THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Guideline

For

the prescribing of donepezil, galantamine, rivastigmine and memantine in the management of Alzheimer's disease.

Shared Care Guideline developed by:

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Based on Shared care protocol originally approved in 2011

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Review Date: 3 years from approval

This is guidance to support the management of a condition and not a commissioning arrangement
Shared Care Guideline for the prescribing of donepezil, galantamine, rivastigmine and memantine in the management of Alzheimer’s disease.

Statement of Purpose
This shared care guideline has been written to enable the continuation of care by primary care clinicians of patients initiated with licensed cognitive enhancing drugs by the Sheffield Health and Social Care Foundation Trust (SHSCFT). Primary care will only be requested to take over prescribing of cognitive enhancing drugs within licensed indications, unless specifically detailed otherwise below.

The use of acetylcholinesterase (AChE) inhibitors or memantine for other indications such as the management of behavioural disturbance is beyond the scope of this protocol.

The use of cognitive enhancer medication should be part of a package to support patients with Alzheimer's disease. Non-pharmacological treatment such as social support, increasing assistance with day-to-day activities, information and education, carer support groups, community dementia teams, home nursing and personal care, community services such as meals-on-wheels, befriending services, day centres, respite care and care homes should also be in place as needed as the disease progresses. See below for useful links.

Indication
This guideline only covers the use of donepezil, galantamine, rivastigmine and memantine in patients diagnosed with Alzheimer’s disease and mixed dementia (vascular dementia and Alzheimer's disease). (Note – See Parkinson’s SCP for use in PD dementia complex and dementia with Lewy Bodies).

The three acetylcholinesterase (AChE) inhibitors, donepezil, galantamine and rivastigmine, are recommended as options for managing mild to moderate Alzheimer's disease. 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 or
- severe Alzheimer's disease.

Combinations will not be prescribed as part of a shared care guideline. There is no evidence to support the use of memantine with any of the AChE inhibitors.

Selection of patients
If a GP suspects that a patient is developing significant cognitive impairment they should be referred to Older Adults Secondary Mental Health Services using the Dementia Protocol (to hyperlink once agreed).

If indicated, the specialist services will prescribe the treatment until the patient is considered stable. The GP will be asked to participate in the shared care of stabilised patient, according to this guideline, including prescribing and review of ongoing medication.

Dosage
Details of dosage will be specified by the consultant and will be in line with licensed indications and BNF recommendations.

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Special considerations

**Memantine**

Patients on memantine should have an annual renal function check.

Renal impairment -

- Reduce dose to 10 mg daily if eGFR 30–49 mL/minute/1.73 m², if well tolerated after at least 7 days dose can be increased in steps to 20 mg daily
- Reduce dose to 10 mg daily if eGFR 5–29 mL/minute/1.73 m².
- Avoid/stop if eGFR less than 5 mL/minute/1.73 m².

If prescribing an AChE inhibitor (donepezil, galantamine or rivastigmine), treatment should normally be started with the drug with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started). There is no evidence to support one AChE being more clinically effective than another, however an alternative AChE inhibitor may be prescribed if it is considered appropriate when taking into account adverse event profile, expectations about adherence, medical comorbidity, possibility of drug interactions and dosing profiles. Based on cost donepezil tablets would generally be first line. Other formulations, such as the orodispersible form, or alternative AchE inhibitors should only be used where there is clinical need or due to patient choice. For example; the orodispersable tablet may be used in patients with dysphagia. Alternative AChE inhibitors may be tried if patient unresponsive to donepezil.

See [table](#) for examples of costs (correct at time of publication – Dec 2016)

**Contra-indications**

The details below are not a complete list and the BNF and the SPC remain authoritative

**Applicable to all** - Known hypersensitivity to the active ingredients or any of the excipients.

Donepezil – patients with a known hypersensitivity to piperidine derivatives

Galantamine – Severe hepatic (Child-Pugh score greater than 9) and severe renal impairment (creatinine clearance less than 9 ml/min). Galantamine is contraindicated in patients who have both significant renal and hepatic dysfunction. BNF Avoid if eGFR less than 9 mL/minute/1.73 m².

Rivastigmine – Hypersensitivity to other carbamate derivatives. Previous history of application site reactions suggestive of allergic contact dermatitis with rivastigmine patch.

Memantine – See special considerations above.

**Side –effects and Precautions**

The details below are not a complete list and the BNF and the SPC remain authoritative

**Acetylcholinesterase inhibitors**

**Side effects**

Common: diarrhoea, muscle cramps, fatigue, nausea, vomiting, insomnia.

Rarely reported: syncope, bradycardia, sinoatrial block, atrioventricular block, psychiatric disturbances.

**Precautions**

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Anaesthesia, cardiac conduction problems, bladder outflow obstruction, seizures, asthma or obstructive pulmonary disease.

**Memantine**

**Side effects**
Hypersensitivity, Hypertension, hallucinations, confusion, dizziness, balance disorders, somnolence, dyspnea, constipation, raised LFTs, headache and tiredness

**Precautions**
Epilepsy, sudden change to a vegetarian diet, recent myocardial infarction, uncompensated congestive heart failure. See above re renal impairment.

**Monitoring**

Following a 6 month trial of treatment the Memory Services will review the efficacy and tolerance to the AChE inhibitor. Those who are benefiting from treatment will be assessed for future care pathway management taking into account the needs, complexity and existing support of each patient. Three broad aftercare pathways have been defined and agreed with NHS Sheffield:

- **Level 1** - Patient assessed to have minimal need. Patient and carer given contact information (see appendix) and patient put on Memory Service case register. Patients will not routinely be seen unless specifically requested by patient/carer or third party (e.g. GP, social worker, voluntary sector)
- **Level 2** - Patient assessed to have low level needs. Patient monitored by Memory Service via patient / carer telephone contact and, where available, via SystmOne.
- **Level 3** - Patients assessed as having active mental health needs and are seen by Memory Service or another Mental Health team.

Patients managed at levels 1 and 2 will require an annual medication review in primary care.

When considering benefits of treatment cognitive, functional and behavioral symptoms should be taken into account as well as considering side effects and interactions with other medicines. Treatment should be continued only when it is considered to be having a worthwhile effect. Consider factors such as life expectancy and discuss treatment goals / benefits / side effects with the patient / carer. If at the review by the GP it is felt there is no longer a worthwhile effect of continuing, or tolerance / adherence is a concern, the GP can consider discontinuation of treatment. If needed, advice can be sought from the specialist service, contact details below. Wherever possible ensure patient, carers and relatives are all involved in decision making.

As well as tolerance / side effects to current cognitive medication the impact of other medication should also form part of the annual review. Examples of medication that may affective cognitive functioning are;

- Antipsychotics
- Anticholinergic medication (See link – consider prescribed and OTC)
- Diuretics – watch for electrolyte disturbance
- Benzodiazepines
- Opioids (consider prescribed and OTC)
- Dopaminergic medication has been reported to enhance and reduce cognitive impairment – discuss with PD specialist

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The GP should inform the specialist services of significant side effects, such as:
- Bradycardia
- Acute asthmatic exacerbations
- Persistent new gastrointestinal symptom, particularly bleeding e.g. melaena

Bradycardia and acute asthmatic exacerbations would be reasons to discontinue treatment.

Patients on memantine should have an annual renal function checked (see advise under dosage).

If the specialist is to discontinue treatment the GP should be informed in timely manner.

**Interactions**
The details below are not a complete list and the current BNF and the SPC remain authoritative.

*Common to all Acetylcholinesterase inhibitors*
Antimuscarinic drugs, neuromuscular blocking agents, cholinergic drugs, beta blocking agents

*Galantamine*
Paroxetine, ketoconazole, erythromycin (plasma concentration of galantamine increased with concomitant use). Galantamine should not be given concomitantly with other cholinomimetics (such as donepezil, neostigmine, pyridostigmine or rivastigmine).

*Rivastigmine*
Rivastigmine should not be given concomitantly with other cholinomimetic substances and rivastigmine might interfere with the activity of anticholinergic medicinal products (e.g. oxybutynin, tolterodine).

*Memantinede*
Amantadine, ketamine and dextromethorphan (avoid concomitant use). L-dopa, dopamine agonists, anticholinergics (effects of these may be enhanced).
Barbiturates and neuroleptics (effects of these may be reduced).
Cimetidine, ranitidine, procainamide, quinine and nicotine (potential risk of increased levels of either drug).
Warfarin - enhance effect possible, closer monitoring of INR advisable.
Baclofen and dantrolene – effects of these may be modified.

**Responsibilities of secondary care service**
- To confirm diagnosis, initiate and stabilise on treatment, initiating acetylcholinesterase inhibitors or memantine in appropriate patients
- To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent. This is particularly important for off label use of products.
- Carry out a cardiac assessment, which may involve carrying out an ECG
- To report any adverse reaction to the CHM– See yellow card.
- To prescribe the first month’s supply or until dose is stable
- To contact patient’s GP to request prescribing under shared care and send a link to or copy of the shared care guideline.
- To advise the GP regarding continuation of treatment, including the length of treatment. Discuss with patient and carers that the benefits of the

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medication will be reviewed over time and there may be a point when the medication will be of no further benefit
- To conduct reviews to assess efficacy and tolerance; and once stabilised to determine and follow case management pathways.
- To discuss any concerns with the GP regarding the patient’s therapy
- The patient to remain under the consultants care whilst ever the patient is being prescribed any medication within this guide (unless individual arrangements agreed).

**Responsibilities of the primary care clinician**
- To refer appropriate patients to secondary care for assessment
- To agree to prescribe for patients in line with the shared care guideline
- To report any adverse reaction to the CHM and the referring consultant – See yellow card.
- To continue to prescribe for the patient as advised by the consultant
- To inform the consultant if the patient discontinues treatment for any reason
- To seek the advice of the consultant / specialist if any concerns with the patient’s therapy
- To conduct an annual face to face medication review or more frequent if required.
- In the event that the GP is not able to prescribe, or where shared care is agreed but the consultant is still prescribing certain items e.g. Hospital only product; the GP will provide the consultant with full details of existing therapy promptly by fax on request.
- For medication supplied from another provider GPs are advised to follow recommendations for Recording Specialist Issued Drugs on Clinical Practice Systems: [http://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/Practice%20resources%20and%20PGDs/Recording_SIDs_on_practice_clinical_systems%20.pdf](http://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/Practice%20resources%20and%20PGDs/Recording_SIDs_on_practice_clinical_systems%20.pdf)

**Responsibilities of Patient / carer**
To report any concern in treatment to GP / specialist
Attend agreed appointments

**Re-Referral guidelines**
All patients will be on the case register at the Memory Service, if there are any concerns at any point regarding treatment / patient or carer safety then the service can be contacted for advice or possible intervention.

**Financial implications**
The table below lists the current (December 2016) costs of preparations if prescribed generically. Wherever clinically appropriate, donepezil tablets should be considered first line. If galantamine, rivastigmine or memantine are prescribed, then prescribers are encouraged to use the most cost effective preparation of the appropriate formulation indicated.

<table>
<thead>
<tr>
<th>Medication / formulation / strength</th>
<th>Cost/28 days treatment (from December 2016 Drug tariff)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil 5mg/10mg tablets</td>
<td>£1.04 /£1.54</td>
</tr>
<tr>
<td>Donepezil 5mg/10mg orodispersible tablets S/F</td>
<td>£6.39/£8.15</td>
</tr>
<tr>
<td>Donepezil 1mg/ml oral solution (S/F)</td>
<td>£48.00/150ml (based on a 5mg dose)</td>
</tr>
<tr>
<td>Galantamine 8mg /12mg tablets</td>
<td>£61.13/£74.10 / 56 (based on BD dosing)</td>
</tr>
<tr>
<td>Galantamine 8mg/16mg/24mg MR</td>
<td>£51.88/£64.90/£79.80</td>
</tr>
</tbody>
</table>

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Ordering information
All medication listed in this guideline are licensed preparations available from all main wholesalers.

Support, education and information
Consultants in Old Age Psychiatry are contactable via Sheffield Health and Social Care Trust switchboard Tel: 0114 271 6310

Main memory clinic number: 0114 2716015
Sheffield Health and Social Care Trust Pharmacy department. Tel: 0114 271 8630

Other useful resources;
- Age UK
- Alzheimer’s Society
- Sheffield Mind
- Sheffield Dementia Information pack
- Age better in Sheffield
- Samaritans
- Safe guarding
- Mental capacity
- Sheffield Carers
- Diagnosing dementia in Care homes
- Dementia Friends

References
NICE technology appraisal guidance TA217 - Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer’s disease

NICE CG 42 - Dementia: supporting people with dementia and their carers in health and social care

Electronic BNF

Electronic Medicines Compendium (EMC)

Quality and Outcomes Framework -
The Sheffield Memory Service is currently reviewing the service it provides to make the experience more user friendly.

We currently find that people would prefer to attend the service for follow up appointments when they are experiencing changes or difficulties to their memory, and/or, their day to day activities of daily living skills, rather than attend when all is well.

To ensure that you receive the service when you want and need it we are planning on providing appointments at your request, rather than sending you routine follow up appointments.

Your next appointment was due in the next 2 – 6 weeks, however, we will be relying on you to contact us if you need to be seen. Again, to reiterate, we feel that this service will offer you access when you need it.

We would like to reassure you that this does not mean that you have been discharged from our service. You will continue to remain with our service and we will send you a bi-monthly news letter and information of drop in sessions and events that we are running.

Should you, at any time, wish to speak with a nurse you can call our

Nurse Help Line on 0114 2718585
(the help line is open 0900-1100hrs and 1300-1500hrs Monday to Friday)

or e mail us on
sheffmemoryservice@shsc.nhs.uk

We would be happy to hear your thoughts or concerns on this new way of providing a service which is bespoke to your needs.

Yours sincerely

This is guidance to support the management of a condition and not a commissioning arrangement
Dear  

The Sheffield Memory Service is currently reviewing the service it provides to make the experience more user friendly.

We currently find that people would prefer to attend the service for follow up appointments when they are experiencing changes or difficulties with their memory, and/or, their day to day activities of daily living skills, rather than attend when all is well.
To ensure that you receive the service when you or your relative want and need it we are planning on providing appointments at your request, rather than sending out routine follow up appointments.

Your relatives next appointment was due in the next 2 – 6 weeks, however, we will be relying on you or your relative to contact us if you need support or advice. Again, to reiterate, we feel that this service will offer you access when you need it.

We would like to reassure you that this does not mean that your relative has been discharged from our service. They will continue to remain with our service and we will send a monthly newsletter and information of drop in sessions and events that we are running.

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