GUIDELINES FOR PRESCRIBING CHOLINESTERASE INHIBITORS
IN THE TREATMENT OF PATIENTS WITH ALZHEIMER’S
DISEASE

INTRODUCTION

The three acetyl cholinesterase inhibitors donepezil, galantamine and rivastigmine are all licensed for the symptomatic treatment of mild to moderate dementia in Alzheimer’s disease. The National Institute for Clinical Excellence (NICE) issued guidelines to the NHS in England and Wales regarding the prescribing of cholinesterase inhibitors in Alzheimer’s disease in January 2001.(1)

These guidelines will be reviewed in the light of any new NICE guidance that may be issued in the future.

PRESCRIBERS

These drugs may only be initiated by Consultants in Old Age Psychiatry. Prescribing by GP’s will only be under agreed shared care protocols.

INDICATIONS

Licensed indications

The current licensed indication for the use of cholinesterase inhibitors is mild to moderate dementia in Alzheimer’s disease, the diagnosis of which must be made in a specialist clinic according to standard diagnostic criteria.

Severity of illness

These drugs are licensed for use in mild to moderate case of dementia. NICE advise that the drugs should be available to NHS patients with Alzheimer’s disease whose mini mental score is above 12 points.
SELECTION CRITERIA

- ICD 10 criteria used for diagnosis of Alzheimer’s disease, and Alzheimer’s disease complicated by vascular disease. For the purposes of this protocol, Dementia with Lewy bodies (DLB) is considered a variant of Alzheimer’s disease (see Appendix). The Consensus Guidelines for the clinical and pathologic diagnosis of DLB should be followed.  
- Guidance mini mental state score between 26-12.

The use of the drugs outside of the mini mental state guidance range may be considered if patients otherwise meet clinical criteria for the diagnosis of mild to moderate Alzheimer’s disease. Under these circumstances, the prescribing Consultant must record the reasons why an exception has been considered, and may undertake further psychometry, such as CAMCOG or WAIS.

It is desirable that patients should be identified early in the course of their illness in order to maximise the period of potential benefit from the use of these drugs, and also to enable greater access to opportunities for counselling and planning of care over time.

TREATMENT GUIDELINES

1. Prior to treatment

1.1 Consent to treatment

Patients should understand the protocol, and in particular, understand not only why the drug is being initiated and the possible limited benefits, but also understand that the drug may be discontinued if it is not showing evidence of efficacy, or if it is thought that the drug is no longer playing a meaningful part in the management of the disorder.

An information leaflet explaining the protocol will be given to patients and their carers.

1.2 Consultants must ensure that structures are in place to ensure compliance before agreeing to initiate treatment.

2. Treatment phase

2.1 Therapeutic monitoring

The following investigations will be undertaken at baseline and subsequent assessments:

- Mini Mental State Assessment (MMSE)
- Abbreviated Bristol ADL scale
- Relatives Stress Scale (Greene et al 1982)
• FAST (baseline only)
• NPI (If Dementia with Lewy bodies suspected)
• CGI undertaken by both carer and Consultant (not at baseline)

2.2 Drug treatment

A number of factors will determine the clinicians choice of drug to be used. Factors that may influence the decision include the dosage regimen of the medication, tolerability, possible interactions with co-morbid medical conditions, possible interactions with the patients’ current medication, pharmacokinetics and mode of action. Patients and carers should be fully involved and informed about the treatment choices. Clinicians may consider switching from one anti dementia drug to another if there is failure to tolerate the initial drug tried at the first review. Each of the three drugs have different pharmacokinetic profiles and the timing of dosage adjustment will vary on which drug is used.

2.3 Prescriptions may be prescribed on hospital outpatients prescriptions or prescriptions FP10(HP) for dispensing at community pharmacies. Drugs prescribed on FP10(HP) are not subject to VAT, and may be cheaper. The initial prescription should be for one months supply, and subsequent prescriptions should be for no more than three months supply at a time.

2.4 Frequency of follow up visits

Week 0: Prescribe drug

Review side effects two weeks after each dose titration (this may be carried out on telephone)

Week 12-14: Assess efficacy using agreed tests (see section 2.1)

• If no evidence of efficacy (within agreed criteria) withdraw treatment
• If evidence of improvement (within agreed criteria) and no other reason for withdrawal, continue treatment and reassess efficacy at 6 monthly intervals, using agreed tests (section 2.1)

3. Criteria for withdrawal of treatment

3.1 The drug will be discontinued if the patient experiences adverse side effects or if his/her immediate family requests cessation of treatment. The drug will also be withdrawn if not efficacious at the three-month assessment.

3.2 If the MMSE falls below 10, a drug holiday should be considered. Similarly, patients showing either no improvement after 12 weeks of treatment could have a
trial discontinuation. Symptomatic deterioration during a drug-free period of upto 6 weeks could be used as an indication to reintroduce and continue treatment. No further deterioration during a drug-free period would be an indicative factor in a decision to stop treatment.

4. Audit.

Data must be collected at each assessment and recorded. It is the responsibility of each Consultant to ensure data collection. Audit will be carried out at agreed intervals and the results fed back to Consultants and PCT’s. The Clinical Director will ensure that all MHSOP staff, including Locum Consultant staff, are inducted into the policy and have access to the relevant assessment forms and data capture forms.

5. References


Date: February 2003

Review Date: February 2005 (or earlier in light of new NICE guidance)
APPENDIX 1

DEMENTIA WITH LEWY BODIES

The clinical syndrome of dementia with Lewy bodies (DLB) is still awaiting classification under the ICD or DSM systems of classification, but is usually classified under Alzheimer’s disease. DLB is the second most common type of degenerative dementia, with a typical prevalence of 15% of dementias.

Core features

- Fluctuating cognition with pronounced variations in attention and alertness;
- Recurrent visual hallucinations which are typically well formed and detailed;
- Spontaneous features of parkinsonism.

Features supportive of diagnosis

- Repeated falls;
- Syncope;
- Transient disturbances of consciousness;
- Neuroleptic hypersensitivity;
- Systemised delusions;
- Hallucinations in other modalities.

Although psychosis is common early in this disease, the neuroleptic hypersensitivity of these patients to both typical and atypical antipsychotics limits therapeutic options. The psychotic and behavioural effects of DLB often lead to patients being admitted to hospital to manage these symptoms, causing major suffering to patients and their carers, and significant cost financially.

Psychopharmacological basis for treatment

The characteristic cognitive deficit in Alzheimer’s disease (AD) is thought to be due to cholinergic deficiencies that occur within the cerebral cortex and basal forebrain. It can be shown that the decline in levels of acetylcholine is correlated with the degree of impairment suffered by the patient. This may also be the case in DLB.

Cholinesterase inhibitors work by increasing the concentration of acetylcholine available for synaptic transmission by blocking the hydrolytic action of acetylcholinesterase present within the synapse. In DLB, neocortical choline acetyltransferase is lower than in AD, but numbers of muscarinic M1 receptors appear elevated. This reflects an upregulation in M1 receptors in response to falling acetylcholine levels. Since cholinergic function in the cortex is impaired but postsynaptic muscarinic receptors remain intact, it is suggested that cholinergic therapy may be particularly effective. Cholinergic deficits in DLB are
thought to manifest themselves more in terms of neuropsychiatric than cognitive symptoms.

Evidence

In 2000, McKeith et al (1) published the results of double-blind, placebo-controlled international study which looked at the efficacy of rivastigmine in DLB. The study showed that patients taking rivastigmine were significantly less apathetic and anxious, and had fewer delusions and hallucinations while on treatment than controls. The conclusion was that rivastigmine 6-12mg daily produces statistically and clinically significant behavioural effects in DLB.

There is also some independent evidence. A letter to the Canadian Journal of Psychiatry reports on the case of a 74-year old man with DLB treated with some success with donepezil and risperidone. (2). Shea et al (3) reported on nine patients with DLB treated with donepezil; cognition improved in seven, hallucinations improved in eight, but parkinsonian symptoms worsened in three patients. Lanctot and Herrman (4) conducted a study in seven patients diagnosed with DLB and treated with donepezil to determine its effect on treating behavioural symptoms. Three of the seven showed marked improvement in behaviour with Neuropsychiatric Inventory scores dropping significantly over time. Sanders et al (5) investigated the treatment of patients with DLB using donepezil. They concluded that there were marked improvements in behavioural symptoms.

To conclude, there is evidence to suggest that cholinesterase inhibitors may be beneficial in both cognitive and behavioural symptoms associated with the condition.

References