons why use of the MMSE, or use of the MMSE by itself, would be an inappropriate tool for assessing the severity of dementia in that individual patient's case.

In such cases healthcare professionals should determine whether the patient has Alzheimer's disease of moderate severity by making use of another appropriate method of assessment. For the avoidance of any doubt, the acetylcholinesterase inhibitors are recommended as options in the management of people assessed on this basis as having Alzheimer's disease of moderate severity.

The same approach should apply in determining for the purposes of section 1.1 above, and in the context of a decision whether to continue the use of the drug, whether the severity of the patient's dementia has increased to a level which in the general population of Alzheimer's disease patients would be marked by an MMSE score below 10 points.

1.3 When the decision has been made to prescribe an acetylcholinesterase inhibitor, it is recommended that therapy should be initiated with a drug with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started). However, an alternative acetylcholinesterase inhibitor could be prescribed where it is considered appropriate having regard to adverse event profile, expectations around concordance, medical comorbidity, possibility of drug interactions and dosing profiles.

1.4 Memantine is not recommended as a treatment option for patients with moderately severe to severe Alzheimer's disease except as part of well designed clinical studies.

1.5 Patients with mild Alzheimer's disease who are currently receiving donepezil, galantamine or rivastigmine, and patients with moderately severe to severe Alzheimer's disease currently receiving memantine, whether as routine therapy or as part of a clinical trial, may be continued on therapy (including after the conclusion of a clinical trial) until they, their carers and/or specialist consider it appropriate to stop.

2 Implementation

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TA111).

- Costing report and costing template to estimate the savings and costs associated with implementation.

Suggestions for audit to measure compliance locally can be found in the full guidance (see 'Further information').

Further information

Quick reference guide

This has been distributed to healthcare professionals working in the NHS in England and Wales (see www.nice.org.uk/TA111distributionlist). It is available from www.nice.org.uk/TA111quickrefguide

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1328).

Full guidance

This contains the following sections:

1 Guidance

2 Clinical need and practice

3 The technologies

4 Evidence and interpretation

5 Implementation

6 Recommendations for further research

7 Related guidance

8 Review of guidance.

The full guidance also gives details of the Appraisal Committee, the sources of evidence considered and suggested criteria for audit. It is available from www.nice.org.uk/TA111guidance

'Understanding NICE guidance'

Information for patients and their carers is available from www.nice.org.uk/TA111publicinfo

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1329).

Related NICE guidance

Dementia: supporting people with dementia and their carers in health and social care. *NICE clinical guideline* no. 42 (2006). NICE in collaboration with Social Care Institute for Excellence (SCIE). Available from: www.nice.org.uk/CG042

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