Integrated Medication Guidelines for the use of Donepezil, Galantamine, Rivastigmine and Memantine in Dementia

Donepezil, Galantamine, Rivastigmine and Memantine for the treatment of Dementia

NOTES to the GP

The information in the integrated medication guideline has been developed in consultation with CCGs in South East London. This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing Donepezil, Galantamine, Rivastigmine and Memantine for the treatment of Dementia. Prescribing should follow requirements in the South East London Interface Prescribing Policy. The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

The objectives of these guideline include the following:

- Safe Prescribing in Dementia
- Innovative thinking in dementia prescribing and care
- Prioritising patient and carer convenience
- Improving efficiencies and timely access to services
- Supporting primary care colleagues
- Rapid re-entry to services on discharge

These integrated medication guidelines form part of a wider management pathway for patients with Alzheimer's disease. Healthcare professionals should also ensure that the patient's social care needs are taken into consideration and that they are referred to local services as and when appropriate.
Ref: APCSCG/012
South East London Shared Care Prescribing Guideline for Donepezil, Galantamine, Rivastigmine and Memantine for
treatment of Dementia
Date approved: March 2019 Review date: March 2022 (or sooner if evidence or practice changes)

1- DEMENTIA MEDICATION PATHWAY

GP identifies possible cognitive impairment
Performs simple cognitive assessment and dementia blood screen (see page 3)

Referral to Memory Clinic

Memory Clinic assessment, diagnosis and further management including
suitability for dementia medication

Inform GP of AD or DLB (or mixed dementia) diagnosis and request GP
initiation of treatment. GP to contact memory service with any concerns

Where GP starts prescribing medication
to contact Memory Clinic with any concerns regarding recommendations

Memory Clinic monitors patient until dose stabilised (3-6 months)

Memory clinic discharges stable patient to GP.

GP continues prescribing dementia medication with 6-12 monthly review
Medication is continued irrespective of cognitive performance1
If medication appears to be causing problems discontinue or refer back for
advice

Any concerns GP calls for advice or refers back to Memory Clinic

Memory Clinic prioritises re-assessment
within 2-4 weeks

*AD = Alzheimer’s Disease
*DLB = Dementia with Lewy Bodies

2. AREAS OF RESPONSIBILITY

## Memory Clinic Consultant / Specialist team responsibilities

### Investigations, assessments and blood tests
1. Confirm diagnosis & communicate cognitive score to the GP. The sMMSE, ACE or other validated tools may be appropriate.
2. Specialist assessment:
   - Tests of cognitive domain
   - Clinical evaluation of non-cognitive domains (e.g. hallucinations, delusions, agitation, behaviour that challenges)
   - Assessment of activities of daily living (ADLs)
   - Assessment of global function
   - Likely compliance with treatment before drug is prescribed.
   - The main therapeutic targets should be confirmed (Cognition, Psychosis, Behaviour that challenges, ADL)
3. When clinically appropriate request CT or MRI brain scan.

### Supporting adherence and ongoing treatment
4. Discuss medication options with patient/carer and provide patient information leaflet (PIL) for drug prescribed.
5. Identify a carer who will undertake monitoring of adherence.
6. Seek agreement that treatment will be stopped if there are adverse effects.
7. Check for interactions with other medicines
8. Contact GP with plan or recommendation to initiate drug treatment.
9. Continue monitoring until patient stabilised on medication at optimum dose.
10. Review treatment at month one and again at month three before discharging patient to GP.
11. Seek carer’s views on patient’s condition at baseline & follow-up.

### Adverse effects and deterioration
12. Stop treatment if any of the following occur:
   - Poor concordance
   - Major adverse effects
   - Patient asks to stop
13. Report serious adverse effects to the MHRA via ‘yellow card system’.
14. Advise patient/carer on future care (for patient in their own home or nursing home) in situations where patient needs further care support.

### Other
15. If patient is prescribed concomitant antipsychotic by specialist team, ensure indication (and preferably duration/need for regular review is communicated to GP) – (see GP responsibilities below)
16. Review medication and cognitive burden with advice to GP.
17. Patients discharged to have easy and timely access back in to Memory Clinic/ alternative mental health service.

## General Practitioner responsibilities

### Before referral:
1. Confirm history of cognitive decline from patient or independent informant.
2. Simple initial cognitive assessment
3. Initial dementia blood screening (HbA1c, FBC, U&E, Bone profile, B12, folate, TFTs, LFTs, CRP - HIV and syphilis if indicated)
4. Urinalysis, BP & heart rate.
5. Consider performing ECG if a cardiac caution to cholinesterase inhibitor treatment is suspected (e.g. sick sinus syndrome or other supraventricular conduction abnormalities); or where indicated. Use community ECG hub if available.
6. Ensure that the patient’s social care needs are taken into consideration and that they are referred to local services as
and when appropriate.

7. Consider minimising the use of medicines associated with increased anticholinergic burden, and if possible look for alternatives when assessing whether to refer a person with suspected dementia for diagnosis and during medication reviews. The Anticholinergic Effect on Cognition (AEC) scale should be used to identify and assess the anticholinergic burden of drugs in patients (www.medichec.com).

After confirmation of diagnosis by Memory Clinic:
8. Initiate medication as recommended or continue prescribing treatment.
9. Check for interactions with other medicines
10. Highlight the importance of adherence to treatment.
11. Support & educate patients/carers

Monitoring of adverse effects and deterioration:
12. Review patients discharged from secondary care [stable on dementia medication] at least 12 monthly.
13. Monitor for adverse effects and report any serious reactions to the MHRA via the ‘yellow card system’.
14. Call Memory Clinic for any concerns regarding memory or dementia medication.
15. Refer back to Memory Clinic if reassessment is required.
16. Stop treatment if urgent need arises.
17. If patient is prescribed concomitant antipsychotic drugs – ensure clear indication and duration of therapy is documented and that antipsychotic is reviewed at least every 6 weeks initially until the patient is clinically stable and tolerating it. Thereafter, antipsychotic review can be every 3-6 monthly but ensure there are procedures in place for regular reviews and reporting of adverse effects.

Other
18. Ensure patient is on the QOF dementia register.

Patient's / Carer’s responsibilities
- Ensure adverse effects, deterioration and response to medicines is reported to Mental Health Team/ consultant and GP
- Report any changes in disease symptoms to the GP or specialist.
- Take medicines as agreed and do not share medicines.

Test Results/ Investigations
Results of all tests and investigations should be copied by/ to both consultant and GP.

3. CLINICAL INFORMATION
NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for Donepezil, Galantamine, Rivastigmine or Memantine prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Place in Therapy
Acetylcholinesterase inhibitors (donepezil) are recommended (and licensed) for the 1st line treatment of people with Alzheimer's Disease (AD) of mild to moderate severity (and treatment of Parkinson's Disease Dementia with rivastigmine only). Memantine monotherapy is recommended as an option (and licensed) for people with moderate AD where acetylcholinesterase inhibitors have not been tolerated or are contraindicated and for severe AD.

In line with NICE guidance¹:
For people with established AD who are already taking an acetylcholinesterase inhibitor:
- Consider memantine in addition to an acetylcholinesterase inhibitor if they have moderate disease
- Offer memantine in addition to an acetylcholinesterase inhibitor if they have severe disease
(GPs may start treatment with memantine without taking advice from specialist clinician)
See appendix 1 for guidance in the use of memantine in combination therapy.

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

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.

Do not offer AChE inhibitors or memantine to people with frontotemporal dementia or to people with cognitive impairment caused by multiple sclerosis.
**Dose & route of administration**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosing</th>
<th>Titration week and dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DONEPEZIL (tablets, orodispersible tablets,</td>
<td>Daily (oral)</td>
<td>1</td>
</tr>
<tr>
<td>oral solution)</td>
<td></td>
<td>5mg</td>
</tr>
<tr>
<td>GALANTAMINE (modified release capsules)</td>
<td>Daily (oral)</td>
<td>8mg</td>
</tr>
<tr>
<td>GALANTAMINE (tablets, oral solution)</td>
<td>Twice daily (oral)</td>
<td>4mg</td>
</tr>
<tr>
<td>RIVASTIGMINE (oral capsules, oral solution)</td>
<td>Twice daily (oral)</td>
<td>1.5mg</td>
</tr>
<tr>
<td>RIVASTIGMINE (patch)</td>
<td>Daily (clean dry</td>
<td>4.6mg/</td>
</tr>
<tr>
<td></td>
<td>skin)</td>
<td>24hrs</td>
</tr>
<tr>
<td>MEMANTINE (scored tablets, oral solution)</td>
<td>Daily (oral)</td>
<td>5mg</td>
</tr>
</tbody>
</table>

**Duration of treatment**

Medication is continued even with evidence of cognitive decline so long as it is tolerated and patient is able to take it regularly.

**Criteria for stopping treatment and how to stop**

If a patient does not tolerate one acetylcholinesterase inhibitor (e.g. due to diarrhoea), it may be reasonable to try another acetylcholinesterase inhibitor (see SPC for full details) prior to changing to memantine. Stop treatment if any of the following occur: • Poor concordance • Major adverse effects • Patient asks to stop

Do not stop acetylcholinesterase inhibitors in people with AD because of severity of disease alone. If stopping treatment, a gradual withdrawal over 1-4 weeks (depending on drug, preparation and dose) is suggested where possible. Keep the patient under regular review. If serious adverse effects occur, stop immediately. Contact specialist or Medicines Information for advice if needed.

**Monitoring Requirements including frequency**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency of monitoring</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini Mental State Examination (sMMSE) / global,</td>
<td>At diagnosis and review within three-six months after</td>
<td>Continue acetylcholinesterase inhibitor (AChEI) treatment unless medication not tolerated</td>
</tr>
<tr>
<td>functional and behavioural assessment</td>
<td>commencing treatment (specialist).</td>
<td>Continue prescribing even where an sMMSE is less than 10, particularly where the medication is tolerated and the score does not represent severe dementia, e.g. patients with learning difficulties, speech problems or where English is not the first language.</td>
</tr>
<tr>
<td>Heart rate (HR)</td>
<td>By primary or secondary care before starting treatment and</td>
<td>If HR is less than 50bpm do not initiate AChEI. If AChEI associated bradycardia occurs (less than 50bpm) stop treatment. Cardiology assessment/ opinion may be required.</td>
</tr>
<tr>
<td></td>
<td>then as and when clinically indicated and annually during a</td>
<td></td>
</tr>
<tr>
<td></td>
<td>patient medication review.</td>
<td></td>
</tr>
</tbody>
</table>
| Blood Pressure (BP)                            | By primary or secondary care before starting treatment and    | Review medication, adjust dose (consider discontinuing) and refer to secondary care for advice if:
|                                               | then as and when clinically indicated and annually during a   | (a) syncope occurs (donepezil and galantamine) or<br>
|                                               | patient medication review.                                    | (b) hypertension occurs (galantamine and memantine)                |
| ECG (in patients with cardiac history)         | By primary or secondary care before initiation of treatment   | If ECG abnormal, suitability for dementia medication will<br>
|                                               | where there are suspected cardiac cautions (e.g. sick sinus   | be considered in secondary care. Cardiac re-assessment/ opinion may be required. |
|                                               | syndrome or other supraventricular conduction abnormalities); |                                                                         |
|                                               | or where indicated. Where there is access to a community hub |                                                                         |
|                                               | refer there for ECG.                                          |                                                                         |
| Renal and liver function                       | By GP before starting treatment.                              | If deterioration in renal or liver function, follow recommendation for individual medicine. Liaise with |

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**South East London Area Prescribing Committee. A partnership between NHS organisations in South East London: Bexley, Bromley, Greenwich, Lambeth, Lewisham and Southwark Clinical Commissioning Groups (CCGs) and GSTFT/KCH /SLAM/ & Oxleas NHS Foundation Trusts/Lewisham & Greenwich NHS Trust**
South East London Shared Care Prescribing Guideline for Donepezil, Galantamine, Rivastigmine and Memantine for treatment of Dementia

Date approved: March 2019 Review date: March 2022 (or sooner if evidence or practice changes)

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review regularly at start of treatment by specialist and GP. By GP annually, or as requested by patient/carer by appointment.</td>
<td>Persist with treatment if mild side effects are experienced during initiation or up-titration of treatment. Stop treatment if severe persistent gastro-intestinal side effects and refer to Memory Clinic specialist. Serious side effects should be reported to the MHRA through the yellow card scheme (yellowcard.mhra.gov.uk).</td>
</tr>
</tbody>
</table>

NB Teams will work together to make sure tests and monitoring are done in a patient-centred way

**Summary of Adverse Effects**
Reminder: this list is not exhaustive - for full details of adverse effects and all potential drug interactions refer to latest Summary of Product Characteristics (SPC) for the drug, available via www.medicines.org.uk.

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Frequency</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholinesterase inhibitors</td>
<td>Very common</td>
<td>Gastro-intestinal symptoms (incl. anorexia, nausea, vomiting, diarrhoea) Generally mild and transient and disappear within a few days of treatment. Can be minimised by taking drug after food. If symptoms persist discuss with/refer to specialist who may reduce dose or try an alternative acetylcholinesterase inhibitor or switch to memantine.</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Headache, fatigue, dizziness and muscle cramps Generally mild &amp; transient. The ability of the patient to continue driving or operating complex machinery should be evaluated. Consult specialist if problematic for the patient. May need dose reduction/discontinuation.</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Agitation, confusion, insomnia, abnormal dreams and nightmares Consult specialist if problematic for the patient. May need dose reduction/discontinuation.</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Syncope Consult specialist. May need dose reduction/discontinuation. In investigating seizures, the possibility of heart block or long sinusal pauses should be considered.</td>
</tr>
<tr>
<td></td>
<td>Common/ Uncommon</td>
<td>Bradycardia Seek urgent review. Stop treatment and consult specialist. Caution in “sick sinus syndrome”, sinoatrial or atrioventricular block or concomitant treatment with digoxin or beta-blockers.</td>
</tr>
<tr>
<td></td>
<td>Uncommon / rare</td>
<td>May enhance predisposition to peptic ulceration Care with active or predisposition to gastric or duodenal ulcers. Consult specialist to consider discontinuation of treatment. Patient should be regularly monitored for symptoms.</td>
</tr>
<tr>
<td></td>
<td>Uncommon / rare</td>
<td>May lower seizure threshold Extreme caution in epilepsy. Review treatment with specialist if seizures develop as may be caused by underlying disease. The possibility of heart block or long sinusal pauses should be considered.</td>
</tr>
<tr>
<td></td>
<td>No data available</td>
<td>May cause bronchoconstriction Caution in COPD or asthma, consult specialist to review treatment.</td>
</tr>
</tbody>
</table>
### Memantine

*See Summary of Product Characteristics (SPC) for full list or BNF*

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memantine continued</td>
<td>Common</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Frequency</th>
</tr>
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<tbody>
<tr>
<td>Somnolence</td>
<td>Common</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Common</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Common</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>Common</td>
</tr>
<tr>
<td>Constipation</td>
<td>Common</td>
</tr>
<tr>
<td>Headache</td>
<td>Common</td>
</tr>
<tr>
<td>Elevated liver function test</td>
<td>Common</td>
</tr>
<tr>
<td>Drug hypersensitivity</td>
<td>Common</td>
</tr>
<tr>
<td>Fungal infections</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Gait abnormal</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Venous thrombosis/thromboembolism</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Confusion, hallucinations, psychosis, fatigue</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Unknown</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>Uncommon</td>
</tr>
<tr>
<td>May lower seizure threshold</td>
<td>Very rare</td>
</tr>
<tr>
<td>Hepatic impairment</td>
<td>No data available</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>No data available</td>
</tr>
</tbody>
</table>

#### May exacerbate bladder outflow problems
- **No data available**
  - **Caution if history of prostatic conditions, urinary retention. (Avoid galantamine in urinary retention or post bladder surgery).**

#### Hepatic impairment
- **No data available**
- **Avoid in severe impairment, caution in mild/moderate impairment. See BNF guidance for each drug and seek advice from consultant hepatologist.**

#### Renal impairment (galantamine, rivastigmine)
- **No data available**
  - **Avoid in severe impairment (except donepezil which is not affected by renal impairment). Caution in mild/moderate impairment. See BNF guidance for each drug and seek advice from consultant nephrologist.**

#### Memantine

*See Summary of Product Characteristics (SPC) for full list or BNF*

<table>
<thead>
<tr>
<th>Common: &gt;1/100, &lt;1/10</th>
<th>Uncommon: &gt;1/1000, &lt;1/100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somnolence</td>
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</tr>
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<td>Renal impairment</td>
<td>No data available</td>
</tr>
</tbody>
</table>

#### Somnolence
- **Common**
  - **The ability of the patient to continue driving or operating complex machinery should be evaluated. Consult specialist if problematic for the patient.**

#### Dizziness
- **Common**
  - **Refer back to specialist if severe or is not self limiting. Consider prn or regular laxative.**

#### Hypertension
- **Common**
  - **Caution in those with uncontrolled hypertension or cardiac disease. Review treatment with a specialist if this develops. May need dose reduction/discontinuation.**

#### Dyspnoea
- **Common**
  - **Caution in those with COPD or asthma, consult specialist to review treatment.**

#### Constipation
- **Common**
  - **Refer back to specialist if severe or is not self limiting. Consider prn or regular laxative.**

#### Headache
- **Common**
  - **Refer back to specialist if severe or is not self limiting.**

#### Elevated liver function test
- **Common**
  - **Refer back to specialist for review.**

#### Drug hypersensitivity
- **Common**
  - **Stop and refer back to specialist.**

#### Fungal infections
- **Common**
  - **Refer back to specialist if severe.**

#### Gait abnormal
- **Uncommon**
  - **Refer back to specialist if severe.**

#### Venous thrombosis/thromboembolism
- **Uncommon**
  - **Refer for treatment of VTE, and review memantine with a specialist.**

#### Confusion, hallucinations, psychosis, fatigue
- **Uncommon**
  - **Refer back to specialist for review.**

#### Pancreatitis
- **Unknown**
  - **Stop if severe, refer back to specialist.**

#### Vomiting
- **Uncommon**
  - **Stop if severe, refer back to specialist.**

#### Cardiac failure
- **Uncommon**
  - **Stop and refer back to specialist.**

#### May lower seizure threshold
- **Very rare**
  - **Extreme caution in epilepsy. Review treatment with specialist if seizures develop as may be caused by underlying disease.**

#### Hepatic impairment
- **No data available**
  - **Avoid in severe impairment. Stop treatment and consult hepatologist.**

#### Renal impairment
- **No data available**
  - **See BNF guidance: Avoid if eGFR <5mL/min/1.73m²; reduce dose to 10mg/day if eGFR 5-29mL/min/1.73m²; reduce dose to 10mg/day if eGFR 30-49mL/min/1.73m² and if well tolerated after 7 days increase to 20mg in 5mg steps.**
The table below is reproduced from the Maudsley Prescribing Guidelines 13th edition. The list of drug interactions presented in the table is not exhaustive, prescribers should also refer to individual SPCs for the medicines concerned for further detail on potential drug interactions (via www.medicines.org.uk). Caution is advised with other drugs that are also inhibitors or enhancers of CYP 3A4 and 2D6 enzymes.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Metabolism</th>
<th>Plasma levels increased by</th>
<th>Plasma levels decreased by</th>
<th>Pharmacodynamic interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil (Aricept®)</td>
<td>Substrate at 3A4 and 2D6</td>
<td>Ketoconazole, Itraconazole, Erythromycin, Quinidine, Fluoxetine, Paroxetine</td>
<td>Rifampicin, Phenytoin, Carbamazepine, Alcohol</td>
<td>Antagonistic with anticholinergic drugs and competitive neuromuscular blockers (e.g. tubocurarine). Potential for synergistic activity with cholinomimetics such as depolarising neuro-muscular blocking agents (e.g. succinylcholine), cholinergic agonists and peripherally acting cholinesterase inhibitors (e.g. neostigmine). Beta blockers, amiodarone or calcium channel blockers may have additive effects on cardiac conduction. Caution with concomitant use of drugs known to induce QT prolongation and/or torsade de pointes. Movement disorders and Neuroleptic Malignant Syndrome have occurred with concomitant use of antipsychotics and cholinesterase inhibitors. Concurrent use with seizure lowering agents may result in reduced seizure threshold.</td>
</tr>
<tr>
<td>Rivastigmine (Exelon®)</td>
<td>Non-hepatic metabolism</td>
<td>Metabolic interactions appear unlikely. Rivastigmine may inhibit the butyrylcholinesterase mediated metabolism of other substances (e.g. cocaine). Smoking tobacco increases the clearance of rivastigmine</td>
<td>None known</td>
<td>Antagonistic effects with anticholinergic and competitive neuromuscular blockers (e.g. tubocurarine). Potential for synergistic activity with cholinomimetics such as depolarising neuro-muscular blocking agents (e.g. succinylcholine) - cholinergic agonists (e.g. ethanecol) or peripherally acting cholinesterase inhibitors (e.g. neostigmine). Synergistic effects on cardiac conduction with beta blockers, amiodarone, calcium channel blockers. Caution with concomitant use of drugs known to induce QT prolongation and/or torsade de pointes. Movement disorders and Neuroleptic Malignant Syndrome have occurred with concomitant use of antipsychotics and cholinesterase inhibitors. Concurrent use with metoclopramide may result in increased risk of EPSEs.</td>
</tr>
<tr>
<td>Galantamine (Reminyl®)</td>
<td>Substrate at 3A4 and 2D6</td>
<td>Ketoconazole, Erythromycin, Ritonavir, Quinidine, Paroxetine, Fluoxetine, Fluvoxamine, Amitriptyline</td>
<td>None known</td>
<td>Antagonistic effects with anticholinergic and competitive neuromuscular blockers (e.g. tubocurarine). Potential for synergistic activity with cholinomimetics such as depolarising neuro-muscular blocking agents (e.g. succinylcholine), cholinergic agonists and peripherally acting cholinesterase inhibitors (e.g. neostigmine). Possible interaction with agents that significantly reduce heart rate (e.g. digoxin, ß blockers, certain calcium-channel blockers and amiodarone). Caution with concomitant use of drugs known to induce QT prolongation and/or torsade de pointes (manufacturer recommends ECG in such cases). Movement disorders and Neuroleptic Malignant Syndrome have occurred with concomitant use of antipsychotics and cholinesterase inhibitors.</td>
</tr>
</tbody>
</table>
Drug-drug interactions’ continued

<table>
<thead>
<tr>
<th>Drug</th>
<th>Metabolism</th>
<th>Plasma levels increased by</th>
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<th>Pharmacodynamic interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memantine (Exiba®)</td>
<td>Primarily non-hepatic metabolism Renally eliminated</td>
<td>Cimetidine Ranitidine Procainamide Quinidine Quinine Nicotine Trimethoprim</td>
<td>None known (Possibility of reduced serum level of hydrochlorothiazide when co administered with memantine).</td>
<td>Effects of L-dopa, dopaminergic agonists, Selegiline and anticholinergics may be enhanced. Effects of barbiturates and antipsychotics may be reduced. Avoid concomitant use with amantadine, ketamine and dextromethorphan -increased risk of CNS toxicity. One published case report on possible risk for phenytoin and memantine combination Dosage adjustment may be necessary for antispasmodic agents, dantrolene or baclofen when administered with memantine. A single case report of myoclonus and confusion when co-administered with co-trimoxazole or trimethoprim</td>
</tr>
</tbody>
</table>

Information provided to the patient

Patient information leaflets (from NHS Choices)

NHS Choices Dementia

Patient information leaflets for specific medicines available at www.medicines.org.uk (patient leaflet) for memantine, rivastigmine, galantamine and donezepil

Evidence Base for treatment and key references

1. NICE Clinical Guideline 42, Dementia: supporting people with dementia and their carers in health and social care (updated June 2018)
### Communication and Support

#### Memory Services

<table>
<thead>
<tr>
<th>Southwark &amp; Lambeth Memory Service (SLMS)</th>
<th>Bexley Memory Service</th>
<th>Bromley Memory Service</th>
<th>Greenwich Memory Service</th>
<th>Lewisham Memory Service</th>
</tr>
</thead>
<tbody>
<tr>
<td>151 Blackfriars Road, London SE1 8EL</td>
<td>Bexleyheath Centre, DA6 8DX</td>
<td>Bridgeways, Turpton Lane BR2 8JA</td>
<td>Memorial Hospital Shooters Hill SE18 3RZ.</td>
<td>91 Granville Park Lewisham SE13 7DW</td>
</tr>
<tr>
<td>Tel: 020 3228 0570</td>
<td>Tel: 020 8301 7900</td>
<td>Tel: 020 8629 4900</td>
<td>Tel: 020 8836 8519</td>
<td>Tel: 020 3228 0939</td>
</tr>
<tr>
<td><a href="mailto:slmsreferrals@slam.nhs.uk">slmsreferrals@slam.nhs.uk</a></td>
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</tbody>
</table>

#### Consultant/Specialist Team

- Dr Justin Sauer, Consultant Psychiatrist
  - Tel: 020 3228 1640
  - Email: Justin.sauer@slam.nhs.uk

#### Medication-Prescribing advice, interactions etc

- Delia Bishara, Consultant Pharmacist, MHOA
  - Tel: 020 3228 1624 / 1629
  - Email: delia.bishara@slam.nhs.uk (Tue, Thu & Fri)

#### Medicines Information

- 01322 625002 or oxl-tr.medicinesinfo@nhs.net

#### Dementia Support Hubs

- Greenwich Dementia information hub: [www.greenwichcommunitydirectory.org.uk](http://www.greenwichcommunitydirectory.org.uk)
  - or call 020 8921 8533
- Bromley Dementia support hub: [https://www.bromleydementiasupporthub.org.uk/](https://www.bromleydementiasupporthub.org.uk/)

#### Links and Referral Options to other Services

These integrated medication guidelines form part of a wider management pathway for patients with dementia. Healthcare professionals should also ensure that the patient’s social care needs are taken into consideration and that they are referred to local services as and when appropriate.

**Social services:**
- Lambeth Duty phone: 020 7926 5555
- Southwark Duty phone: 020 7525 3324

**Alzheimer’s Society:** [http://www.alzheimers.org.uk/](http://www.alzheimers.org.uk/)

- Alzheimer’s Society for Southwark & Lambeth Tel: 020 7735 5850  southwarkandlambeth@alzheimers.org.uk
- Alzheimer’s Society for Greenwich Tel: 01322 559308 Email: dagreenwich@alzheimers.org.uk

You can request a dementia advisor at the society branch who can signpost and organise peer support, carer support and advice.

**Age UK:** [https://www.ageuk.org.uk/](https://www.ageuk.org.uk/)

- Lambeth: [https://www.ageuk.org.uk/lambeth](https://www.ageuk.org.uk/lambeth)
  - Ring 020 7346 6800
  - Ring 020 7701 9700

**National dementia helpline:** 0300 222 1122 can provide information, support, guidance and signposting to other appropriate organisations. The Helpline is usually open from:

- 9am - 8pm Monday to Wednesday
- 9am - 5pm on Thursday and Friday
- 10am - 4pm on Saturday and Sunday
Guidance for healthcare professionals in primary care on the use of Memantine for Dementia – in line with updated Dementia NICE guidelines 2018

Monotherapy
Memantine monotherapy is recommended as an option for managing Alzheimer’s disease (AD) in people with:

- moderate Alzheimer’s disease who are intolerant of or have a contraindication to acetylcholinesterase inhibitors (AChEIs) or
- severe Alzheimer’s disease. Prescribers should only start memantine (or an AChEI) on the advice of a specialist, but a GP can do so if they have specialist expertise in diagnosing and treating AD.

Memantine should also be considered:

- for people with dementia with Lewy bodies if AChE inhibitors are not tolerated or are contraindicated and
- for people with vascular dementia but only if they have suspected comorbid Alzheimer’s disease, Parkinson's disease dementia or dementia with Lewy bodies.

Once a decision has been made to start memantine (or AChEI), the first prescription may be made in primary care (in line with the local integrated care guideline for dementia).

Combination therapy
For people with an established diagnosis of AD who are already taking an AChE inhibitor:

- consider memantine in addition to an AChEI if they have moderate disease
- offer memantine in addition to an AChEI if they have severe disease

If a person has an established diagnosis of AD and is already taking an acetylcholinesterase inhibitor, primary care prescribers may start treatment with memantine without taking advice from a specialist.

What is memantine?
NMDA receptor antagonist which blocks the effects of glutamate. Glutamate is released in increased amounts in Alzheimer’s disease and this excessive stimulation causes neuronal damage.

What are the therapeutic effects of memantine?
It can slow progression of symptoms, like disorientation. It may help with delusions, aggression and agitation.

Dosage and how to start?
Starting dose is 5mg daily. Increasing the dose weekly by 5mg until maximum dose of 20mg daily.

Precautions and contraindications?
Caution is recommended in patients with epilepsy, former history of convulsions or patients with predisposing factors for epilepsy.

Renal impairment
In patients with mildly impaired renal function (creatinine clearance 50 – 80 ml/min) no dose adjustment is required. In patients with moderate renal impairment (creatinine clearance 30 – 49 ml/min) daily dose should be 10 mg per day. If tolerated well after at least 7 days of treatment, the dose could be increased up to 20 mg/day according to standard titration scheme. In patients with severe renal impairment (creatinine clearance 5 – 29 ml/min) daily dose should be 10 mg per day. Avoid if eGFR less than 5 mL/minute/1.73 m².

Hepatic impairment
In patients with mild or moderate hepatic impaired function (Child-Pugh A and Child-Pugh B), no dose adjustment is needed. No data on the use of memantine in patients with severe hepatic impairment are available. Administration of memantine is not recommended in patients with severe hepatic impairment.

What are the possible side effects of memantine?
In general, the observed side effects are mild to moderate.

Common (affects 1 to 10 users in 100):
- Headache, sleepiness, constipation, elevated liver function tests, dizziness, balance disorders, shortness of breath, high blood pressure and drug hypersensitivity
**Uncommon (affects 1 to 10 users in 1,000):**
- Tiredness, fungal infections, confusion, hallucinations, vomiting, abnormal gait, heart failure and venous blood clotting (thrombosis/thromboembolism)

**Very Rare (affects less than 1 user in 10,000):**
- Seizures

**Not known (frequency cannot be estimated from the available data):**
- Inflammation of the pancreas, inflammation of the liver (hepatitis) and psychotic reactions

**Drug interactions (prescribers should also refer to individual product information for specific drugs):**
- L-dopa, dopaminergic agonists, and anticholinergics may be enhanced by concomitant treatment with 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 dose adjustment may be necessary.
- Concomitant use of memantine and amantadine, ketamine or dextromethorphan should be avoided, owing to the risk of pharmacotoxic psychosis. There is one published case report on a possible risk also for the combination of memantine and phentyoin.
- 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.
- There may be a possibility of reduced serum level of hydrochlorothiazide (HCT) when memantine is co-administered with HCT or any combination with HCT.
- In post-marketing experience, isolated cases with international normalized ratio (INR) increases have been reported in patients concomitantly treated with warfarin. Although no causal relationship has been established, close monitoring of prothrombin time or INR is advisable for patients concomitantly treated with oral anticoagulants.

**What needs to happen when the person is stable on treatment?**
A person with dementia continues to benefit from a regular review of their condition and update of their care plan. This should also include a check of BP and pulse rate and assessment of changes in cognition and social needs. Review of care plan should be at least annually, and at any point when a significant change has occurred for the person with dementia.

**When to stop treatment?**
Memantine should not be stopped because of severity of illness alone; it should be continued even if there is evidence of cognitive decline, so long as it is tolerated and patient is able to take it regularly.

**References:**
- NICE Clinical Guideline 42, [Dementia: supporting people with dementia and their carers in health and social care](https://www.nice.org.uk/guidance/cg42) (June 2018)
- British National Formulary: [www.BNF.org](http://www.BNF.org) (last updated August 2018)