Information for Prescribing Anti-dementia Drugs
November 2012

The aim of this document is to provide information about the prescribing of anti-dementia medication for adult patients with dementia following an assessment and stabilisation of treatment in the memory clinic.

The information will ensure there is a consistent rationale for prescribing in memory clinics across the Health Board and that GPs will have sufficient information to enable them to safely undertake ongoing prescribing of anti-dementia medication.

NICE Recommendations


In summary, the review advises that:

- The three acetylcholinesterase (AChE) inhibitors, donepezil, galantamine and rivastigmine are recommended as options for the treatment of mild to moderate Alzheimer’s disease (AD).
- Memantine is recommended as an option for people with moderately severe to severe Alzheimer’s disease
- The medication with the lowest acquisition cost should be initiated however, if this is not suitable for the patient, another medication could be prescribed.

Choice of treatment

All anti-dementia medication will be prescribed by the approved name, not by proprietary (brand) name.

A generically available preparation of donepezil, galantamine or rivastigmine (chosen according to current acquisition cost and specialist preference / experience), will be considered for patients with mild to moderate Alzheimer’s disease, unless contra-indicated.

A patient with Alzheimer’s disease may be offered one of the other two drugs if the first is not tolerated or due to lack of clinical efficacy.
Donepezil Hydrochloride

**Licensed indications:** symptomatic treatment of mild to moderately severe Alzheimer’s dementia.

**Pharmacology:** Reversible inhibitor of acetylcholinesterase.

**Preparations available:** 5mg and 10mg tablets. Orodispersible tablets are available for those patients with swallowing difficulties.

**Recommended dosage and administration**

**Initial dose:** 5 mg once daily, increased if necessary after one month to 10mg once daily.

**Usual maintenance dose:** 5mg to 10mg once daily.

**Maximum dose:** 10mg once daily.

* Orodispersible tablets should be placed on the tongue, allowed to disperse and swallowed.

**Contra-indications:** Patients with a known hypersensitivity to donepezil (or other piperidine derivatives), or to any of the excipients used in the formulations. Breastfeeding.

**Cautions:** Sick sinus syndrome or other supraventricular conduction abnormalities; susceptibility to peptic ulcers; asthma, chronic obstructive pulmonary disease, pregnancy.

**Hepatic impairment:** caution in mild to moderate impairment, no information available for severe impairment.

**Drug interactions:** Check current BNF Appendix 1 before co-prescribing other drugs. Acetylcholinesterase inhibitors act as **parasympathomimetics**

- Antimuscarinics - Effects of Acetylcholinesterase inhibitors antagonised by antimuscarinics.
- Muscle Relaxants – Acetylcholinesterase inhibitors can also enhance the effect of the depolarising muscle relaxants and antagonise the effects of non-depolarising muscle relaxants.
- Ketoconazole, quinidine, itraconazole, erythromycin, fluoxetine inhibit donepezil metabolism (in vitro studies).
- Rifampicin, phenytoin, carbamazepine and alcohol may reduce the levels of donepezil (in vitro studies).

**Adverse effects:** most common – diarrhoea, muscle cramps, fatigue, nausea, vomiting, headache and insomnia.

**If the patient develops seizures, pancreatitis, cardiac, gastrointestinal or ophthalmological disorders withhold drug and discuss with the specialist team**
Galantamine

**Licensed indications:** symptomatic treatment of mild to moderately severe dementia of the Alzheimer type.

**Pharmacology:** competitive and reversible inhibitor of acetylcholinesterase, and also an enhancer of the intrinsic action of acetylcholine on nicotinic receptors.

**Preparations available:** 8mg and 12mg galantamine tablets, 8mg, 16mg and 24mg modified release capsules and oral solution.

The modified release preparations are now initiated first line however an oral solution is available for those patients with swallowing difficulties.

**Recommended dosage and administration**

**Initial dose:**
- Galantamine XL Capsules: 8mg once daily for 4 weeks, increased to 16mg once daily for 4 weeks.
- Galantamine Oral solution: 4mg twice daily for 4 weeks, increased to 8mg twice daily for 4 weeks.

**Usual maintenance dose:**
- Galantamine XL Capsules: 16 to 24mg once daily.
- Galantamine Oral solution: 8 to 12mg twice daily.

**Maximum dose:**
- Galantamine XL Capsules: 24mg once daily.
- Galantamine Oral solution: 12mg twice daily.

**Contra-indications:** Patients with a known hypersensitivity to galantamine (or other carbamate derivatives) or to any of the excipients used in the formulations. Breastfeeding.

Avoid in urinary retention, gastro-intestinal obstruction, and while recovering from bladder or gastro-intestinal surgery.

Severe hepatic (Child –Pugh score >9) and severe renal (creatinine clearance < 9ml/min).

**Hepatic impairment:**
- for *immediate-release* preparations in moderate impairment, initially 4 mg once daily (preferably in the morning) for at least 7 days, then 4 mg twice daily for at least 4 weeks; max. 8 mg twice daily; avoid in severe impairment.
- for *modified-release* preparations in moderate impairment, initially 8 mg on alternate days (preferably in the morning) for 7 days, then 8 mg once daily for 4 weeks; max. 16 mg daily; avoid in severe impairment.
(Galantamine continued)

**Cautions:** Cardiac disease (including sick sinus syndrome or other supraventricular conduction abnormalities), unstable angina, congestive heart failure); electrolyte disturbances; susceptibility to peptic ulcers; asthma, chronic obstructive pulmonary disease, pulmonary infection; history of seizures, pregnancy.

**Drug interactions:** Check current BNF Appendix 1 before co-prescribing other drugs. Acetylcholinesterase inhibitors act as *parasympathomimetic*:

- Antimuscarinics - Effects of Acetylcholinesterase inhibitors antagonised by antimuscarinics.
- Muscle Relaxants – Acetylcholinesterase inhibitors can also enhance the effect of the depolarising muscle relaxants and antagonise the effects of non-depolarising muscle relaxants. Galantamine enhances the effects of suxamethonium.
- Erythromycin - can increase plasma concentration of galantamine.
- Ketoconazole - can increase plasma concentration of galantamine.
- Paroxetine - can increase plasma concentration of galantamine.

**Adverse effects:** Most common - nausea, vomiting, diarrhoea, abdominal pain, dyspepsia, anorexia, fatigue, dizziness, headache, somnolence and weight decrease.

**If the patient develops seizures, pancreatitis, cardiac, gastrointestinal or ophthalmological disorders withhold drug and discuss with the specialist team**
Rivastigmine

**Licensed indications:** symptomatic treatment of mild to moderately severe Alzheimer's dementia.

*Rivastigmine capsules (not the transdermal patches) are also licensed for the treatment of mild to moderately severe dementia in Parkinson's disease.

**Pharmacology:** Pseudo-irreversible acetylcholinesterase inhibitor.

**Preparations available:** 1.5mg, 3mg, 4.5mg and 6mg capsules, 2mg in 1ml oral solution and patches of 4.6mg / 24hour  9.5 mg / 24hour.

**Recommended dosage and administration**

**Initial dose:**
Rivastigmine capsules / oral solution: 1.5mg twice daily, increased in steps of 1.5mg twice daily at intervals of at least 2 weeks according to response and tolerance.

Rivastigmine patches: 4.6mg/24 hours; if well tolerated increase to 9.5mg/24 hours patch daily after at least 4 weeks.

**Usual maintenance dose:**
Rivastigmine capsules / oral solution:  3 to 6mg twice daily. If treatment is interrupted for more than several days, treatment should be retitrated from 1.5mg twice daily.
Rivastigmine patches: 4.6 to 9.5mg/24 hours; if patch not applied for more than several days, treatment should be restarted with 4.6mg/24 hours patch.

**Maximum dose:**
Rivastigmine capsules / oral solution: 6mg twice daily.
Rivastigmine patches: 9.5mg/24 hours.

Note - When switching from oral to transdermal therapy, patients taking 3–6 mg by mouth daily should initially switch to 4.6 mg/24 hours patch (then titrate as above); patients taking 9–12 mg by mouth daily should switch to 9.5 mg/24 hours patch. The first patch should be applied on the day following the last oral dose.

**Contra-indications:** Patients with a known hypersensitivity to rivastigmine (or other carbamate derivatives) or to any of the excipients used in the formulations. Breastfeeding.
Previous application site reactions suggestive of allergic contact dermatitis (for patches).
Patients with severe hepatic impairment (no studies in theses patients).
(Rivastigmine continued)

**Cautions:** Gastric or duodenal ulcers (or susceptibility to ulcers); monitor
body-weight; sick sinus syndrome, conduction abnormalities; history of
asthma or chronic obstructive pulmonary disease; history of seizures; bladder
outflow obstruction.

**Hepatic and renal impairment:** use with caution as patients may experience
more adverse reactions.

**Drug interactions:** Check current BNF Appendix 1 before co-prescribing
other drugs. Acetylcholinesterase inhibitors act as *parasympathomimetics*:

- Muscle Relaxants – rivastigmine antagonise the effects of non-
depolarising muscle relaxants.
- Suxamethonium – rivastigmine enhances the effects of
suxamethonium.
- Antimuscarinics - Effects of Acetylcholinesterase inhibitors antagonised
by antimuscarinics.

**Adverse effects:** most common – nausea, vomiting, diarrhoea, dyspepsia,
anorexia, weight loss, increased salivation, abdominal pain, bradycardia,
dizziness, headache, drowsiness, malaise, agitation, anxiety, tremor,
confusion, insomnia, extrapyramidal symptoms (and worsening of Parkinson’s
disease), sweating. Female patients were found to be more susceptible to
nausea, vomiting, loss of appetite and weight loss.

Note - Transdermal administration less likely to cause gastro-intestinal
disturbance.

Note - Treatment should be interrupted if gastro-intestinal side-effects occur
and withheld until their resolution - retitrate dose if necessary.

**If the patient develops seizures, pancreatitis, cardiac, gastrointestinal
or ophthalmological disorders withhold drug and discuss with the
specialist team**
Memantine

Licensed indications: symptomatic treatment of patients with moderate to severe Alzheimer’s disease.

Pharmacology: Memantine acts as an antagonist at N-methyl-D-aspartate (NMDA) receptors, an action which, in theory, may be neuroprotective and thus disease modifying.

Preparations available: 10mg and 20mg film coated tablets, a Treatment Initiation pack containing 5mg, 10mg, 15mg and 20mg tablets and an oral solution 5mg per actuation (10mg in 1ml).

Recommended dosage and administration:
Initial dose (adult): Memantine is initially given as 5 mg once daily and then increased in steps of 5 mg at weekly intervals to a maximum of 20 mg daily.

Usual maintenance dose: 20mg once daily.

Maximum dose: 20mg once daily.

Contra-indications: Patients with a known hypersensitivity to memantine or to any of the excipients used in the formulations. Breast feeding.

Cautions: patients with epilepsy, former history of convulsions or patients with predisposing factors for epilepsy. Concomitant use of N-methyl-D-aspartate (NMDA)-antagonists such as amantadine, ketamine or dextromethorphan should be avoided. These compounds act at the same receptor system as memantine, and therefore adverse drug reactions (mainly CNS-related) may be more frequent or more pronounced.

Risk in pregnancy is unknown therefore should be avoided unless absolutely necessary.

Hepatic impairment: in patients with mild or moderate hepatic impaired function no dosage adjustment is needed. There is no data available on the use of memantine in patients with severe hepatic impairment. Avoid in severe hepatic impairment.

Renal impairment: reduce dose to 10 mg daily if eGFR 30-49 mL/minute/1.73 m², if well tolerated after at least 7 days dose can be increased in steps to 20 mg daily; reduce dose to 10 mg daily if eGFR 5–29 mL/minute/1.73 m²; avoid if eGFR less than 5 mL/minute/1.73 m².
Drug interactions:

- Amantadine - increased risk of CNS toxicity when memantine given with amantadine (manufacturer of memantine advises avoid concomitant use).

- Antimuscarinics - memantine possibly enhances effects of antimuscarinics.

- Antipsychotics - memantine possibly reduces effects of antipsychotics.

- Baclofen - memantine possibly modifies effects of baclofen.

- Barbiturates - memantine possibly reduces effects of barbiturates.

- Dantrolene - memantine possibly modifies effects of dantrolene.

- Dextromethorphan - increased risk of CNS toxicity when memantine given with dextromethorphan (manufacturer of memantine advises avoid concomitant use).

- Dopaminergics - memantine possibly enhances effects of dopaminergics.

- Ketamine - increased risk of CNS toxicity when memantine given with ketamine (manufacturer of memantine advises avoid concomitant use).

- Selegiline - memantine possibly enhances effects of selegiline.

- Warfarin – memantine possibly enhances anticoagulant effect of warfarin.

Adverse effects: most common – constipation, hypertension, dyspnoea, headache, dizziness and drowsiness.
NOTES for all medication

** If the patient develops seizures, pancreatitis, cardiac, gastrointestinal or ophthalmological disorders withhold drug and discuss with the specialist mental health team

- Please report adverse events to the CSM using the yellow card system. [www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm](http://www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm)
- Please refer to the SPC for full prescribing information (available at [www.medicines.org.uk](http://www.medicines.org.uk)).

Date of Preparation: November 2012       Review Date: November 2014

References:
BNF 64 September 2012
Maudsley Prescribing Guidelines in Psychiatry 11th edition
SmPCs accessed via [www.medicines.org](http://www.medicines.org) 15.11.2012

Contact Details for Memory Clinics

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<thead>
<tr>
<th>Clinic</th>
<th>Telephone Number</th>
<th>Fax Number</th>
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<tr>
<td><strong>Carmarthen</strong></td>
<td>Medical Secretary: 01267 674042</td>
<td>01267 674040</td>
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<tr>
<td>Memory Clinic Nurse</td>
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<tr>
<td>Margaret Tooby</td>
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<td>Consultant Psychiatrist</td>
<td>Dr Graham O’Connor</td>
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<tr>
<td><strong>Llanelli</strong></td>
<td>Medical Secretary: 01554 779310</td>
<td>01554 779312</td>
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<tr>
<td>Memory Clinic Nurse</td>
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<tr>
<td>Ann Pearce</td>
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<tr>
<td>Consultant Psychiatrist</td>
<td>Dr Toyin Adeyemo</td>
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<tr>
<td><strong>Ammanford</strong></td>
<td>Medical Secretary : 01267 674034</td>
<td>01267 674039</td>
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<tr>
<td>Memory Clinic Nurse</td>
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<tr>
<td>Barbara Davies</td>
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<tr>
<td>Consultant Psychiatrist</td>
<td>Dr Apparao Biradar</td>
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<td>Aberystwyth</td>
<td><strong>Enilli Unit</strong>&lt;br&gt;Memory Clinic Nurse&lt;br&gt;Clive Thomas&lt;br&gt;Dr Anke Cupok&lt;br&gt;Consultant Psychologist&lt;br&gt;Becci Dow&lt;br&gt;Medical Secretary&lt;br&gt;01970 635844/635842&lt;br&gt;<a href="mailto:Richard.Thomas4@wales.nhs.uk">Richard.Thomas4@wales.nhs.uk</a>&lt;br&gt;<a href="mailto:Anke.cupok@wales.nhs.uk">Anke.cupok@wales.nhs.uk</a>&lt;br&gt;<a href="mailto:Rebecca.dow@wales.nhs.uk">Rebecca.dow@wales.nhs.uk</a></td>
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<td>Cardigan</td>
<td><strong>Cardigan Hospital (Monthly)</strong>&lt;br&gt;Memory Clinic Nurse&lt;br&gt;Clive Thomas&lt;br&gt;Dr Anke Cupok&lt;br&gt;Consultant Psychologist&lt;br&gt;Becci Dow&lt;br&gt;Medical Secretary&lt;br&gt;01970 635844/635842</td>
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<tr>
<td>Pembrokeshire Memory Clinic</td>
<td><strong>Bro Ceryn Centre</strong>&lt;br&gt;Memory Clinic Nurse&lt;br&gt;Helen Goodchild&lt;br&gt;Consultant&lt;br&gt;Dr C James&lt;br&gt;Medical Secretary&lt;br&gt;01437 772828&lt;br&gt;Clinic&lt;br&gt;01437 772844</td>
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<tr>
<td>Pembrokeshire Older Adults CMHT</td>
<td><strong>Bro Ceryn Centre</strong>&lt;br&gt;CMHT Co-ordinator&lt;br&gt;Judith Radbourne&lt;br&gt;Consultant Psychiatrist&lt;br&gt;Dr Pansari&lt;br&gt;Medical Secretary&lt;br&gt;01437 772828&lt;br&gt;Clinic&lt;br&gt;01437 772844</td>
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ANTI-DEMENTIA MEDICATION PRESCRIPTION REQUEST FORM

Part A: To be completed by Specialist Memory Assessment Service

Dear Dr...........................................................................................

GP Practice..........................................................................................

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<td>Date of birth</td>
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<td>Address</td>
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The above patient has been assessed by the specialist memory service and has been stabilised on the following treatment for their dementia.

I am requesting your agreement to continue prescribing this medication

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<tr>
<td>Date of most recent issue of medicine(s)</td>
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<td>Date next issue is due</td>
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<td>Date of next Memory Clinic Review appointment</td>
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<td>Name of consultant</td>
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Part B: To be completed by GP Practice

ACKNOWLEDGEMENT OF TRANSFER OF PRESCRIBING

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<td>Date of Next Issue</td>
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I AGREE / DO NOT AGREE TO CONTINUING THE PRESCRIPTION OF THE ABOVE MEDICATION TO THIS PATIENT (PLEASE INDICATE)

Signed........................................................................................................

Print Name...................................................................................................

Date..............................................................................................................

GP Practice....................................................................................................

Please return to
Eileen Richards
Mental Health Pharmacy
Glangwili Hospital
Carmarthen
SA31 2AF
Tel: 01267 227367

Or FAX to SAFE HAVEN FAX on 01267 227720