

Somerset Healthcare Community Shared Care Protocol for the use of **Acetylcholinesterase Inhibitors or Memantine in the Management of Alzheimer's Disease**



This shared care protocol (SCP) sets out details for the sharing of care for patients prescribed any of the following drugs in the management of

Disease – donepezil, rivastigmine, galantamine or memantine. It should be read in conjunction with the latest Summary of Products Characteristics (SPC) available for each drug at <http://www.medicines.org.uk/emc/>

As outlined in NHS England Guidance 2018 (07573), 'Responsibility for Prescribing Between Primary, Secondary and Tertiary Care.' When a consultant considers a patients' condition is stable or predictable he/she may seek the agreement of the patients and their GP to "share" the patients' care. This document provides information on drug treatment for the shared commitment between the consultant and GP concerned. GPs are invited to participate. If the GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. The doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

N.B. If the GP decides not to participate in shared care for a particular patient, they must inform the relevant specialist in writing, within 2 weeks of receipt of a request to share care.

Introduction

This shared care guideline sets out details to support the transfer of responsibility for prescribing acetylcholinesterase inhibitors or memantine from secondary to primary care.

It is intended to apply to patients who have been initiated on treatment, (and who have been assessed as benefiting) by secondary care services experienced in the care of people with dementia in accordance with the guidance from the National Institute for Health & Clinical Excellence.

In Somerset, GPs should refer appropriate patients to the Somerset Partnership old age psychiatry service for assessment within a specialist service. Where indicated, treatment should be initiated in secondary care. Secondary care services should continue to prescribe for the first three months while response is assessed. In referring patients, GPs should be willing to continue prescribing after the first three months, as part of a shared care arrangement, for those patients who have been assessed as benefiting.

A separate protocol is required for those in primary care who wish to initiate the medication themselves.

Drug treatment for Alzheimer's disease should form part of a wider package of support and information for the patient and their carer.

Treatment with an acetylcholinesterase inhibitor or memantine should only be initiated if reasonable steps are taken to ensure adequate compliance.

For further information please click on the links below or visit;

[British National Formulary](http://www.medicines.org.uk/emc/)

<http://www.medicines.org.uk/emc/>

[NICE TA217](#) and [NICE NG97](#) Recommended Indications:

Acetylcholinesterase Inhibitor Monotherapy

Cognitive Symptoms of Alzheimer's Disease

Donepezil, Rivastigmine and Galantamine are recommended as options in the management of the cognitive symptoms of Alzheimer's disease of mild to moderate severity.

Acetylcholinesterase inhibitors are not recommended for patients who have vascular dementia.

For people who are not taking an AChE inhibitor or memantine, prescribers should only start treatment on the advice of a clinician who has the necessary knowledge and skills.

Acetylcholinesterase Inhibitors in the management of Cognitive Symptoms of non-Alzheimer's Dementia

Dementia with Lewy Bodies

- Offer donepezil or rivastigmine to people with mild to moderate dementia with Lewy bodies.
- Only consider galantamine for people with mild to moderate dementia with Lewy bodies if donepezil and rivastigmine are not tolerated.
- Consider donepezil or rivastigmine for people with severe dementia with Lewy bodies.

Parkinson's Disease Dementia

- Offer a cholinesterase inhibitor for people with mild or moderate Parkinson's disease dementia.
- Consider a cholinesterase inhibitor for people with severe Parkinson's disease dementia.

Vascular Dementia

- Only consider AChE inhibitors or memantine for people with vascular dementia if they have suspected comorbid Alzheimer's disease, Parkinson's disease dementia or dementia with Lewy bodies.

Frontotemporal Dementia

- **Do not** offer AChE inhibitors or memantine to people with frontotemporal dementia

Cognitive impairment caused by multiple sclerosis

- **Do not** offer AChE inhibitors or memantine to people with cognitive impairment caused by multiple sclerosis.

Memantine Monotherapy

Managing Cognitive Symptoms of Alzheimer's Disease

Memantine is recommended as an option for:

- managing moderate Alzheimer's disease in patients who are intolerant of or, have a contra-indication to acetylcholinesterase inhibitors.
- managing severe Alzheimer's disease

Memantine in the management of Cognitive Symptoms of non-Alzheimer's Dementia

Dementia with Lewy Bodies

- Consider memantine for people with dementia with Lewy bodies if AChE inhibitors are not tolerated or are contraindicated.

Parkinson's Disease Dementia

- Consider memantine for people with Parkinson's disease dementia, only if cholinesterase inhibitors are not tolerated or are contraindicated.

Vascular Dementia

- Only consider AChE inhibitors or memantine for people with vascular dementia if they have suspected comorbid Alzheimer's disease, Parkinson's disease dementia or dementia with Lewy bodies.

Frontotemporal Dementia

- **Do not** offer AChE inhibitors or memantine to people with frontotemporal dementia

Cognitive impairment caused by multiple sclerosis

- Do not offer AChE inhibitors or memantine to people with cognitive impairment caused by multiple sclerosis.

Combined Acetylcholinesterase Inhibitor and Memantine Therapy

For people with an established diagnosis of Alzheimer's disease who are already taking an AChE inhibitor:

- consider memantine in addition to an AChE inhibitor if they have moderate disease
- offer memantine in addition to an AChE inhibitor if they have severe disease.

For people with an established diagnosis of Alzheimer's disease who are already taking an AChE inhibitor, primary care prescribers may start treatment with memantine without taking advice from a specialist clinician.

Do not stop AChE inhibitors in people with Alzheimer's disease because of disease severity alone.

Dose (posology & method of administration): see individual SPCs at <http://www.medicines.org.uk/emc/>

Please refer to the individual manufacturers summaries of product characteristics for full prescribing information on dose, including dose in impaired renal function. Only licensed doses should be used.

Rivastigmine patches should be reserved for patients with a particular clinical need

Contra-indications: see individual SPCs for detail at <http://www.medicines.org.uk/emc/>

The summaries of product characteristics include the following contra-indications:

- patients with hypersensitivity to Donepezil (or piperidine derivatives), Rivastigmine (or carbamate derivatives), Galantamine or the excipients and Memantine or excipients
- Galantamine is contra-indicated in patients with severe renal and/or hepatic impairment.

Special warnings and precautions for use: see individual SPCs at <http://www.medicines.org.uk/emc/>

Acetylcholinesterase inhibitors should be given with caution in:

- cardiovascular conditions - the potential for vagotonic actions may be particularly important for patients with "sick sinus syndrome," patients with conduction defects, those who take drugs that significantly.
- reduced heart rate, or those who have uncorrected electrolyte imbalance.
- gastrointestinal conditions - patients at increased risk of developing ulcers should be monitored for symptoms.
- neurological conditions - the drugs are believed to have some potential to cause generalised convulsions (seizure activity may also be a manifestation of Alzheimer's disease).
- patients with a history of asthma or obstructive pulmonary disease.
- patients with urinary outflow obstruction or recovering from bladder surgery.
- consult individual SPCs for renal and hepatic impairment.

Memantine should be given with caution in:

- patients who have a history of epilepsy.
- avoid in severe hepatic impairment as no information available.
- in 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 if eGFR less than 5 mL/minute/1.73 m²
- patients where a rise in urinary pH due to drastic changes in diet, e.g. from a carnivore to a vegetarian diet, a massive ingestion of alkalisating gastric buffers, renal tubular acidosis (RTA) or severe infections of the urinary tract with *Proteus* bacteria.
- patients with recent myocardial infarction, uncompensated congestive heart failure (NYHA III-IV), or uncontrolled hypertension as only limited data are available on use in these groups so patients with these conditions should be closely supervised.

Drug interactions: see individual SPCs for full details at <http://www.medicines.org.uk/emc/>

Acetylcholinesterase inhibitors

- Acetylcholinesterase inhibitors should not be administered with anticholinergic medication due to the antagonism of effect. When the patient is taking a drug with anticholinergic properties (e.g. antipsychotics, tricyclics) the relative benefits of taking acetylcholinesterase inhibitors alongside these should be assessed.
- Acetylcholinesterase inhibitors are likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia.
- The summary of product characteristics for **rivastigmine** states: Additive effects leading to bradycardia (which may result in syncope) have been reported with the combined use of various beta-blockers (including atenolol) and rivastigmine. Cardiovascular beta-blockers are expected to be associated with the greatest risk, but reports have also been received in patients using other beta-blockers. Therefore, caution should be exercised when rivastigmine is combined with beta-blockers and also other bradycardia agents (e.g. class III antiarrhythmic agents, calcium channel antagonists, digitalis glycoside, pilocarpin).
- The summary of product characteristics for **rivastigmine** states Since bradycardia constitutes a risk factor in the occurrence of torsades de pointes, the combination of rivastigmine with torsades de pointes-inducing medicinal products such as antipsychotics i.e. some phenothiazines (chlorpromazine, levomepromazine), benzamides (sulpiride, sultopride, amisulpride, tiapride, veralipride), pimozide, haloperidol, droperidol, cisapride, citalopram, diphemanil, erythromycin IV, halofantrin, mizolastin, methadone, pentamidine and moxifloxacin should be observed with caution and clinical monitoring (ECG) may also be required

- The summary of product characteristics for Galantamine states that during initiation of treatment with potent inhibitors of CYP2D6 (e.g. quinidine, paroxetine, fluoxetine or fluvoxamine) or CYP3A4 (e.g. ketoconazole, ritonavir), patients may experience an increased incidence of cholinergic side-effects, mainly nausea and vomiting and a reduction in the dose of the acetylcholinesterase inhibitor may be considered.
- The summary of product characteristics for donepezil states that drug interaction studies performed in vitro show that ketoconazole and quinidine inhibit donepezil metabolism. Other drugs that could also inhibit the metabolism of donepezil are itraconazole, erythromycin and fluoxetine. Enzyme inducers such as rifampicin, phenytoin, carbamazepine and alcohol may reduce the levels of donepezil.

Memantine

- Memantine should **not** be prescribed for patients taking N-methyl-D-aspartate (NMDA)-antagonists such as amantadine, ketamine or dextromethorphan. These compounds act at the same receptor sites as memantine, and therefore adverse drug reactions (mainly CNS-related) may be more frequent or more pronounced.
- The mode of action suggests that the effects of L-dopa, dopaminergic agonists, and anticholinergics may be enhanced by concomitant treatment with NMDA-antagonists such as memantine. The effects of barbiturates and neuroleptics may be reduced. Concomitant administration of memantine with the antispasmodic agents, dantrolene or baclofen, can modify their effects and a dosage adjustment may be necessary.
- Other active substances such as cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine that use the same renal cationic transport system as amantadine may also possibly interact with memantine leading to a potential risk of increased plasma levels.

Pregnancy and lactation: see individual SPCs for full details at <http://www.medicines.org.uk/emc/>

- Very limited data are available- consult specialist.

Adverse effects: see individual SPCs at <http://www.medicines.org.uk/emc/>

Acetylcholinesterase inhibitors

- The most common adverse effects include diarrhoea, nausea, vomiting, muscle cramps, dyspepsia, fatigue, insomnia, anorexia, weight loss, dizziness, headache and somnolence.
- Other side-effects include confusion, fall, injury, syncope, upper respiratory tract infection and urinary tract infection.
- Weight loss is also associated with Alzheimer's disease itself and therefore patients' weight should be monitored during therapy (if clinically appropriate).

Memantine

- The most common adverse effects include constipation; hypertension; dyspnoea; headache, dizziness, drowsiness Other side-effects include vomiting, thrombosis, heart failure, confusion, fatigue, hallucinations, and abnormal gait and very rarely seizures, pancreatitis, psychosis, depression, and suicidal ideation.

Shared Care Responsibilities

Responsibilities of Old Age Psychiatry Service

1. Diagnosis of probable or possible Alzheimer's disease (excluding other forms of dementia) and any appropriate assessments required.
2. Ensure that the patient has access (if needed) to care and support through the multidisciplinary team.
3. Assess the patient's suitability for acetylcholinesterase inhibitor or memantine therapy as defined by NICE guidelines.
4. Ensure patient/carer understands what the drug is, and why it has been prescribed
5. Ensure patient/carer understands how and when it should be given, and any potential side-effects
6. Either provide the first prescription or, ask the GP to prescribe. NICE guidance states that once a decision has been made to start an AChE inhibitor or memantine, the first prescription may be made in primary care.
7. Assess the patient during the first three months.
8. Assess the patient after three months and approach the GP with regard to continued prescribing if treatment is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms.
9. Discontinue treatment after 3 months where there has not been benefit or where there has been a deterioration of the condition.
10. When treatment is to be continued after 3 months, to undertake regular reviews (every 6-12 months) as clinically appropriate to assess ongoing benefit.
11. If discontinuing treatment, care should be taken to phase out the medication gradually and monitor for a potentially significant deterioration of patient functioning or a worsening of behavioural symptoms.
12. Treatment should be discontinued if the drug becomes unsuitable e.g. due to side-effects, inter-current illness or compliance issues.

General Practitioner responsibilities

1. It is recommended good practice for there to be a pre-referral assessment including physical examination and baseline blood tests (FBC, U&E's, LFT's, glucose, TFT's, B12, folate and calcium) in accordance with the "Dementia assessment pathway" for primary care.
2. To refer appropriate patients to Somerset Partnership Old Age Psychiatry services.
3. To reinforce educational points in 2 and 3 above.
4. To prescribe an acetylcholinesterase inhibitor and/ or memantine for those patients who the psychiatrists believe would benefit from treatment. NICE guidance now states that the first prescription can be made in primary care. It is recommended that there should be consultation with the responsible Old Age Psychiatrist before discontinuation of an established acetylcholinesterase inhibitor or memantine.
5. To undertake any necessary monitoring including weight, as agreed with the Old Age Psychiatry service.

6. To consider any side-effects reported by the patient and to discuss with the old age psychiatry department if necessary.
7. To undertake any necessary monitoring including weight, as agreed with the Old Age Psychiatry service.

Patient/carer responsibilities

To report any significant signs or symptoms relating to their condition, including side effects, to the GP or member of the Old Age Psychiatry team.

Further support

- Medicines Information department, Musgrove Park Hospital: 01823 342253
- Medicines Information department, Yeovil District Hospital: 01935 384327
- Prescribing & Medicines Management Team, NHS Somerset: 01935 384123
- Medicines Management Team, Somerset Partnership: 01823 368265

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Approved by:	Somerset Prescribing Forum, NHS Somerset	
	Drug & Therapeutics Committee, Taunton & Somerset NHS FT	
	Drug & Therapeutics Committee, Yeovil and District NHS FT	
	Medicines in clinical practice Committee, Somerset Partnership NHS FT	
Review required by:		Sept 2021

References

[NICE Guidance NG97](#) - Dementia: assessment, management and support for people living with dementia and their carers

[NICE TA217](#) - Donepezil, galantamine, rivastigmine and memantine in the management of Alzheimer's disease

Summaries of Product Characteristics at (accessed August -18): <http://www.medicines.org.uk/emc/>

[British National Formulary No. 74 \(March 2018\)](#)