South West Yorkshire Partnership NHS Foundation Trust

Barnsley Hospital NHS Foundation Trust

Barnsley Clinical Commissioning Group

Donepezil, Galantamine, Rivastigmine and Memantine
Shared Care Guideline for Dementia

Introduction

Indication/Licensing information (NICE Guidance TAG 217[1])
The three acetylcholinesterase (AChE) inhibitors **donepezil, galantamine and rivastigmine** are recommended as options for managing mild to moderate Alzheimer's disease. **Rivastigmine** is also licensed for Lewy Body and Parkinson's Dementia

Memantine is recommended as an option for managing Alzheimer's disease for people with:

- Moderate Alzheimer's disease who are intolerant of or have a contraindication to AChE inhibitors
- Severe Alzheimer's disease.

Treatment should be 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 older people) should initiate treatment. Carers' views on the patient's condition at baseline should be sought.

NICE Guidance 2016 update 1.6.2.3: Prescribers should only start treatment with donepezil, galantamine, rivastigmine or memantine on the advice of a clinician who has the necessary knowledge and skills. These could include secondary care medical specialists (eg psychiatrists, geriatricians and neurologists) and other healthcare professionals (eg GPs, nurse consultants and advanced nurse practitioners with specialist expertise in diagnosing and treating AD).

Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms.

Patients who continue on treatment should be reviewed regularly using cognitive, global, functional and behavioural assessment. Treatment should be reviewed by an appropriate specialist team, unless there are locally agreed protocols for shared care. Carers' views on the patient's condition at follow-up should be sought.

Dosage, administration, treatment duration and storage

Donepezil initially 5 mg once daily at bedtime, increased if necessary after one month to max. 10 mg daily

Galantamine initially 4 mg twice daily for 4 weeks increased to 8 mg twice daily for 4 weeks; maintenance 8–12 mg twice daily

Rivastigmine (oral) Initially 1.5 mg twice daily, increased in steps of 1.5 mg twice daily at intervals of at least 2 weeks according to response and tolerance; usual range 3–6 mg twice daily; max. 6 mg twice daily

Rivastigmine (patches) Initially apply 4.6 mg/24 hours patch to clean, dry, non-hairy, non-irritated skin on back, upper arm, or chest, removing after 24 hours and siting a replacement patch on a different area (avoid using the same area for 14 days); if well tolerated increase to 9.5 mg/24 hours patch daily after no less than 4 weeks; if patch not applied for more than several days, treatment should be restarted with 4.6 mg/24 hours patch
Note:*When switching a patient from oral to transdermal therapy, patients taking 3–6 mg daily should be prescribed the 4.6 mg/24 hours patch; patients taking 9 mg daily who do not tolerate the dose well should be prescribed the 4.6 mg/24 hours patch, while those taking 9 mg daily who tolerate the dose well should be prescribed the 9.5 mg/24 hours patch; patients taking 12 mg daily should be prescribed the 9.5 mg/24 hours patch. The first patch should be applied on the day following the last oral dose.*

Memantine (oral) Initially 5 mg once daily, increased in steps of 5 mg at weekly intervals to max. 20 mg daily (this is determined by creatinine clearance tests)

Responsibilities of the specialist initiating treatment

Summary

- To assess the suitability of the patient for treatment. Confirm that dementia is due to Alzheimer's Disease (using standard diagnostic criteria).
- To discuss the benefits and side effects of treatment with the patient/carer and the need for long term monitoring if applicable.
- To perform baseline tests and if appropriate routine tests until the patient is stable.
- To ensure there are no interactions with any other medications initiated in primary care.
- To prescribe for the first 12 weeks of treatment or for longer until patient is on a stable dose with clear benefits
- To ask the GP whether they are willing to participate in shared care.
- To provide the GP with a summary of information relating to the individual patient to support the GP in undertaking shared care (See Shared care request form in Appendix A).
- To provide the GP with details of who their dementia advisers are (each surgery has named designated senior dementia adviser and support worker). The role of the senior dementia adviser is to provide clinical advice or information within primary care. The role of the support worker/dementia advisor is to offer support and advice to the patient's carer.
- To advise the GP of any dosage adjustments required, monitoring required, when to refer back, and when and how to stop treatment (if appropriate).
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow card scheme).
- To provide the GP with contact details in case of queries.
- **Patients once stable will be discharged back to primary care. However these patients can be referred back to specialists if there are any problems through rapid access clinics.**

Responsibilities of other prescribers

Acceptance of Responsibility by the Primary Care Clinician
It is optional for GPs to participate in taking on responsibility for shared care for the patient. GPs will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible.
- To prescribe as recommended by the specialist.
- To refer back to the specialist where appropriate. For example:
  - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects.
  - Advice in respect of concordance.
  - Special situations – Behavioural and psychological symptoms of dementia etc

There are no special monitoring requirements for patients on cognitive enhancers. However suggested parameters are identified under section "Routine Monitoring".

Routine Monitoring

Parameter	*By Whom*
Compliance checks	Primary and Secondary care
Adverse effects	Primary and Secondary care
Check for interactions with newly prescribed drugs	Primary and Secondary care

- Discontinue the drug as directed by the specialist if required
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow card scheme).
- To check interactions with newly prescribed medication in primary care

Advice on when to discontinue the medication:

- Patient and/or proxy decision-maker decide to stop
- Patient refuses medication or non-adherence is an insurmountable problem
- No apparent response to therapy
    - Note that this is difficult to judge in practice; evidence shows that patients on treatment do better than those on no treatment, even in some with severe AD
- Intolerable side effects
- Co-morbidities make continued use too risky or futile (eg, terminal illness)
- Dementia is very advanced and terminal care is appropriate
- Withdraw treatment slowly and consider reinstating if deterioration occurs.

Clinical Particulars

BNF therapeutic class	BNF 4.11 Drugs used for Dementia
Cautions and Contraindications	**Contraindications** There are no contraindications listed in the BNF **Cautions** **Donepezil** sick sinus syndrome or other supraventricular conduction abnormalities; susceptibility to peptic ulcers; asthma, chronic obstructive pulmonary disease **Galantamine** cardiac disease (including sick sinus syndrome or other supraventricular conduction abnormalities, unstable angina, congestive heart failure); electrolyte disturbances; susceptibility to peptic ulcers; asthma, chronic obstructive pulmonary disease, pulmonary infection; avoid in urinary retention and gastro-intestinal obstruction; **Rivastigmine** gastric or duodenal ulcers (or susceptibility to ulcers); monitor body-weight; sick sinus syndrome, conduction abnormalities; history of asthma or chronic obstructive pulmonary disease; history of seizures; bladder outflow obstruction; **Memantine** (oral) history of convulsions **Please Note:** If any of the above treatments are interrupted for more than several days, re-introduce with initial dose and increase gradually (see Dose)

Adverse Drug Reactions	**Donepezil** nausea, vomiting, anorexia, diarrhoea; fatigue, insomnia, headache, dizziness, syncope, hallucinations, agitation, aggression; muscle cramps; urinary incontinence; rash, pruritus; *less commonly* gastric and duodenal ulcers, gastro-intestinal haemorrhage, bradycardia, seizures; *rarely* sino-atrial block, AV block, hepatitis, extrapyramidal symptoms; potential for bladder outflow obstruction **Galantamine** nausea, vomiting, diarrhoea, abdominal pain, dyspepsia; syncope; rhinitis; sleep disturbances, dizziness, confusion, depression, headache, fatigue, anorexia, tremor; fever; weight loss; *less commonly* arrhythmias, palpitation, myocardial infarction, cerebrovascular disease, paraesthesia, tinnitus, and leg cramps; *rarely* bradycardia, seizures, hallucinations, agitation, aggression, dehydration, hypokalaemia, and rash; *very rarely* gastro-intestinal bleeding, dysphagia, hypotension, exacerbation of Parkinson's disease, and sweating **Rivastigmine** nausea, vomiting, diarrhoea, dyspepsia, anorexia, abdominal pain; dizziness, headache, drowsiness, tremor, asthenia, malaise, agitation, confusion; sweating; weight loss; *less commonly* gastric or duodenal ulceration, bradycardia, syncope, depression, insomnia; *rarely* angina pectoris, seizures; *very rarely* gastro-intestinal haemorrhage, pancreatitis, cardiac arrhythmias, hypertension, hallucinations, extrapyramidal symptoms (including worsening of Parkinson's disease), and rash; ***Patches:*** application-site reactions. ***Note:***Gastro-intestinal side-effects more common in women **Memantine** (oral) constipation; hypertension; dyspnoea; headache, dizziness, drowsiness; *less commonly* vomiting, thrombosis, heart failure, confusion, fatigue, hallucinations, and abnormal gait; *very rarely* seizures; pancreatitis, psychosis, depression, and suicidal ideation also reported **Pregnancy and Lactation** Not Applicable
Monitoring	No monitoring required with drug other than monitoring of disease progression
Interactions	**Donepezil** possibly antagonises effects of non-depolarising muscle relaxants and possibly enhances effects of suxamethonium. **Galantamine** the plasma concentration of galantamine increased by erythromycin, ketoconazole, paroxetine. Galantamine enhances effects of suxamethonium **Rivastigmine** antagonises effects of non-depolarising muscle relaxants and possibly enhances effects of suxamethonium. **Note:** The effects of parasympathomimetics such as donepezil, galantamine and rivastigmine are antagonised by antimuscarinics. Many drugs have antimuscarinic effects; concomitant use of two or more such drugs can increase side-effects such as dry mouth, urine retention, and constipation; concomitant use can also lead to confusion in the elderly. Interactions do not generally apply to antimuscarinics used by inhalation **Memantine** (oral) increased risk of CNS toxicity when memantine given with amantadine (manufacturer of memantine advises avoid concomitant use) increased risk of CNS toxicity when memantine given with dextromethorphan and or ketamine (manufacturer of memantine advises avoid concomitant use) See notes above regarding antimuscarinic side effects.

Communication

Specialist to GP
The specialist will inform the GP when they have initiated dementia drugs. When the patient is near completing the satisfactory initiation period, the specialist will write to the GP to request they take over prescribing and where possible give an indication as to the expected length of treatment. The Specialist will also send a Shared care request form to support the GP in undertaking shared care. (Appendix A)

GP to specialist
If the GP has concerns over the prescribing of drug dementia drugs, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	Telephone number	Email
Sarah Hudson Lead Pharmacist	01226 644339	Sarah.hudson@swyt.nhs.uk
Medicines Information	01924 327619	Med.Information@swyt.nhs.uk
Dr Kalyan Seelam/ Dr Eve Randall	01226 644250	Kalyan.Seelam@swyt.nhs.uk Eve.Randall@swyt.nhs.uk
Mr Andrew Stones	01226 644250	Andrew.stones@swyt.nhs.uk

References

BNF www.medicinescomplete.org. Accessed on 5/1/16
NICE Guidance www.NICE.org.uk . Accessed on 5/1/16
SPC arricept http://www.medicines.org.uk/emc/medicine/577 Accessed on 5/1/16
SPC rivastigmine http://www.medicines.org.uk/emc/medicine/25361 Accessed on 5/1/16
SPC galatamine http://www.medicines.org.uk/emc/medicine/10335 Accessed on 5/1/16
SPC Memantine http://www.medicines.org.uk/emc/medicine/27720 Accessed on 5/1/16

Development Process

This guidance has been produced by Sarah Hudson, Lead Pharmacist following an AMBER classification status of dementia drugs *by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 8th March 2017 and the LMC on 9th May 2017.*

Appendix A – Shared Care request form (Amber)

- Specialist to complete when requesting GP to enter a shared care arrangement.
- GP to return signed copy of form.
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**GP**): _____

Patient details

Name: _____ ID Number: _____

Address:_____ DOB: _____

Diagnosed condition: _____

ICD Code: _____ GP Read Code:_____

Amber Drug details

Drug name:_____ Dose: _____

Date of initiation: _____ Length of treatment: _____

The patient will be reviewed by the Consultant/Specialist on: _____

The patient should be reviewed by the GP by: _____

Monitoring

The following monitoring should be undertaken by the GP:

Parameter	Date next test due	Frequency

Communication

Consultant:

Telephone number: _____ Fax number:_____

Specialist Nurse

Telephone number: _____ Fax number: _____

Senior Memory Worker:

Telephone number: _____ Fax number:_____

Dementia Advisor:

Telephone number: _____ Fax number: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, Dr ……., can confirm I :

☐ accept the request to participate in shared care for the patient named above.

☐ reject the request to participate in shared care for the patient named above. The reason for this being ……..

GP signature: _____ Date: _____