Dementia Care Pathway: Guidance for prescribing acetylcholinesterase inhibitors and memantine

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1st Line Treatment – Donepezil

Mild / Moderate Alzheimer's Disease

Donepezil tablets 5mg daily

1 month (weeks 1 to 4)

Not tolerating → **2nd line treatment**

Donepezil tablets 10mg daily

Unable to tolerate higher dose → **Donepezil tablets 5mg daily**

2 months (weeks 5 to 12)

Review at week 8

Oro-dispersible tablets are recommended for those who are secreting tablets, require supervised administration or have swallowing difficulties where donepezil is effective and tolerated; and should be considered ahead of rivastigmine patches.

Prescribing Guidance – see NICE

- All 3 Acetylcholinesterase Inhibitors (AChEI) have broadly similar clinical effects. Treatment should usually be initiated using the drug with the lowest acquisition cost
- An alternative AChEI could 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
- No important differences between drugs in respect of type or frequency of adverse effects. Due to excess cholinergic stimulation (nausea, vomiting, diarrhoea, insomnia), most likely to occur at start of treatment and when dose is increased. See Dementia Care Pathway (link) for monitoring requirements at initiation and during titration. Risk of drug interactions also needs to be considered. Due to AChEI mode of action can increase anticholinergic burden (see Frailty CLiP)

Prescribing responsibilities:

- For people who are not taking an AChEI or memantine, prescribers should only start treatment with these on the advice of a clinician who has the necessary knowledge and skills. This could include:
  - secondary care medical specialists such as psychiatrists, geriatricians and neurologists
  - other healthcare professionals (such as GPs, nurse consultants and advanced nurse practitioners), if they have specialist expertise in diagnosing and treating Alzheimer's disease.

Cost effective 2nd line treatment option – Rivastigmine

Mild / moderate Alzheimer's disease

Preferred in: *Parkinson's disease and those prescribed an interacting drug (see overleaf)*
Titrate according to response and tolerance

Rivastigmine capsules 1.5mg twice daily

At least 2 weeks

Rivastigmine capsules 3mg twice Daily

At least 2 weeks — **Unable to tolerate higher dose**

Rivastigmine capsules 4.5mg twice daily

At least 2 weeks — **Unable to tolerate higher dose**

Rivastigmine capsules 6mg twice Daily

From 6 weeks

Review once on a stable, tolerated dose

Patches reserved for *those who are unable to tolerate or swallow an oral AChEI, or those with a significant co-morbidity which increases the risk of side effects from oral preparations*

Rivastigmine patches 4.6mg / 24 hours

1 month (weeks 1 to 4)

Rivastigmine patches 9.5mg / 24hours

2 months (weeks 5 to 12)

Review at week 8

After 6 months on 9.5mg/24 hours if well tolerated and cognitive or functional decline demonstrated increase to 13.3mg / 24 hours

Alternative 2nd line treatment option - Galantamine

Mild / moderate Alzheimer's disease

Galantamine 8 mg daily (MR capsules)

1 month (weeks 1 to 4)

Galantamine 16 mg daily (MR capsules) or **8mg twice daily** (tablets)

1 month (weeks 5 to 8)

Unable to tolerate higher dose

Galantamine 24 mg daily (MR capsules) or **12 mg twice daily** (tablets)

2 months (weeks 9 to 16)

Review at week 12

Galantamine oral solution should only be considered for patients who are secreting tablets, require supervised administration or have swallowing difficulties, and do not tolerate Donepezil orodispersible tablets

3rd line treatment – Memantine

Moderate / severe Alzheimer's disease

Monotherapy for:

- *Moderate Alzheimer's disease unable to take AChEIs*
- *Severe Alzheimer's disease*

Memantine initiation - 4 weeks (5mg daily increased in steps of 5mg every 7 days to 20mg daily). For slower titration prescribe 10mg tablets (scored)

1 month (weeks 1 to 4)

Memantine tablets 20mg per day (or maximum tolerated dose)

Review at week 8

AChEI + memantine combinations for treatment of Alzheimer's disease

- Moderate disease* – consider memantine in addition to AChEI
- Severe disease* – **OFFER** memantine in addition to AChEI

In patients with an established diagnosis of Alzheimer's disease Primary care prescribers may start memantine without taking advice from a specialist clinician.

*See assessment of severity

Switching between drugs:
Failure to benefit from one AChEI does not necessarily mean that a patient will not respond to another. Similarly, poor tolerance of one agent does not rule out good tolerance of another
Intolerance - switching to another agent should be done only after complete resolution of adverse effects following discontinuation of initial agent.
Lack of efficacy – switching can be done overnight with a quicker titration scheme thereafter
Loss of benefit – switching to another AChEI not recommended
See BNF for dose equivalence when switching from oral to transdermal rivastigmine

Lewy Body Dementia (LBD)

Disease severity	1st line treatment	Not tolerated
Mild to moderate	Donepezil* or Rivastigmine*	Galantamine*
Severe	Donepezil* or Rivastigmine*	Memantine*

*unlicensed in Lewy Body Dementia

Parkinson's disease dementia (PDD)
- Mild to Moderate PDD **offer** AChEI (only Rivastigmine licensed)
- Severe PDD consider an AChEI
- Memantine – only consider in PDD if AChEI not tolerated or contra-indicated

Vascular Dementia – Only consider AChEI or memantine if co-morbid Alzheimer's disease, PDD or LDB

***Assessment of severity of Alzheimer's disease:**
In determining the severity of Alzheimer's disease or need for initiation or continuation of treatment the most appropriate method of assessment which takes into account any physical, sensory or learning disabilities, or communication difficulties that could affect the results should be used. Sole reliance on cognition scores in these circumstances would be inappropriate. Services need to ensure equality of access to treatment for patients from different ethnic groups, in particular those from different cultural backgrounds. Explanation of the assessment method used should be included in GP communications. In TEWV Dementia severity links to cluster.

Safe Transfer of Prescribing:
AChEI and memantine are classified as Green + when prescribed as per NICE guidance and can either be recommended by a specialist for initiation in primary care; or be initiated by a specialist and transferred to primary care once the patient is stabilised (as per local commissioning arrangements)
See also Dementia Care Pathway for any additional information to be provided (link).

Assessing the need for continued treatment:
When assessing the severity of Alzheimer's disease and the need for treatment, healthcare professionals should not rely solely on cognition scores in circumstances in which it would be inappropriate to do so. These include:
- if the cognition score is not, or is not by itself, a clinically appropriate tool for assessing the severity of that patient's dementia because of the patient's learning difficulties or other disabilities (for example, sensory impairments), linguistic or other communication difficulties or level of education **or**
- if it is not possible to apply the tool in a language in which the patient is sufficiently fluent for it to be appropriate for assessing the severity of dementia **or**
- if there are other similar reasons why using a cognition score, or the score alone, would be inappropriate for assessing the severity of dementia.

In such cases healthcare professionals should determine the need for initiation or continuation of treatment by using another appropriate method of assessment.

Do not offer AChEI or memantine in frontotemporal dementia or to people with cognitive impairment caused by multiple sclerosis

Drug Interactions
NB list not exhaustive check current BNF

Drug	Plasma levels increased by	Plasma levels decreased by	Pharmacodynamic interaction
Donepezil	Fluoxetine Erythromycin Ketoconazole Itraconazole Quinidine Paroxetine	Carbamazepine Phenytoin Rifampicin Alcohol	Interaction with anticholinergic drugs Potential for synergistic activity with B-blockers
Galantamine	Fluoxetine Fluvoxamine Paroxetine Amitriptyline Erythromycin Ketoconazole Ritonavir Quinidine	None known	Avoid use with anticholinergics Possible interaction with drugs affecting heart rate e.g. digoxin, B-blockers, certain calcium channel blockers and amiodarone
Rivastigmine	Metabolic interactions appear unlikely Smoking tobacco increases clearance of rivastigmine		Avoid use with anticholinergics
Memantine	Warfarin - Isolated cases of INR increase, close monitoring advised. Cimetidine Ranitidine Procainamide Quinidine Quinine Nicotine Trimethoprim	None known	Effects L-dopa, dopaminergic agonists, selegiline and anticholinergics may be enhanced. Effects of antipsychotics and barbiturates may be reduced Dose adjustment may be needed with antispasmodics, dantrolene and baclofen

Patient /Carer Information:

Information about individual medicines is available on the *Choice and Medication* website https://www.choiceandmedication.org/tees-esk-and-wear-valleys/