

## **\_For use in South and West Hertfordshire and East and North Hertfordshire**

### **NICE TECHNOLOGY APPRAISALS – RECOMMENDED**

**NICE TA 217 – DONEPEZIL, GALANTAMINE, RIVASTIGMINE AND MEMANTINE FOR THE  
TREATMENT OF ALZHEIMER’S DISEASE (REVIEW), MARCH 2011, UPDATED SEPTEMBER  
2015, OCTOBER 2018, JULY 2020 AND FEBRUARY 2021**

**AMBER INITIATION - RECOMMENDED FOR RESTRICTED USE.**

**SPECIALIST INITIATION AND TITRATED TO AN OPTIMAL DOSE AND STABILISED BY SPECIALIST  
SERVICES. PRIMARY CARE PRESCRIBING UNDER PRESCRIBING SUPPORT DOCUMENT**

#### **RECOMMENDATIONS:**

- Patients with all grades of dementia should be referred to a specialist for assessment.
- There has been a statutory duty to commission this TA from 23 June 2011.
- **Patients referred to Hertfordshire Partnership University NHS Foundation Trust (HPFT)**
  - HPFT are responsible for initiation and stabilisation of dementia treatment. Dose is titrated and patient is monitored and reviewed for 6-8 months by HPFT before asking GP to take over prescribing responsibility.
  - GPs may be requested to undertake the responsibility for the continued prescribing **and** annual monitoring of dementia treatment in primary care as detailed in the ‘**Prescribing support document**’ below.
- **Patients referred to other Provider Trusts**
  - Prescribing responsibility may be accepted by GPs in the presence of appropriate ‘**Shared Care/Transfer of Care/Prescribing Support**’ guidelines supplied by the Provider.
  - The ‘Shared Care/Transfer of Care/Prescribing Support’ guidelines supplied:
    - ❖ must have been ratified by the Host Commissioner of the Provider Trust.
    - ❖ must detail the responsibilities of the different parties sharing care.
    - ❖ must contain **stopping criteria** that have been discussed with the patient and carer(s) **at the time of treatment initiation**.

NICE Technology Appraisal Guidance 217 is available at: [www.nice.org.uk/TA217](http://www.nice.org.uk/TA217)

This recommendation is based upon the evidence available at the time of publication.  
The recommendation will be reviewed upon request in the light of new evidence becoming available.

# Prescribing Support Document: Management of Dementia Drugs Process Summary

Following assessment under EMDASS, patient is diagnosed with mild to severe Alzheimer’s disease and is suitable for treatment with donepezil, galantamine, rivastigmine or memantine (as recommended by NICE TA217/NG97)

Drug for dementia is initiated by EMDASS/SMHTOP team.  
Dose is titrated and patient is monitored and reviewed for 6-8 months

Good therapeutic response and patient is stable on treatment

Patient either does not have a good therapeutic response or cannot be stabilised on treatment

- EMDASS to send clinic letter to the GP to include: -
- Clear diagnosis and care plan
  - Details of drug treatment and dose
  - Patient is confirmed to be stable on a maintenance dose and benefitting from treatment
  - 8 week prescription of on-going medication
  - Specialist team contact details for back up advice/support
  - Patient consent to treatment documented
  - Advice on any medication or co-morbidity that may worsen cognition and should be reviewed (if applicable)
  - Link to the prescribing support document (for additional information)

Patient is retained by HPFT  
Information continues to be passed onto GP about patient’s care

Referral made to SPA:  
Crisis referrals seen by Crisis Assessment and Treatment Team (CATT) within 4 hours  
Urgent referrals contacted by SMHTOP Team within 72 hours  
Standard referrals assessed within 4 weeks in E&N and 6 weeks in SWH by SMHTOP

- GP accepts the responsibility for the on-going prescribing and monitoring of the dementia medication and assumes the responsibilities as detailed in the prescribing support document
- GP monitors adverse effects and drug interactions and takes the appropriate actions with access to back up advice/support

- There is a trigger for referral of patient to secondary care specialist service:
- Difference of opinion GP and carer about stopping medication
  - Consideration of use of dual pharmacology therapy in patients with moderate or severe Alzheimer’s disease, and a global impression that cognitive enhancement would be of benefit for the service user
  - Uncertainty about side effects or benefits
  - Behavioural issues requiring community team input (whether or not the patient is taking anti-dementia medication)

GP conducts an annual monitoring review in primary care including the cognitive, functional, behavioural and global assessment and takes appropriate actions

Worthwhile effect on cognitive, global, functional or behavioural symptoms?

**Yes:** continue dementia medication

**No:** AChEIs should not be stopped because of disease severity alone; refer to specialist for review/support

## Prescribing Support Document: Drugs for the Management of Dementia (donepezil, galantamine, rivastigmine, memantine)

### Change History

| Version number | Change details   | Date          |
|----------------|--|---------------|
| V 1.0          | Transfer of Care Guidelines  | June 2016     |
| V 2.0          | Document updated to Prescribing support document.<br>Transfer of care form removed. This is replaced by a clinic letter sent by Psychiatrist to the GP.<br>GP fax back reply for refusal of transfer of care – removed.  | November 2018 |
| V 3.0          | Document updated following publication of NICE guideline (NG97) - Dementia: assessment, management and support for people living with dementia and their carers; changes include: <ul style="list-style-type: none"> <li>• potential use of dual pharmacological treatment in patients with moderate or severe Alzheimer's disease;</li> <li>• acetylcholinesterase (AChE) inhibitors should not be stopped in people with Alzheimer's disease because of disease severity alone.</li> </ul> Additional minor updates made where necessary (e.g. removal of references to Local Incentive Scheme, updated weblinks and drug costs).<br>Additional information added as suggested by ENHCCG mental health prescribing lead/HPFT (to aid clarity). | July 2020     |
| V 4.0          | Minor typographical error corrected (page 8, galantamine section)  | February 2021 |
| V 5.0          | Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include: <ul style="list-style-type: none"> <li>• Rebadging with HWE ICB and removal of ENHCCG and HVCCG headers</li> <li>• Removal of reference to CCGs and change HV to SWH</li> </ul>   | December 2023 |

## 1. Introduction

The clinical management of patients with dementia in Hertfordshire, including the prescribing of dementia drugs, has been the responsibility of the Specialist Mental Health Teams for Older People (SMHTOP), Hertfordshire Partnership University NHS Foundation Trust (HPFT) since the implementation of NICE guidance (TA 217) in 2011. The Early Memory Diagnosis and Support Service (EMDASS) is responsible for the diagnosis and initiation of medication.

There is an agreement between both South west Herts place and East and North Herts place and HPFT for appropriate patients who are maintained on a stable dose of dementia medication to be transferred to the General Practitioner (GP) for on-going prescribing and monitoring in primary care.

The aim of this guideline is to ensure that the transfer of care of the patient with dementia from EMDASS to the GP is safe and appropriate by providing the following information: -

- The roles and responsibilities of the secondary care specialist team, the GP, the ICB and patient/carer.
- Criteria for the transfer of prescribing from secondary care to the GP.
- Clinical information on the drugs used in the management of dementia including the monitoring requirements of these medications in primary care.
- Cognitive, global, functional and behavioural assessment scales (where appropriate).
- Criteria for when medication should be stopped.

- When and how to refer back to specialist services.
- Secondary care contact details for support and back-up advice.

The GP will assume both the clinical and legal responsibility of prescribing the dementia drugs and the clinical management of the patient. Patients considered complex by the HPFT Old Age Psychiatrist will be excluded from the transfer of care arrangement.

## 2. NICE guidance

**NICE TA 217 (Mar 2011)** recommends: -

- The three anticholinesterase (AChE) inhibitors donepezil, galantamine and rivastigmine as options for managing mild to moderate Alzheimer's disease.
- The glutamate receptor antagonist, memantine, alone (monotherapy) 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

**(PLEASE SEE BELOW [NG97] REGARDING UPDATED ADVICE ON DUAL PHARMACOLOGICAL THERAPY)**

- Patients who continue on treatment should be reviewed regularly using cognitive, global, functional and behavioural assessment. Carer's views on the patient's condition on follow-up should be sought\*.
- AChE inhibitor treatment should normally be started with the drug with the lowest acquisition cost (taking into account required daily dose and the price per dose). However, an alternative AChE inhibitor could be prescribed if considered appropriate taking into account adverse event profile, expectations about adherence, medical comorbidity, possibility of drug interactions and dosing profiles.
- Except as part of properly constructed clinical studies, do **not** use:
  - acetylcholinesterase inhibitors or memantine for cognitive decline in vascular dementia
  - acetylcholinesterase inhibitors in mild cognitive impairment.

**\*Please see Section 9 (Monitoring Requirements in Primary Care) for further details**

**NICE guideline [NG97]** - Dementia: assessment, management and support for people living with dementia and their carers was published in June 2018. This included two changes surrounding pharmacological treatment options as follows:

- For people with an established diagnosis of Alzheimer's disease who are already taking an acetylcholinesterase (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

Following discussion at the Hertfordshire Medicines Management Committee (in June and October 2019), the committee supported dual pharmacological therapy (with AChE inhibitor and memantine) for both moderate and severe Alzheimer's disease (in line with NICE guidance). Dual pharmacological therapy to be initiated only by specialists in the care of patients with dementia (where clinically appropriate).

## 3. Criteria for transfer of prescribing and monitoring to primary care

The following must apply before the GP is asked to accept on-going prescribing responsibility and monitoring of the patient in primary care: -

- The patient must have undergone the appropriate assessments and shown a beneficial response to treatment
- The patient is stable on a maintenance dose of dementia drug
- The patient's care plan is stable\* or predictable

The **inclusion** criteria include:

- *The patient must have undergone the appropriate assessments and shown an ongoing overall benefit from treatment*
- *The patient is <sup>\*</sup>stable on a maintenance dose of dementia drug*
- *The patient's care plan is stable or predictable*

- *Alzheimer's Disease*
- *Dementia in Parkinson's Disease*
- *Dementia with Lewy Bodies*
- *Mixed dementia (has to include one of the above types of dementias)*

The **exclusion** criteria include: -

- *Vascular dementia*
- *Fronto-temporal dementia*
- *Memantine for mild dementia (unlicensed)*

\*'Stable' for the purpose of the transfer of care arrangement is defined as when the patient is living at their usual address without requiring any additional psychiatric service other than the memory clinic (EMDASS).

The request for the transfer of care will usually be made when the patient has been on 6-8 months of treatment.

#### 4. Areas of responsibility

| ICB RESPONSIBILITIES  |   |
|---|---|
| 1   | ICB will review the prescribing support document annually.  |
| SPECIALIST RESPONSIBILITIES (HPFT Consultant and associated team) |   |
| 1   | Initial assessment of patient to include tests of cognitive (MMSE or alternative score), global, functional and behavioural symptoms and activities of daily living.  |
| 2   | Confirm the diagnosis of dementia. Ensure patient has access to an overall programme of care.   |
| 3   | Counsel patients and carers on the implications of the diagnosis, the likelihood of potential benefits and side effects of treatment and treatment endpoints and include the consequence of poor compliance. Provide patient with comprehensive advice and information. HPFT's Choice and Medication website can be used:<br><a href="https://www.choiceandmedication.org/hertfordshire/condition/dementia-and-alzheimers-disease/">https://www.choiceandmedication.org/hertfordshire/condition/dementia-and-alzheimers-disease/</a><br><a href="https://www.choiceandmedication.org/hertfordshire/printable-leaflets/">https://www.choiceandmedication.org/hertfordshire/printable-leaflets/</a>   |
| 4   | Initiate and stabilise treatment with donepezil, galantamine, rivastagmine and/or memantine if clinically appropriate, and ensure compliance. <ul style="list-style-type: none"> <li>• The preferred option is <b>generic donepezil standard tablets</b> for mild to moderate severity Alzheimer's disease. Generic rivastigmine tablets would normally be a 2<sup>nd</sup> line choice if donepezil cannot be tolerated.</li> <li>• Where there are specific patient reasons where these preferred choices cannot be used, the rationale for the choice of drug/formulation must be communicated to the GP and documented in the patient's notes.</li> <li>• Memantine monotherapy is an option in moderate Alzheimer's disease for people who are intolerant or have a contraindication to AChE inhibitors, or in severe Alzheimer's disease.</li> <li>• <b>Dual pharmacological therapy:</b> for people with an established diagnosis of Alzheimer's disease who are already taking an acetylcholinesterase (AChE) inhibitor: <ul style="list-style-type: none"> <li>• consider memantine in addition to an AChE inhibitor if they have moderate disease</li> <li>• offer memantine in addition to an AChE inhibitor if they have severe disease.</li> </ul> </li> <li>• HPFT fully supports the use of equivalent cost-effective 'branded generics' in primary care i.e. galantamine XL.</li> </ul> |
| 5   | Advise GP on any medication or co-morbidity that may worsen cognition and should be reviewed.   |
| 6   | During the first 6-8 months of treatment: - <ul style="list-style-type: none"> <li>• Monitor patient regularly for compliance, side-effects and signs of deterioration. Report adverse events via the yellow card scheme, if appropriate.</li> <li>• Increase the dose at appropriate intervals or switch to alternative drug/formulation if there are signs of intolerance.</li> </ul>   |
| 7   | Assessment of patient for evidence of treatment efficacy at approximately 3 months (2 – 4 months depending on time spent at sub-therapeutic doses during titration). Medication should be continued only where there has been an improvement or no deterioration in MMSE (or alternative) score, together with evidence of global improvement on the basis of behavioural and/or functional assessment.   |

|    |  |
|----|--|
| 8  | Discontinue treatment where there has not been benefit or where there has been deterioration of the condition.   |
| 9  | <p>If appropriate for patient to continue with medication, GP to be promptly informed to take on further prescribing and monitoring in primary care after 6-8 months. The following information (as a minimum) to be provided to the GP in order that the on-going prescribing and monitoring can be taken on in primary care - see checklist in Section 5 – Communication and Handover from secondary to primary care:-</p> <ul style="list-style-type: none"> <li>• Prescribing support document</li> <li>• Clear diagnosis and care plan</li> <li>• Confirmation that the patient is stable on a maintenance dose and there has been ongoing overall benefit from treatment</li> <li>• Eight weeks' prescription of on-going medication from last appointment</li> <li>• Specialist team contact details for GPs to obtain advice and support</li> <li>• Patient has been fully informed with regards to their treatment and consent has been discussed and documented including the change in where their future prescriptions will be issued from (GP not HPFT). This includes informing patients that their medication (i.e. galantamine XL) may be switched to an equivalent 'branded generic' product by the GP. The 'branded generic' is a preferred ICB choice which is cost-effective in primary care.</li> </ul> |
| 10 | Specialist to ensure that patient/carer is informed and made aware of their responsibilities (as detailed under patient/carer responsibilities in these guidelines) for when transfer of care to the GP occurs.  |

| <b>GP RESPONSIBILITIES</b> |  |
|----------------------------|--|
| 1                          | <p>Review the request from the specialist to take on the transfer of prescribing and monitoring of the patient. Acceptance is assumed.</p> <p>Prompt communication to EMDASS if prescribing responsibility is not accepted (within 2 weeks), including the clinical reason for not taking on the transfer of care. Responsibility cannot be declined on grounds of cost of medication.</p>   |
| 2                          | Check sufficient information has been provided to take on the responsibility of continued prescribing and monitoring – see Section 5 'Communication and handover from secondary to primary care' checklist. Request any missing information to be provided from EMDASS consultant before taking on the prescribing in primary care. Transfer of care can be declined by GP if insufficient detail is received following request for further information. |
| 3                          | Prescribe donepezil, galantamine, rivastigmine and/or memantine at the maintenance dose recommended. Switch to the ICB preferred cost-effective 'branded generic' product where relevant i.e. galantamine XL.  |
| 4                          | Monitor treatment as stated in Section 9 'Monitoring in Primary Care' in the prescribing support document. Report adverse events via the yellow card scheme, if appropriate.   |
| 5                          | Seek advice from the specialist on any aspect of patient care of concern to the GP that may affect treatment. See Section 6 and 7 'Contact details for backup advice and support' in the prescribing support document.   |
| 6                          | Check for possible drug interactions when newly prescribing or stopping concurrent medication.   |
| 7                          | Discontinue treatment if patient develops side-effects, or seek advice if progression of disease is noted, indicating need for a review of management plan. AChEIs should not be stopped because of disease severity alone – see Section 10 'Stopping Medication' in the prescribing support document.   |
| 8                          | Refer patient back to secondary care when appropriate, clearly highlighting that the referral relates to a patient under this transfer scheme – see Section 11 'Triggers for re-referral to secondary care' in the transfer of care guidelines.  |

| <b>PATIENT/CARER RESPONSIBILITIES</b> |  |
|---------------------------------------|--|
| 1                                     | Report to their GP if they do not have a clear understanding of or have any concerns with their treatment with donepezil, rivastigmine, galantamine or memantine.  |
| 2                                     | Inform their GP of any over the counter products (the GP will know all the other medications that are being prescribed for the patient) and tell the pharmacist of their prescribed medication when buying over the counter medications. |
| 3                                     | Report any adverse effects to the GP or whilst taking donepezil, galantamine, rivastigmine or memantine.   |
| 4                                     | Report any changes in disease symptoms to the GP.  |
| 5                                     | Following the transfer of prescribing, obtain further prescriptions for dementia medication from the GP and not HPFT.  |

## 5. Communication and Handover from Secondary to Primary care

The following information should be provided/action undertaken when requesting the transfer of prescribing of the patient with dementia to primary care

- Clear diagnosis and care plan including information that has been discussed with patient and carer.
- Details of drug treatment and dose.
- Confirmation that the patient is \*stable on a maintenance dose and there has been benefit from treatment.
- Eight weeks prescription of on-going medication from last appointment.
- Specialist team contact details for GPs to obtain advice and support.
- Confirmation that patient has been fully informed with regards to their treatment and consent has been discussed and documented including the change in where their future prescriptions will be issued from (GP not EMDASS).
- The post-diagnostic support service will work in parallel with the secondary care titration clinic. The post-diagnostic support service will provide the following information to the GP (if consent from the patient is obtained):
  - Confirmation of the standard information handed to the patient.
  - Details of whether advanced care plan has been agreed or discussed.
  - Any patient or carer specific information (at discretion of professional).
  - Any useful telephone numbers.
  - Report at discharge.
  - Specialist team contact details for back-up advice and support.
- Advice on any medication or co-morbidity that may worsen cognition and should be reviewed (if applicable).
- Link to the prescribing support document (to provide additional information for GPs).

## 6. The Principles of Access to Back-Up Advice:

- GPs are expected to use the usual crisis pathway for crisis support (as with other patients).
- The EMDASS/SMHTOP team will respond to GP requests for back-up advice by telephone **within 24 hours** and will provide access to consultant clinics **within 2 weeks** (when needed).
- The GP will be able to contact the post-diagnostic support service (Inc. the dementia carers support nurse) to enable targeted support when patients/carers may be approaching crisis. The GP will be able to refer to the Alzheimer's Society, or other community based organisations (as usual) for signposting and support.

## 7. EARLY MEMORY DIAGNOSIS & SUPPORT SERVICE (EMDASS)

| EAST  |   |
|---|---|
| <p><b>Team Manager:</b> Jan Gardiner</p> <p><b>Team Lead:</b> Jennifer Miller</p> <p><b>Doctors:</b><br/>           Dr Virender Marwah<br/>           Dr Hema Ananth<br/>           Dr Kaushik Mukhopadhaya<br/>           Dr Sujatha Merve</p> | <p>Rosanne House<br/>           Parkway<br/>           Welwyn Garden City<br/>           Herts AL8 6HG</p> <p><b>T:</b> 01707 364 012</p> <p><b>E:</b> <a href="mailto:ENHERTS.SMHTOP@NHS.NET">ENHERTS.SMHTOP@NHS.NET</a></p>   |
| NORTH   |   |
| <p><b>Team Manager:</b> Michael Cruz</p> <p><b>Team Lead:</b> Amanda Lewis</p> <p><b>Doctors:</b><br/>           Dr Kunle Ashaye<br/>           Dr K Shankar</p>  | <p>SMHTOP North<br/>           1st Floor, Saffron Ground<br/>           Ditchmore Lane<br/>           Stevenage<br/>           Herts<br/>           SG1 3LJ</p> <p><b>T:</b> 01438 792120</p> <p><b>E:</b> <a href="mailto:Emdass.north@nhs.net">Emdass.north@nhs.net</a></p> |

| SOUTH WEST   |  |
|--|--|
| <b>Team Manager:</b> Rob Standen<br><br><b>Team Lead:</b> Alfred Asimeng<br><br><b>Doctors:</b><br>Dr Amirtha Pasupathy<br>Dr Shaheen Shora          | Colne House<br>21 Upton Road<br>Watford<br>Herts WD18 0JP<br><br><b>T:</b> 01923 837 154<br><b>E:</b> <a href="mailto:hpft.swherts.emdass@nhs.net">hpft.swherts.emdass@nhs.net</a>                           |
| NORTH WEST   |  |
| <b>Team Manager:</b> Matt Stewart<br><br><b>Team Lead:</b> Robin Firminger<br><br><b>Doctors:</b><br>Dr Mike Walker<br>Dr Arun Jha<br>Dr Rahul Tomar | The Marlowes Health and Wellbeing Centre<br>39-41 Marlowes<br>Hemel Hempstead<br>Hertfordshire<br>HP1 1LD<br><br><b>T:</b> 01442275628<br><b>E:</b> <a href="mailto:emdass.nw@nhs.net">emdass.nw@nhs.net</a> |

## 8. Supporting Information

(For full details, please refer to the current individual drug Summary of Product Characteristics, SmPC, and BNF)

| Dosage and administration  |   |
|--|---|
| Treatment should be started at the lowest dose and built up to a tolerable dose within the effective range |   |
| Donepezil  | 5mg once daily in the evening, just before bed, increased if necessary after 1 month to 10mg once daily.<br>Orodispersible tablet available (significantly more expensive).   |
| Rivastigmine   | <u>Capsule and liquid</u><br>Starting dose 1.5mg twice daily with meals. Increase dose to maximum tolerated up to 6mg twice daily. Minimum of 2 weeks between dose increases.<br><u>Patch (only if capsule/liquid cannot be administered)</u><br>4.6mg/24hours increasing to 9.5mg/24hours after a minimum of 4 weeks. After a further 6 months may be increased to 13.3mg/24 hours if clinically appropriate.                |
| Galantamine  | <u>Standard release tablet and liquid</u><br>Start at 4mg twice daily preferably with meals. Increase to maximum tolerated up to 12mg twice daily. Minimum of 4 weeks between dose increases.<br><u>Modified release tablet</u><br>8mg once daily increasing to maximum tolerated up to 24mg once daily. Minimum of 4 weeks between dose increases.   |
| Memantine  | <u>Tablet/orodispersible tablet and oral solution</u><br>5mg once daily, increased in steps of 5mg at weekly intervals, until reaching the recommended maintenance dose of 20mg once daily.<br>Orodispersible tablets and oral solution available (significantly more expensive); orodispersible tablets used in preference to oral solution at HPFT.<br>Oral solution should be dosed onto a spoon or into a glass of water. |

| Absolute Contraindications |   |
|----------------------------|---|
| All drugs                  | Where there is hypersensitivity to the active substance or any of the excipients.   |
| Donepezil                  | Known sensitivity to piperidine derivatives   |
| Galantamine                | Severe hepatic/renal impairment or those who have both significant renal and hepatic dysfunction. Urinary retention or history of prostatic condition |
| Donepezil & galantamine    | Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption                       |
| Rivastigmine               | Known hypersensitivity to carbamate derivatives or severe liver impairment  |
| Memantine                  | Patients with rare hereditary problems of fructose intolerance should not take oral solution (contains sorbitol).                                     |



| Cautions – to be used with caution in the following    |   |  |   |
|--|---|--|---|
| AChE inhibitors (donepezil, galantamine, rivastigmine) | <ul style="list-style-type: none"> <li>Sino-atrial, AV node block or sick sinus syndrome</li> <li>Severe asthma</li> <li>Concomitant beta-blocker therapy</li> <li>Urinary symptoms (avoid use of galantamine)</li> </ul>   | <ul style="list-style-type: none"> <li>People at increased risk of peptic ulcers (those with history of ulcer disease or on concomitant NSAIDs)</li> </ul> | <ul style="list-style-type: none"> <li>Chronic obstructive pulmonary disease or active pulmonary infections</li> <li>Epilepsy</li> <li>CVD</li> </ul> |
| Memantine  | <ul style="list-style-type: none"> <li>History of convulsions</li> <li>Patients with recent MI, uncontrolled hypertension or uncompensated congestive heart failure were excluded from the clinical trials and there is limited data for the use in these patients. These patients should be closely supervised.</li> <li>Patients who have had drastic diet changes e.g. carnivore to vegetarian or a massive ingestion of alkalinising gastric buffers since this causes alkalinisation of urine which reduces elimination of memantine.</li> </ul> |  |   |

| Adverse effects of AChE inhibitors (donepezil, galantamine, rivastigmine) and suggested actions   |  |                      |  |
|---|--|----------------------|--|
| There are two practically important groups of adverse effects:  |  |                      |  |
| 1. GI – common S/Es include abdominal pain, nausea, vomiting, diarrhoea, anorexia, weight loss  |  |                      |  |
| 2. Cardiac  |  |                      |  |
| <ul style="list-style-type: none"> <li>heart block (sino-atrial block, AV block) – this is rare but potentially serious and easily missed</li> <li>bradycardia – if this occurs, carry out an ECG. If symptoms of collapse or dizzy spells and PR interval &gt;200ms, then stop AChE inhibitor</li> </ul> |  |                      |  |
| Adverse effects   | Symptoms/signs   | Frequency            | Suggested actions  |
| GI symptoms   | Anorexia, nausea, vomiting and diarrhoea   | Very common          | Generally mild and transient. Can be minimised by taking drug after food. If symptoms persist, reduce dose. If unsuccessful, consider switch to alternative AChE inhibitor.  |
|   | May enhance predisposition to gastric or duodenal ulceration   | Uncommon/rare        | Discontinue treatment if ulcer develops. Care with those at risk of or with active gastric or duodenal ulcer. Patient should be monitored regularly for symptoms.  |
| Cardiovascular symptoms   | Bradycardia  | Uncommon/rare        | <b>Seek urgent review.</b> Carry out an ECG. If symptoms of collapse or dizzy spells and PR interval >200ms then stop AChE inhibitor.  |
| Neurological symptoms   | Dizziness, headache, insomnia, somnolence  | Very common / common | Generally mild and transient. If symptoms persist, reduce dose. If unsuccessful, consider switch to alternative AChE inhibitor/memantine.  |
|   | Syncope  | Common/uncommon      | Reduce dose. If symptoms persist, consider switch to alternative AChE inhibitor/memantine.   |
|   | Extrapyramidal symptoms (including worsening of Parkinson's disease)   | Rare                 | Reduce dose. If symptoms persist, consider switch to alternative AChE inhibitor/memantine.   |
|   | Decreased seizure threshold  | Rare                 | Extreme caution in epilepsy  |
| Skin  | Galantamine <i>has been associated with <b>serious skin reactions</b> including Stevens Johnson Syndrome (SJS), acute generalised exanthematous pustulosis</i> | Rare                 | <i>It is recommended that patients and carers are advised to <b>monitor</b> for skin reactions. In the advent of an apparent skin reaction patients should be advised to <b>stop treatment and seek medical advice</b></i> |

|                      |  |                   |   |
|----------------------|--|-------------------|---|
|                      | <i>(AGEP) and erythema multiforme.</i> |                   |   |
| General disorders    | Asthenia, fatigue                      | Common            | Generally mild and transient. If symptoms persist, reduce dose. If unsuccessful, consider switch to alternative AChE inhibitor/memantine. |
| Respiratory symptoms | May cause bronchoconstriction          | No available data | Caution in patients with history of asthma or COPD or those with an active pulmonary infection (pneumonia).                               |
| Psychiatric symptoms | Agitation, confusion and insomnia      | Common            | Reduce dose. If symptoms persist, consider switch to alternative AChE inhibitor/memantine.  |

#### Adverse effects of memantine and suggested actions

Appears to be well tolerated in practice but it is important to note that it might be easy to miss distressing side effects when it is used in a population with moderate/severe dementia.

| <b>Adverse effects</b>  | <b>Symptoms/signs</b>           | <b>Frequency</b> | <b>Suggested actions</b>                                  |
|-------------------------|---------------------------------|------------------|---|
| GI symptoms             | Constipation                    | Common           | PRN or regular laxative                                   |
| Cardiovascular symptoms | Hypertension                    | Common           | Reduce dose and review BP. Consider discontinuation       |
| Neurological symptoms   | Dizziness, headache, drowsiness | Common           | Reduce dose and review symptoms. Consider discontinuation |
| Respiratory symptoms    | Dyspnoea                        | Common           | Reduce dose and review symptoms. Consider discontinuation |

#### Drug Interactions

|                           |  |
|---------------------------|--|
| All AChE inhibitors       | <ul style="list-style-type: none"> <li>May interact (antagonism of effects) with medicines that have anticholinergic activity e.g. oxybutynin, antipsychotics and tricyclics.</li> <li>Potential for synergistic activity with medicines such as succinylcholine (suxamethonium) and other neuromuscular blocking agents, cholinergic agonists or beta-blocking agents that have effects on cardiac conduction.</li> <li>Potential for additive effects with other drugs that share the same side effects e.g. beta blockers and bradycardia, SSRIs and anorexia)</li> </ul> |
| Donepezil and galantamine | Metabolised via CYP3A4 and CYP2D6 pathways in the liver. Inhibitors of these pathways (e.g. erythromycin, clarithromycin, ketoconazole, fluvoxamine, fluoxetine, paroxetine) may increase drug levels and patients may experience increased side effects. A dose reduction may be required. Enzyme inducers (e.g. rifampicin, phenytoin, carbamazepine and alcohol) may reduce levels so care should be taken with concurrent prescribing.   |

#### Costs (Source: Drug Tariff and Dictionary of Drugs & Medical Devices June 2020)

All costs below are quoted for maximum doses. Treatment is often at maximum dose although practice varies. In the case of oral rivastigmine, the maximum is often not reached.

| Drug         | Formulation                         | Dose         | 28 days cost             | Annual Cost |
|--------------|-------------------------------------|--------------|--------------------------|-------------|
| Donepezil    | Tablets                             | 10mg od      | £1.36                    | £18         |
|              | Orodispersible tablets              | 10mg od      | £10.43                   | £136        |
| Rivastigmine | capsules                            | 6mg bd       | £33.00                   | £430        |
|              | Oral solution 2mg/ml (120ml bottle) | 6mg bd (6ml) | £193.64 (120ml = £96.82) | £2524       |
|              | Patches                             | 13.3/24      | £77.97                   | £1016       |

|                                     |   |                     |                        |       |
|-------------------------------------|---|---------------------|------------------------|-------|
|                                     |   | 9.5/24              | £19.97                 | £260  |
|                                     |   | 4.6/24              | £77.97                 | £1016 |
| <b>Galantamine</b>                  | Standard release tablets                                | 8mg bd              | £63.29                 | £825  |
|                                     |   | 12mg bd             | £77.27                 | £1007 |
|                                     | Modified release capsules (prescribed generically)      | 16mg od             | £64.90                 | £846  |
|                                     |   | 24mg od             | £79.80                 | £1040 |
|                                     | Modified release capsules (branded generic Gatalin XL®) | 16mg od             | £32.45                 | £423  |
|                                     |   | 24mg od             | £39.90                 | £520  |
| Oral solution 4mg/ml (100ml bottle) | 8mg bd (4ml)  | £240 (100ml = £120) | £1800                  |       |
|                                     | 12mg bd (6ml)   | £240                | £2640                  |       |
| <b>Memantine</b>                    | Tablets   | 20mg od             | £10.48                 | £136  |
|                                     | Orodispersible tablets                                  | 20mg od             | £49.98                 | £652  |
|                                     | Oral solution 10mg/ml                                   | 20mg od             | £61.77 (50ml = £55.15) | £741  |

## 9. Monitoring requirements in primary care.

Monitor for adverse effects and drug interactions (see section 8 for details and suggested actions). The most relevant are:

- Exacerbation of asthma and COPD
- Anorexia and weight loss
- GI ulcer or bleed
- AV node block as a possible cause of collapse
- Potential additive effects with other drugs that share the same side effects (e.g. beta-blockers and bradycardia; SSRIs and anorexia)

### Annual Monitoring Review in Primary Care

The following is a summary of the components to be included in the annual monitoring review of the patient:-

|  |   |   |
|--|---|---|
| <b>1. Compliance</b> - is the medication being taken properly?   |   |   |
| <b>2. Physical Health Monitoring</b>   |   |   |
| <b>Weight</b>  | If weight loss has started or accelerated after starting AChE inhibitor medication, this may be the cause   |   |
| <b>Pulse</b>   | If <60, carry out an ECG. If PR interval > 200ms, stop drug or discuss with mental health specialist  |   |
| <b>U+Es and LFTs</b>   | Renal or hepatic impairment may reduce an individual's tolerability to rivastigmine and/or donepezil  |   |
| <b>Overall tolerance to medication</b>   | GI symptoms - anorexia, nausea, vomiting and diarrhoea<br>Neurological symptoms – headaches, dizziness, drowsiness, syncope<br>See section 8 for full details and suggested actions |   |
| <b>3. Impact on global functioning</b>   |   |   |
| Functional and behavioural assessment is best made via a discussion with the patient and carer (it might be important to see the carer alone to elicit behavioural problems). [Rating scales do exist for functional, behavioural and global assessment but most were designed for research purposes and none has become widely established for practical clinical use. See Appendix 1 for available assessment scales.] |   |   |
| <b>Functional assessment</b>   | Impact on daily living. Is there declining function?  | Review whether referral to Social Services (HCS) is required for declining function |

|   |   |   |
|---|---|---|
| <b>Carer Impact</b>   | Does the carer value the effect of the medication?  | It is important to take into account the impact of the medication to the carer                      |
| <b>Behavioural assessment</b>   | New behavioural problems?<br>Is the patient displaying behavioural and psychological symptoms of dementia (BPSD)? | Review whether standard or urgent referral to SMHTOP via SPA is needed for new behavioural problems |
| <b>4. Cognitive Assessment</b>  |   |   |
| <ul style="list-style-type: none"> <li>Some patients are distressed by repeated use of formal cognitive scoring tests. Therefore, it is not always necessary to repeatedly use a formal scale to measure cognition as this can also be assessed via patient and carer interview. Use of formal cognitive scales is not mandatory.</li> <li>It is also important to consider the global functioning of the patient by discussion with the carer/relatives. It is often the case that no management change is likely whatever the result of the test (i.e. the global functional, behavioural and global assessments are positive and the dementia is not severe).</li> <li>However, in some cases a formal test can help find severe dementia and highlight that ongoing benefit of treatment is unlikely. An unexpectedly large change in a test score might prompt a conversation about other problems that need management – e.g. increased care package.</li> <li>When the use of a formal cognitive scoring test is appropriate (e.g. when there has been a significant deterioration in the global functioning), consider using either of the following open access primary care validated scales – 6CIT (six item cognitive impairment test) or GPCOG (the General Practitioner assessment of Cognition).<br/>See Appendix 1</li> </ul> |   |   |
| <b>5. Is the medication still of overall benefit?</b>   |   |   |

## 10. Stopping Medication

AChEIs should not be stopped because of disease severity alone in people with Alzheimer's disease. For GP management it is anticipated that if there is still an **overall** benefit and providing the patient is tolerating the treatment and there are no contraindications, the treatment will be maintained until such a time as it becomes inappropriate such as in extreme frailty or a severely impaired stage of dementia (e.g. swallowing difficulties).

Treatment should be stopped if the patient cannot tolerate side effects (see section 8 – adverse effects).

It is advisable to give reducing doses – e.g. donepezil 5 mg od for a month if the patient has been taking 10mg. Similar gradual reduction with other drugs may be used. Research evidence suggests there might not be a withdrawal reaction from AChEI medication (AD 2000 trial) but anecdotally these have been reported and therefore appears to be a reasonable precaution.

## 11. Triggers to consult with/refer to secondary care

- Difference of opinion between primary care team and carer about stopping medication
- Consideration of use of dual pharmacology therapy in patients with moderate or severe Alzheimer's disease, and a global impression that cognitive enhancement would be of benefit for the service user
- Uncertainty about side effects
- Behavioural problems that would require the community team whether or not the patient is taking anti-dementia medication.

### Appendix 1

### References and Assessment Scales

- **NICE TA 217** - Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease. NICE March 2011
- **NICE Dementia: assessment, management and support for people living with dementia and their carers (NG97)**. NICE June 2018: <https://www.nice.org.uk/guidance/ng97>
- **Mini-mental state examination** – (Folstein and Folstein 1974) – the publishers do not allow free use for health professionals
- **6CIT** – This is free to use for health professionals and easy to find online – (Brooke P, Bullock R; Validation of a 6 item cognitive impairment test with a view to primary care usage. Int J Geriatr Psychiatry. 1999 Nov; 14(11):936-40) <http://www.patient.co.uk/doctor/six-item-cognitive-impairment-test-6cit>
- **GPCOG** - This is free to use for health professionals and easy to find online (Brodaty et al, JAGS 2002; 50:530-534) <http://www.patient.co.uk/doctor/general-practitioner-assessment-of-cognition-gpcog-score>
- **Abbreviated Mental Test Score (AMTS)** – This is quick and popular in general hospitals. It is not validated in primary care, though compares well against MMSE in some research. (Hodgkinson HM (1972) Evaluation of a mental test score for assessment of mental impairment in the elderly. Age and Ageing 1, 233-8) <http://www.patient.co.uk/doctor/abbreviated-mental-test-amt>
- **Functional Activities Questionnaire (FAQ) in Older Adults with Dementia** – This measures instrumental activities of daily living (IADLs), such as preparing balanced meals and managing personal finances. Since functional changes are noted earlier in the dementia process with IADLs that require a higher cognitive ability compared to basic activities of daily living (ADLs), this tool is useful to monitor these functional changes over time. The FAQ may be used to differentiate those with mild cognitive impairment and mild Alzheimer's disease. <https://www.alz.org/careplanning/downloads/functional-activities-questionnaire.pdf>
- **Assessment of Motor and Process Skills (AMPS)**: a standardised observation-based evaluation of a person's quality of performance of relevant and chosen personal or domestic activities of daily living.
- **Model of Human Occupation Screening Tool (MoHOST)**: The MOHOST addresses client's motivation for occupation, pattern of occupation, communication/interaction, process, and motor skills, and environment. The MOHOST was designed to be used to document progress towards occupational therapy intervention goals as well as to screen for occupational therapy services.
- **Pool Activity Level (PAL) © 2015 Jackie Pool Associates**: The PAL Instrument contains a valid and reliable tool for assessing level of ability which is recommended in the National Clinical Practice Guideline for Dementia (NICE, 2006), for activities of daily living and for leisure activity. The instrument also contains profiling tools for interpreting the assessment in order to plan and deliver effective, enabling care and support.
- **Just checking** (<http://www.justchecking.co.uk/>) an activity monitoring system which can be used to establish routines and patterns of movement within the home. The information gained from this assessment can help inform decision making about future interventions and/or support needed, provide reassurance or as a baseline to compare against in the future if behaviours change.
- **Medichec Tool** (South London and Maudsley NHS Foundation Trust): a tool to assess anticholinergic burden, as medications with anticholinergic effects are known to increase the risk of cognitive impairment and dementia. Can be used to help clinicians identify which drugs have a cholinergic effect on cognition and defines the extent of this effect. <https://medichec.com/>

|         |   |
|---------|---|
| Version | 5.0 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include: <ul style="list-style-type: none"> <li>• Rebadging with HWE ICB and removal of ENHCCG and HVCCG headers</li> </ul> |
|---------|---|

|                       |  |
|-----------------------|--|
|                       | <ul style="list-style-type: none"> <li>Review date removed and replaced with standard statement.</li> </ul>  |
| Developed by          | ENH & SWH PMOT   |
| Approved by           | HMMC   |
| Date approved/updated | June 2016 updated Feb 2021   |
| Review date:          | The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available. |
| Superseded version    | 4.0  |