Dementia Medication Shared Care Guideline (v3 September 2018)

Background

This guideline sets out details for the appropriate prescribing of medicines for dementia ie acetylcholinesterase inhibitors (ACIs) **donepezil**, **galantamine**, **rivastigmine** and/or **memantine**. Relevant prescribing issues are highlighted as far as practical but prescribers should use in conjunction with relevant NICE guidance, the BNF and summary of product characteristics for the most up to date information. This guideline is based on the NICE Technology Appraisal (TA217) and NICE Guideline NG97 June 2018.

A. Memory Assessment Service (Memory Clinic)

Responsibilities of the specialist initiating treatment

- Seek carers views on the patient's condition at baseline
- Advise the patient or carer on benefits and side-effects of treatment
- Ensuring that patient/carer have appropriate information about anti-dementia drug and contact details for responsible service, Community Dementia Nurse (CDN) / Care Home In-Reach Team (CHIRT) or CMHT
- Initiate the first month's treatment and ask the GP if they are willing to participate in shared care
- Regular review by the community specialist nurse team (CDN or Care Home Support Team)
- Advise the GP on when to adjust the dose, stop treatment, or consult with the specialist
- Ensure that clear backup arrangements exist for GPs to obtain advice and support

General Practitioner Responsibilities

- Reply to the request for shared care as soon as possible
- Prescribe and adjust the dose as recommended by the specialist [28 day prescriptions recommended]
- Arrange annual U&Es for patients on memantine to check dose is appropriate for renal function eg at regular review, for QOF or other purposes
- Report adverse events to the specialist team and serious adverse effects to the MHRA www.yellowcard.gov.uk
- Refer back to the specialist where appropriate – this will usually be done by the CDN / CHIT

GP practices will be supported by the relevant specialist team:

Memory Clinic – Memory Clinic Nurses

Primary Care – Community Dementia Nurses and Care Home In-reach Team

Older Peoples Community Mental teams – Community Psychiatric Nurses

Care Home In- reach team – Specialist Nurses

Other prescribers for example geriatric services can access the CDN service for support with any patient with dementia not under the care of secondary care mental health services.

Patient / carer responsibilities:

- Ensure they have a clear understanding of how and when to take their medicines
- Request further supplies, store appropriately and take/administer as directed
- Report any adverse effects to the prescriber
- Report back to specialist nurse if problems with medication adherence.

B. Medication Initiation in other scenarios

In line with NICE guidance the Herefordshire dementia pathway allows for initiation of dementia medication in the community via specialist nurse recommendation e.g. memory clinic nurse, Community Dementia Nurse, Care Home In-Reach Team nurse.

Initiation of new medication in these cases (where referral to a psychiatrist would provide no additional clinical benefit) will be by recommendation from the specialist nurse to the GP. It is recognised that moving away from a medical shared care model will take time to embed and depends upon GP clinical confidence with prescribing these medications.

Addition of memantine for patients experiencing behavioural and psychological symptoms of dementia (BPSD) often reduces the need for prescribing antipsychotics. All review and monitoring will be undertaken by the specialist nurse team who will liaise closely with the GP practice and ensure EMIS notes are updated. Clinical supervision for the CDN and CHIT teams is provided by the 2gether psychiatrist team.

Initiation of dementia medication may be requested by the following:

- Memory Clinic (as outlined on page 1)
- GPs with the support of the Community Dementia Nurse Team, Care Home In-Reach Team (for primary care patients), with access to advice on request from secondary care specialists. It is important to note that these patients are not under secondary care but are managed in the community by CDNs/CHIT advising GPs
- Older Peoples Community Mental Health Team
- Learning Disabilities Service
- Care Home In-reach Team working with secondary care patients.

This includes non-medical prescribers working in any of the above settings.

Initiation in Wye Valley NHS Trust acute and community settings may be made by the following, including those working under their supervision:

- Consultant geriatricians
- Psychiatric liaison team
- Consultant neurologists

Clinical Information

NICE Guideline NG97 recommends the use of the ACIs donepezil, galantamine and rivastigmine as options for mild to moderate Alzheimer's disease and in other forms of dementia with the exception of a predominantly Vascular 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 ACIs **OR**
- severe Alzheimer's disease. Memantine may help manage BPSD and reduce the need for antipsychotic medication in this patient group.

Dosage and administration (see table 1 overleaf)

Ensuring good medicines adherence is essential otherwise the drug is unlikely to have any beneficial effect and side effects are more frequent.

***Donepezil*:** 5mg once daily at bedtime, increased if necessary after 1 month to 10mg once daily. Orodispersible tablets are available.

Galantamine*: *Standard release tablets: 4mg twice daily for 4 weeks, with the morning and evening meals; increased to 8mg twice daily for 4 weeks. An increase to 12 mg twice a day may be considered following assessment including evaluation of clinical benefit and tolerability. If there is no increased response or tolerability is poor, reduce dose back to 8mg twice daily. Ensure adequate fluid intake.
Modified release capsules: Initially 8mg once daily for 4 weeks each morning with food, increased to 16mg once daily for 4 weeks; maintenance 16-24mg once daily (reviewed as per standard tablets). **Gatalin XL®** is the most cost effective way of prescribing galantamine in primary care, more cost effective than standard release tablets.

***Rivastigmine*:** 1.5mg twice daily, with the morning and evening meals; increased in steps of 1.5mg twice daily at intervals of at least 2 weeks up to a maximum of 6mg twice daily. Re-titration from 1.5mg twice daily should be undertaken if treatment is interrupted for more than several days. Liquid and transdermal patch available for patients with swallowing difficulties; prescribe patches as brand **Alzest®** in primary care.

Memantine: 5mg once daily, increased in steps of 5mg at weekly intervals, until reaching the recommended maintenance dose of 20mg once daily. Oral solution is available (NB solution should be dosed onto a spoon or into a glass of water).

Dosing in Renal Impairment

In general for ACIs no dosage adjustment is required. Galantamine is contraindicated in eGFR <10ml/min. Memantine max dose in severe renal impairment (eGFR 5-29ml/min) is 10mg. Dose should be increased cautiously when eGFR 30-49ml/min. NB eGFR overestimates renal function in frail older people particularly those with low weight so CrCl is preferred for these patients – see CrCl calculator.

Table1: Prescribing Information (See SPC for full list of cautions)

AChE Inhibitors	Usual Maintenance Dose	Formulations	Adverse effects / contra-indications
Donepezil	5-10mg once daily at bedtime	Tablets *Orodispersible tablets	Dose-related cholinergic effects (eg GI upset) on initiation, hence low starting dose and incremental titration. Care in patients with asthma/COPD, severe hepatic failure, CV conditions eg heart block, SVT, urinary obstruction and history of peptic ulceration.
Galantamine (Gatalin XL)	8-12mg twice daily 16-24mg MR once daily	Tablets, *liquid 4mg/ml MR capsules	
Rivastigmine	3-6mg twice daily 4.6mg – 9.5mg/24hr once daily	Capsules, *liquid 2mg/ml *Transdermal patches[#] (Alzest® brand)	
Glutamate modulators			
Memantine	20mg once daily	Tablets *Liquid 10mg/ml	Most common side effects headache, somnolence, and constipation. Caution in people with history of seizures.

*Orodispersible tablets, liquids and patch formulations are reserved for those patients experiencing difficulty with standard preparations.

[#]**Rivastigmine Patch (Alzest®)** starting dose 4.6mg/24hr once daily, ensure patches are removed after 24 hours (see MHRA warning) and resite patch in different area (avoid using the same site for 14 days). After 4 weeks if well tolerated increase dose to 9.5mg/24hr patch once daily. If patch is not applied for more than 3 days re-titrate with 4.6mg/24hr patch. Incorrect use of patches has been associated with overdose (eg not removing patch or applying more than one patch at the same time).

Monitoring

No routine ongoing monitoring is required for AChIs. Renal function should be checked at least annually for patients prescribed memantine – maximum recommended dose for eGFR 5-29ml/min is 10mg daily.

A routine pre-treatment ECG is unnecessary; ECG usually done if history of heart disease, pulse <60, syncope, suspicion of heart block, sometimes if on digoxin or beta blockers which can impair AV conduction. Specialist can advise on whether this is necessary.

***QOF exception reporting**:* the tests outlined in QOF are designed to aid differential diagnosis for new patients. It may be appropriate to exception report patients whose diagnosis is Read coded in later stages of dementia eg patients with known dementia moving to a practice but not previously coded eg new care home residents. The importance of confirming diagnosis even for patients with advanced disease is well researched with improved outcomes if patients transfer between care environments. The DiADeM tool supports GPs in diagnosing dementia for people living with advanced dementia in a care home setting – available for download.

Toxicity

AChIs have been associated with weight loss; consider this and any symptoms of peptic ulcer disease or gastrointestinal bleeding when reviewing, especially patients at increased risk of developing peptic ulcers e.g. those with a history of ulcer disease or prescribed medicines which increase bleeding risk e.g. NSAIDs, aspirin, anticoagulants, SSRIs, steroids.

Efficacy

A principal role of the Community Dementia Service or Care Home In-reach Team is to support the prescriber in the monitoring of the medication. Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms – this will be assessed by the Community Dementia Service or Care Home In-reach Team. Once established on the medication it should be reviewed in line with the repeat prescription policy of the prescribing practice.

Pregnancy & Lactation

Not recommended in pregnancy and lactation.

Common / Significant Drug interactions (See BNF for full list of interactions)

All drugs with anticholinergic effects (eg drugs for urinary incontinence, tricyclic antidepressants) should be avoided wherever possible in people with dementia as they exacerbate symptoms and reduce efficacy of AChIs.

All ACIs caution with the following:

- drugs that have effects on cardiac conduction e.g. beta blockers
- other cholinomimetics (e.g. neostigmine, pyridostigmine, bethanecol)
- neuromuscular blockers

Donepezil*:* CYP3A4 inhibitors eg itraconazole, ketoconazole and erythromycin, and CYP2D6 inhibitors, such as fluoxetine, quinidine may inhibit the metabolism of donepezil. Enzyme inducers eg rifampicin, phenytoin, alcohol and carbamazepine may reduce the levels of donepezil - SPC recommends caution as unknown magnitude of effect.

Galantamine*:* potent inhibitors of CYP2D6 or CYP3A4 (as above for donepezil) may experience an increased incidence of cholinergic adverse reactions, mainly nausea and vomiting.

Rivastigmine: no additional interactions. The patch carries a risk of local irritation hence advice to change site every day and not reuse site for 14 days.

Memantine may exacerbate effects of levodopa, selegilene, dopamine agonists and anticholinergics in Parkinson's disease. Effects of barbiturates and neuroleptics may be reduced. Avoid amantadine, ketamine or dextromethorphan - risk of pharmacotoxic psychosis. Monitor warfarin closely particularly during initiation – potential for increase in INR.

Stopping Treatment

- When medication is reduced or stopped patients should be monitored for negative effects on cognitive, global, functional or behavioural symptoms. In General Practice this will typically be a task delegated to the Community Dementia Nurse (CDN) or Care Home In-reach Team (CHIRT). Patients on lower doses may be stopped abruptly, patients on usual maintenance doses should be reduced to a lower dose for 4 weeks before stopping completely
- In later stages of Alzheimer's ACI's are associated with driven or overactive behaviour, but stopping the drugs is associated with more rapid functional decline and probably institutionalisation
- Follow-up after reducing or stopping the medication can be by telephone or in person. Patients and carers should be counselled to report any potential adverse effects. Reviews should be held at least every two weeks until the patient has been successfully withdrawn for 6 weeks in total.
- The exceptions will be in the event of an adverse drug reaction which necessitates immediate cessation or a serious change in the patient's physical health which makes ACI treatment inappropriate for example if the patient is dying.

New Patients registering with a practice who are established on treatment should generally have their prescriptions continued by their new practice and a routine review arranged by CDN, partly to ensure that appropriate support arrangements are in place.

Availability of back-up advice and support

Contact relevant local dementia specialist as previously indicted where possible.

Memory Clinic & CHIRT	01432 842203
CMHT North	01432 842201
CMHT South	01432 842202
Learning Disabilities	01432 383400
Wye Valley Trust	01432 355444

This guideline, agreed between NHS Herefordshire CCG, Wye Valley NHS Trust and 2gether NHS Trust, attempts to reflect the changes in pathways for diagnosis and prescribing across Herefordshire.
The information contained in this guideline is issued on the understanding that it is the best available from the resources at our disposal on the date of issue. Further information may be obtained from the specialist or your local medicines information centre (01432 364017). This guideline does not contain a complete list of indications, precautions, warnings etc. For further information please refer to the product Summary of Product Characteristics http://emc.medicines.org.uk/
Internet link to shared care guidelines:
https://www.herefordshireccg.nhs.uk/your-services/medicines-optimisation/shared-care