Management of medications for Alzheimer's disease

DOCUMENT TO BE SCANNED INTO ELECTRONIC RECORDS / FILED IN NOTES

Patient Name: **Date of Birth:** **NHS No:**

Name of Referring Consultant: **Contact Number:**

INTRODUCTION

These guidelines have been produced to clarify the roles of primary and secondary care in the management of medications for Alzheimer's disease. They are based on the National Institute for Health and Care Excellence (NICE) Technology Appraisal 217 (March 2011) regarding donepezil, rivastigmine and galantamine (acetylcholinesterase inhibitors, or AChEIs) and memantine and an appraisal of more recent evidence relating to the prescription on combination treatment the most recent of which is a 2014 systematic review and meta-analysis (see references).

NICE GUIDANCE 2011

1. The three AChEIs are recommended as options for managing mild to moderate Alzheimer's disease under all the conditions specified in 3 and 4 below.
2. Memantine is an option for people with:
    - Moderate Alzheimer's disease who are intolerant of or have a contraindication to AChEIs, or
    - Severe Alzheimer's disease.
3. Treatment should be under the following conditions:
    - Initiation of treatment should be by a specialist in the care of patients with dementia. Carers' views on the patient's condition at baseline should be sought.
    - Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms. Again, carers' views should be sought.
    - Patients who continue on treatment should be reviewed at least annually. These reviews may be by an appropriate specialist team, for example during hospital admission, or by the primary care team where appropriate.

The 2011 guidance places less emphasis on mini-mental state examination scores in assessing severity, pointing out that educational attainment, sensory problems and language barriers need to be taken into account. Combination of an AChEI and memantine may occur where deemed clinically appropriate and switching between or combining the two is a clinical decision.

Combination treatment

More recent evidence demonstrates that the addition of Memantine to treatment with either donepezil or Rivastigmine (combination treatment) has significant benefits in terms of cognition, activities of daily living, neuropsychiatric symptoms and global assessment for people with mild-moderate Alzheimer's disease. Combination treatment may be considered in those with moderate to severe Alzheimer's disease with rapid progression and/or behavioural disturbance despite treatment with an AChEI. The decision to prescribe combination treatment should be made on an individual patient basis and with consideration of the overall severity of the illness, the nature and severity of behavioural symptoms, the rate of progression, and carer and patient views. All patients prescribed combination treatment will be reviewed within three months.

PATIENT PATHWAY

Clinical Speciality/ Indication	Prescribing Initiated By	Prescribing Continued By	Monitored By	Duration of Treatment
Alzheimer's disease, Dementia with Lewy bodies and Parkinson's disease dementia.	Old Age or Learning Disability Psychiatrist, Neurologist or Geriatrician	GP.	Old Age Psychiatry, Learning Disability Psychiatry, Neurology, Geriatric medicine or GP. Reviews should be at least annually or sooner if clinically indicated.	Determined on a case by case basis as clinically appropriate/as per NICE guidelines.

ORAL DOSE AND ADMINISTRATION

Current medications for Alzheimer's disease can have modest but significant effects on cognition, psychiatric and behavioural symptoms and function in individuals. There is also evidence to support their use in mixed (Alzheimer's disease and vascular) dementia and Lewy body dementia.

Donepezil
- Tablets/orodispersible tablets
- Dose: 5 mg/day for 4 weeks, maintenance 10 mg/day
- Common side effects include: diarrhoea, muscle cramps, fatigue, nausea, vomiting, headache and insomnia
- Caution in: supraventricular conduction abnormalities, particularly bradyarrythmias; gastric ulcers or people on non-steroidal anti-inflammatory drugs (NSAIDs); seizures; asthma or chronic obstructive pulmonary disease (COPD); patients on cholinergic agonists; patients on beta blockers

Galantamine
- Tablets/oral solution/modified release capsules
- Dose: 8 mg/day for 4 weeks, 16 mg/day for 4 weeks, then if tolerated 24 mg/day
- Tablets and oral solution need to be given in divided doses
- Side effects and cautions: see under donepezil

Rivastigmine
- Capsules/oral solution – dose: 1.5 mg bd for 4 weeks, then 3 mg bd for 4 weeks, then 4.5 mg for 4 weeks and then if tolerated 6 mg bd
- Patches – dose: 4.6 mg/24 hours for 4 weeks then 9.5 mg/24 hours. Dose can be increased to 13.3 mg/24 hours if required
- Side effects and cautions: see under donepezil

Memantine
- Differs from the AChEIs in being an NMDA antagonist
- Tablets/oral drops
- Dose: 5 mg/day for 1 week, then 10 mg/day for 1 week, then 15 mg/day for 1 week, then 20 mg/day
- Side effects: dizziness, headache, constipation, somnolence, hypertension

Drug Product	Cheapest Price in Primary Care (BNF68)
Donepezil tablets	5 mg x28 – £1.20 10 mg x28 – £1.60
Donepezil orodispersible tablets	5 mg x28 – £9.04 10 mg x28 – £12.00
Galantamine tablets	8 mg x56 – £59.29 12 mg x56 – £74.10
Galantamine oral solution	4 mg/mL x100 mL – £437.00
Galantamine MR capsules	8 mg x56 – £51.88 16 mg x56 – £64.90

	24 mg x56 – £79.80
Memantine tablets	10 mg x28 – £14.42 10 mg x56 – £69.01 20 mg x28 – £28.85
Memantine oral solution	5 mg/actuation (10 mg/mL) x50 mL – £61.61 5 mg/actuation (10 mg/mL) x100 mL – £123.23
Rivastigmine capsules	1.5 mg x28 – £3.43 1.5 mg x56 – £11.98 3 mg x28 – £3.40 3 mg x56 – £6.80 4.5 mg x28 – £16.62 4.5 mg x56 – £15.00 6 mg x28 – £16.62 6 mg x56 – £14.76
Rivastigmine oral solution	2 mg/mL x120mL – £99.14
Rivastigmine patches	4.6 mg/24 hours x30 – £77.97 9.5 mg/24 hours x30 – £77.97 13.3 mg/24 hours x30 – £77.97

MONITORING

1. Pre-treatment pulse check is required before treatment with AChEIs and pre-treatment electrocardiogram (ECG) (usually carried out in secondary care) is advised in some cases to look for supraventricular conduction abnormalities and bradyarrythmias.
2. Monitoring of cognitive function, global functional abilities and behavioural problems (taking in to account views of carers). These domains are assessed clinically. Frequency not specified in NICE guideline. Good practice suggests this should be at least yearly for stable patients. This monitoring can be carried out in primary care or in secondary care for those who need on-going specialist follow up.
3. No requirement for regular blood tests in relation to the prescription of medication for Alzheimer's disease.

The table below only lists the key important adverse drug reaction – for comprehensive information on cautions, contra-indications and interactions. Please refer to the current British National Formulary and Summary of Product Characteristics.

Adverse Effects	**Symptoms/Signs**	**Actions**
For donepezil, galantamine and rivastigmine: Common side effects include: diarrhoea, muscle cramps, fatigue, nausea, vomiting, headache and insomnia. Caution in: supraventricular conduction abnormalities, particularly bradyarrythymias; gastric ulcers or people on NSAIDs; seizures; asthma or COPD; people on cholinergic agonists; people on beta blockers.	Severe and/or persistent common side effects that outweigh benefits of treatment should prompt consideration regarding discontinuation. New or worsening cardiovascular symptoms (if they occur are usually secondary to bradycardia), e.g. dizziness, syncope. Exacerbation of COPD/asthma/epilepsy/peptic ulcer disease associated with starting these drugs should prompt review.	Discontinue if side effects severe, otherwise discuss with Old Age Psychiatry, Learning Disability Psychiatry or Neurology regarding appropriate action. For symptoms suggestive of cardiovascular side effects examine cardiovascular system and consider ECG.

For memantine: Side effects: dizziness, headache, constipation, somnolence, hypertension.	Severe and/or persistent common side effects that outweigh benefits of treatment should prompt consideration regarding discontinuation.	Discontinue if side effects severe, otherwise discuss with Old Age Psychiatry, Learning Disability Psychiatry or Neurology regarding appropriate action.

SHARED CARE

This shared care guideline is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibilities for each party. The intention to shared care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use.

CONSULTANT

1. Ensure that the patient/carer is an informed recipient in therapy. For patients who lack capacity to consent to treatment a decision should be made in the patients best interests in line with Mental Capacity Act guidance.
2. Take account of the patient's medical history / comorbid conditions that may impact on prescribing Acetylcholinesterase inhibitors or Memantine.
3. With regard to Acetylcholinesterase inhibitors, aim to prescribe the drug with the lowest acquisition cost unless there is a clinical reason to prescribe an alternative drug / formulation.
4. Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate).
5. Ensure baseline investigations are normal before commencing treatment. Initiate treatment or advise the GP on the initiation of treatment, as appropriate.
6. Send letter/results notification to the GP after each clinic attendance ensuring current dose stated.
7. Evaluation of any reported adverse effects by GP or patient.
8. Advise GP on review, duration or discontinuation of treatment where necessary.
9. Inform GP of patients who do not attend clinic appointments.
10. Document assessment, management plan and treatment in the patient notes and inform the GP.
11. Ensure that all patients on combination treatment (Memantine and AcetylCholinesterase inhibitor) are reviewed within three months.

GENERAL PRACTITIONER

1. Reinforce the patient's understanding of the nature, effect and potential side effects of the drug before prescribing it as part of the shared care programme and contact the specialist for clarification where appropriate.
2. Report any adverse events to the consultant, where appropriate.
3. Report any adverse events to the Committee on Safety of Medicines via the Yellow Card system, where appropriate.
4. Help in monitoring the progression of disease.
5. Prescribe the drug treatment as described.
6. Carry out annual reviews for those patients no longer under specialist care

CCG

1. To provide feedback to Trusts via Trust Medicines Committees.
2. To support GPs in making decisions on whether or not to accept clinical responsibility for prescribing.
3. To support Trusts in resolving issues that may arise as a result of shared care.

PATIENT/CARER

1. Report any adverse effects to their GP and/or specialist.
2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist.
4. Alert GP and/or specialist of any changes of circumstance which could affect management of disease.
5. Take/administer the medication as prescribed.
6. Undertake any monitoring as requested by the GP and/or specialist.

RESOURCES AVAILABLE

BHRUT switchboard (request the initiating consultant or a member of the clinical team caring for the patient)	01708 435 000
NELFT switchboard (requesting the initiating consultant)	03005551200
Memory Services	
Redbridge	0300 555 1179 Dr David Hinchcliffe – 07713 164801
Havering	0300 555 1135 x66700 Dr Amber Selwood – 07725 218681 Dr Janet Carter – 07725 218680 Dr Sima Shende – 07424 739647 Dr Jo Rodda – 07718 118138
Barking and Dagenham	0300 555 1016 Dr Hilary Kinsler -07939 251345 Dr Mike Devine – 07939 569812 Dr Mohan Bhatt – 07713 094797
Waltham Forest	03005551279 Dr. Samir Shah 07976605854
Learning Disabilities	
Redbridge	020 8708 7018 Dr Rehana Akhter – 07899 053691
Havering	01708 433446 Dr Bini Thomas – 07950 906088
Barking and Dagenham	020 8227 5434 Dr Shaun Gravestock - 0774142 71999
Waltham Forest	Dr Afia Ali and Dr Boni Iparragirre 020 8521 0337

REFERENCES

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- British National Formulary edition 68 (September 2014 – March 2015)
- Refer to the NHS Barking, Havering and Redbridge CCG website to obtain the latest version of this guideline
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Guideline adapted from *NHS ONEL and NELFT Shared Care Guidelines for management of medication for Alzheimer's disease* by: Elsy Gomez Campos (Pharmacist), Stuart Hill (Pharmacist) and Dr Alberto Cifelli (Consultant Neurologist), Dr Jo Rodda (Consultant Old age Psychiatrist), Dr Janet Carter (Consultant Old Age Psychiatrist), Dr Stephen O'Connor (Consultant Old Age Psychiatrist) Final amendments made March 2016 following APC review.

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