## Memantine for the treatment of moderate to severe Alzheimer’s disease

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs). This guideline reinforces the basic premise that:

- When clinical and/or prescribing responsibility for a patient is transferred from the Wirral Memory Assessment Service (WMAS) to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the “sharing of information with the individual GP and their mutual agreement to the transfer of care.”

These are not rigid guidelines. On occasions, Consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

### Licensed indication:

Memantine is licensed for the treatment of moderate to severe Alzheimer’s dementia.

NICE Guidance recommends that treatment should only be used 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 or
- Severe Alzheimer’s disease

NICE Guidance recommends that treatment should only be prescribed under the following conditions:

- Alzheimer’s disease must be diagnosed and treatment initiated by a specialist; treatment can be continued by general practitioners under a shared-care protocol;
- The carers’ views of the condition should be sought before and during treatment;
- Treatment should continue only if it is considered to have a worthwhile effect on cognitive, global, functional, or behavioural symptoms.

### Dosage and administration:

#### Adults/Elderly:

The recommended starting dose is 5mg once daily, increased in steps of 5mg at weekly intervals to a maximum daily dose is 20 mg daily (treatment initiation pack available)

The recommended maintenance dose is 20 mg per day.

#### Renal impairment:

- Mildly impaired renal function (creatinine clearance 50 - 80 ml/min) no dosage adjustment is required.
- Moderate renal impairment (creatinine clearance 30 - 49 ml/min) daily dose should be 10 mg. 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.
- Severe renal impairment (creatinine clearance 5 - 29 ml/min) daily dose should be 10 mg per day.

#### Hepatic impairment:

In patients with mild or moderate hepatic impaired function no dosage adjustment is needed. Administration of memantine is not recommended in patients with severe hepatic impairment

The solution must not be poured or pumped into the mouth directly from the bottle or the pump, but should be dosed onto a spoon or into a glass of water using the pump. The solution and film-coated tablets can be taken with or without food.

#### Note: Combination treatment with memantine and an acetylcholinesterase inhibitor is not recommended

**Children and adolescents under 18 years:** Memantine is not recommended for use in children below 18 years.

### Contra-indications:

Hypersensitivity to the active substance or to any of the excipients and in severe hepatic impairment.

### Cautions:

Recommended in patients with epilepsy, history of convulsions or patients with predisposing factors for epilepsy.
Some factors that may raise urine pH may necessitate careful monitoring of the patient. These factors include drastic changes in diet, e.g. from a carnivore to a vegetarian diet, or a massive ingestion of alkalisating gastric buffers. Also, urine pH may be elevated by states of renal tubulalry acidosis (RTA) or severe infections of the urinary tract with *Proteus* bacteria.

In most clinical trials, patients with recent myocardial infarction, uncompensated congestive heart failure (NYHA III-IV), or uncontrolled hypertension were excluded. As a consequence, only limited data are available and patients with these conditions should be closely supervised.

*Excipients - oral solution:* The oral solution contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

For full information see the current edition of the British National Formulary (BNF)

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<tr>
<th><strong>Adverse effects:</strong></th>
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<td>For full information see the current edition of the British National Formulary (BNF).</td>
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<tr>
<td><strong>Common (10-15%)</strong>     constipation, hypertension, dyspnoea, headache, dizziness and drowsiness</td>
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<tr>
<td><strong>Less Common</strong>     vomiting, thrombosis, heart failure, confusion, fatigue, hallucinations, and abnormal gait</td>
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<tr>
<td><strong>Very Rare</strong>     seizures, pancreatitis, psychosis, depression and suicidal ideation</td>
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Report suspected adverse drug reactions via the Yellow Card Scheme, either online at [https://yellowcard.mhra.gov.uk/](https://yellowcard.mhra.gov.uk/) or by using the yellow forms at the back of a current BNF

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<th><strong>Monitoring requirements:</strong></th>
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<td>The NICE Health Technology Appraisal on these medications mandates the monitoring of cognition, and global functioning. The recommended scales for this locally are the Montreal Cognitive Assessment (<a href="http://www.mocatest.org">www.mocatest.org</a>) and the Global Deterioration Scale.</td>
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Practices will continue to monitor a patient’s cognitive level, as per NICE guidelines, using the MoCA until certain criteria are met:

The patient is no longer able to complete this test, due to:

- Significant communication difficulties so that they can no longer understand the instructions for the test, or
- Experiencing significant distress as part of the testing process

The patient’s cognitive level falls below 10/30 on this test

In these cases, the reason for the cessation of the cognitive testing must be recorded, and an overall assessment of the patient’s condition made on the Global Deterioration Scale (GDS)

**Action to be taken if abnormal results/adverse effects:** In the event of any adverse effects please contact the Wirral Memory Assessment Service (WMAS) for advice on 0151 488 7758. In the case of serious adverse events the medication should not be continued until that advice has been received.

**Drug interactions:** 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.

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 related with oral anticoagulants.

The mode of action suggests that the effects of L-dopa, dopaminergic agonists, and anticholinergics may be enhanced by concomitant treatment with NMDA-antagonists such as memantine. The effects of barbiturates and neuroleptics may be reduced. Concomitant administration of memantine with the antispasmodic agents, dantrolene or baclofen, can modify their effect and a dosage adjustment may be necessary.

For full information see the current edition of the BNF.
Specialist responsibilities:
1. Confirm the diagnosis of Alzheimer’s disease following full assessment. Provide confirmation of this to the patient and carer, and communicate this to the referrer.
2. Ensure that baseline tests and investigations required have been provided by referrer.
3. Initiate and titrate memantine for six months ensuring that the client is stable on the medication prior to transfer back to the referrer on the shared care protocol.
4. Monitor for side effects
5. Provide the referrer with details needed to continue the care of the client under the shared care protocol, to include details of the monitoring and prescriptions required for the client.

GP responsibilities:
1. Initial referral to the Memory Clinic after an initial assessment that raises the possibility of dementia. This initial assessment should include a test of cognition, physical examination and the agreed initial investigations of Full Blood Count, Chemical Profile, Thyroid Function Tests, B12 and folate, and an up to date Electrocardiogram (ECG).
2. Provide the patient with monthly repeat prescriptions of medication once the specialist has recommended continuation therapy following stabilisation. The patient should allow at least 48 hours for the prescription from the GP to be generated once they have agreed to take on prescribing.
3. Review the patient every six months, including their cognitive assessment, global assessment, functional assessment, behavioural assessment, mental health and medication.
4. Provide ongoing support and management for physical health issues
5. Report any adverse effects of medication to consultant.
6. Contact the specialist if they do not agree with the treatment recommendation or if there is a perceived problem with compliance or concordance, or if they have any questions about the management plan.
7. Refer on to appropriate agencies e.g. Social Services or the Alzheimer’s Society (0151 630 5206) if additional support is needed for the client or their carer.

Patient and parent/carer responsibilities:
• Agree to request prescriptions from the GP in good time; obtain the first GP prescription within 2 weeks of being informed that shared care will be in operation.
• Report any concerns or adverse effects to the GP or Pharmacist.

Secondary care review:
Refer back to secondary mental health services through Single Point of Access if deterioration in behaviours or significant risks that cannot be safely managed in the community.

References:
Summary of Product characteristics (SPC) for Ebixa® at http://www.medicines.org.uk/emc/default.aspx
NICE Technology Appraisal – Donepezil, galantamine, rivastigmine & memantine for the treatment of Alzheimer’s disease, issued March 2011 (TA217)
Mims April 2013
Drug Tariff, April 2013 available online at http://www.ppa.org.uk/ppa/edt_intro.htm

Availability:
Memantine 10mg tablets, 56 tablet pack costs £69.01 (Drug Tariff, April 2013)
N.B Exiba 10mg tablets, 28 tablet pack = £34.50 & 112 tablet pack = £138.01 (Mims April 2013)
Memantine 20mg tablets, 28 tablet pack costs £69.01 (Drug Tariff, April 2013)
N.B Ebixa Treatment Initiation Pack, containing a 7 day supply of 5/10/15/20mg tablets, 28 day pack, costs £43.13 (Mims April 2013)
N.B Ebixa 5 mg/pump actuation (10mg/ml) oral solution, 50g pump pack costs £61.61, 100g costs £123.23 (Mims April 2013) – Once opened, the contents of the bottle should be used within 3 months

Back up advice and support

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<tr>
<th>Specialist</th>
<th>Telephone/Fax</th>
<th>Email address</th>
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<tbody>
<tr>
<td>Dr Andrew Ellis, Consultant Psychiatrist</td>
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<td><a href="mailto:Andrew.Ellis@cwp.nhs.uk">Andrew.Ellis@cwp.nhs.uk</a></td>
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