NHS

Nottinghamshire Area Prescribing Committee

Memantine

Traffic light classification – Amber 2
Information Sheet for Primary Care Prescribers

Licensed Indications
Memantine is indicated for the symptomatic treatment of patients with moderate to severe dementia in Alzheimer's disease.

Therapeutic Summary
Memantine monotherapy is recommended by NICE as an option for managing Alzheimer's disease for patients with: moderate Alzheimer's disease who are intolerant of or have a contraindication to acetylcholinesterase inhibitors (donepezil, galantamine or rivastigmine), or severe Alzheimer's disease[1,2].

Memantine is now recommended for people with an established diagnosis of Alzheimer's disease who are already taking an acetylcholinesterase inhibitor if they have moderate or severe disease[1]. Primary care prescribers may start treatment with memantine in these patients without taking advice from a specialist clinician.

Memantine works primarily through its action upon glutamate transmission and more specifically on particular subtypes of receptors within glutamate systems particularly related to memory (N-methyl-D-aspartate [NMDA] receptors)[1,2].

Medicines Initiation and Continuation
For people who are not taking an acetylcholinesterase inhibitor, treatment with memantine should be initiated by specialists in the care of patients with dementia (that is, psychiatrists including those specialising in learning disability, neurologists, and physicians specialising in the care of older people) following a comprehensive assessment and diagnosis[1,2].

Once a decision has been made to start memantine, the first prescription may be made in primary care.

Products Available[3,4]
Initiation packs of film-coated tablets and orodispersible tablets are available containing 5mg, 10mg, 15mg and 20mg tablet strengths.

Film-coated tablets: 5mg, 10mg, 15mg and 20mg
Oral solution sugar free: 10mg/1mL
Orodispersible tablets (Valios®): 5mg, 10mg, 15mg and 20mg

For patients with swallowing difficulties, oral solution is the most cost-effective product[3]. The orodispersible tablets should only be used when a patient is unable to use the oral solution.

Dosages and Route of Administration[2,4]
- A slow titration is necessary to minimise side effects.
- Treatment should be initiated at 5mg once a day for 7 days with or without food. Memantine initiation packs are available which contain 5mg tablets. Alternatively, half a 10mg tablet can be used.
- If tolerated, the dose should be increased by 5mg daily every 7 days i.e. 10mg daily for 7 days, 15mg daily for 7 days, 20mg daily thereafter.
- Maintenance dose is 20mg once a day.
- No dose adjustment is required for patients with mild renal impairment.
- For those with moderate renal impairment (creatinine clearance 30-49 ml/min) the target maintenance dose is 10-20mg once a day depending on tolerability - see titration above.
- For those with severe renal impairment (creatinine clearance 5-29 ml/min) the target maintenance dose is 10mg once daily.
- No dose adjustment is required for those with mild to moderate hepatic impairment. Use in severe hepatic impairment is not recommended in view of a lack of data.

Duration of Treatment
Treatment should be continued only when it is considered to be having a worthwhile effect on cognitive, global, functional or behavioural symptoms[1]. The prescriber would be required to discuss with the patient, carer and other professionals involved in the care of the patient before making the decision to stop treatment where there is no worthwhile effect. Gradual withdrawal over a 4-week period would be preferable to abrupt discontinuation[1].

Primary Care Prescribers may refer back to the Specialist Service if changes or progress are cause for concern, or to discontinue memantine treatment.

Monitoring Requirements and Responsibilities

Baseline screening / investigations to exclude other causes of cognitive impairment will have been carried out by the GP before initial referral to specialist.

No routine plasma monitoring is required during memantine treatment.

The Primary Care Prescriber will carry out an annual patient review for all dementia patients[1].

For those prescribed pharmacological treatment, this will include a medication review as well as cognitive, global, functional and behavioural assessments, as per NICE guidance[1].

Contraindications[2]

- Known hypersensitivity to any ingredient.
- Pregnancy and breastfeeding.

Precautions[2]

- Cardiovascular conditions: use with caution and monitor use closely in patients with recent myocardial infarction, uncompensated congestive heart failure (NYHA III-IV), or uncontrolled hypertension – limited data.
- Neurological conditions: Memantine should be used with caution in those with epilepsy, former history of convulsions or those with predisposing factors for epilepsy**.**
- Raised urine pH: alkaline urine conditions may reduce the elimination rate of memantine (requires careful monitoring). Factors that may raise urine pH include drastic changes in diet e.g. carnivore to vegetarian diet, large ingestion of alkalising gastric buffers, renal tubulary acidosis or severe infections of the urinary tract with *Proteus* bacteria
- Use of oral solution should be avoided in those with rare hereditary problems of fructose intolerance- contains sorbitol

Explicit Criteria for Review and Discontinuation of the Medicine[2]

ADVERSE EFFECT	**ACTION**
Common (≥ 1/100 to < 1/10)	
Headache	• Treat with a simple analgesic e.g. paracetamol.
Constipation	• Treat with laxatives. • Ensure patient takes plenty of fluids.
Somnolence	• Consider a dose reduction.
Dyspnoea	• Discuss with psychiatrist.
Dizziness, unsteadiness	• Advise patient to take time to stand up. • Advise patient not to drive. • May subside during continued therapy. • Consider a dose reduction.
Hypertension	• Consider a dose reduction. Monitor BP.
Elevated liver function tests	• Discuss with psychiatrist. Monitor LFTs.
Hypersensitivity Reactions	• If severe, consider discontinuation.
Uncommon (≥ 1/1000 to < 1/100)	
Vomiting	• Ensure patient takes plenty of fluids. • Discuss with psychiatrist. • If severe consider prescribing an antiemetic
Fatigue	• Consider a dose reduction.
Hallucinations (esp. in severe Alzheimer's disease) Confusion	• Symptoms have resolved after a dose reduction or discontinuation of treatment. • Discuss with psychiatrist.
Abnormal gait	• Consider a dose reduction.

Cardiac failure	• Discuss with psychiatrist.
Venous thrombosis / thromboembolism	• Discuss with psychiatrist.
Fungal Infections	• Discuss with Psychiatrist
Very Rare (< 1/10,000) or unknown	
Seizures (action: discontinue unless taking anticonvulsants and discuss with psychiatrist). Psychotic reactions (action: withhold and discuss with psychiatrist). Pancreatitis or hepatitis (action: withhold and discuss with psychiatrist).	

Report suspected adverse drug reactions via the Yellow Card Scheme, either online at https://yellowcard.mhra.gov.uk/ or by using the yellow forms at the back of a current BNF.

Clinically Relevant Medicine Interactions and Their Management[2]

- Amantadine, ketamine, dextromethorphan – use of NMDA antagonists together with memantine should be avoided (increased CNS adverse effects)
- L-dopa, dopaminergic agonists, anticholinergics – enhanced effect when prescribed with memantine
- Neuroleptics and barbiturates – reduced effect when prescribed with memantine.
- Antispasmodic agents, dantrolene or baclofen – the effects of these medicines may be modified by memantine and dose adjustments may be necessary.
- Cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine – may lead to increased plasma levels of memantine (may require dose adjustment, monitor for adverse effects).
- Hydrochlorothiazide – serum level may be reduced when prescribed with memantine.
- Oral anticoagulants – monitor INR closely with memantine use (isolated cases of INR increases)

Information Given To Patient

Further written information sheets on memantine can be accessed via the following sites:
https://www.choiceandmedication.org/nottinghamshirehealthcare/medication/memantine/

https://www.alzheimers.org.uk/about-dementia/treatments/dementia-medication/medication-dementia-symptoms

Patient / Carer's Role

The following should be discussed with the patient on initiation or during review/consultation:

- The patient/carer will report any suspected adverse reactions to the GP for assessment.
- The patient/carer will report to their GP or specialist signs of clinical worsening.
- The patient/carer will attend all follow-up appointments with GP and specialist. If they are unable to attend any appointments they should inform the relevant practitioner as soon as possible and arrange an alternative appointment.

Pharmacy Contacts - Nottinghamshire Healthcare NHS Foundation Trust

Wells Road Centre Pharmacy 01159 555 357
Nottinghamshire Healthcare Pharmacy Advisory Line - 0300 303 5808
Email MI@nottshc.nhs.uk

References

1. National Institute for Health and Care Excellence (NICE). *Dementia: assessment, management and support for people living with dementia and their carers [NG97].* 2018. Available from: https://www.nice.org.uk/guidance/ng97 [Accessed 06th December 2023].

2. Electronic Medicines Compendium (EMC). *Memantine Ebixa Lundbeck 10mg film-coated tablets SmPC.* Available from: https://www.medicines.org.uk/emc/product/8222/smpc [Accessed 6th December 2023].

3. The Electronic Drug Tariff. http://www.drugtariff.nhsbsa.nhs.uk/#/00786378-DD/DD00786373/Home [Accessed 6th December 2023].

4. Joint Formulary Committee. *British National Formulary*. 2023. Available at: http://www.medicinescomplete.com [Accessed: 6th December 2023]

5. Nottinghamshire Area Prescribing Committee (NAPC). *Managing Behaviour and Psychological Problems in Patients with Diagnosed or Suspected Dementia in Primary and Secondary care.* 2021). Available from*:* https://www.nottsapc.nhs.uk/media/p0jlee5o/bpsd-guideline.pdf?UNLID=913286040202311231242 2 [Accessed 6th December 2023].

6. National Institute for Health and Care Excellence (NICE). *Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease [TA217].* 2011. Available from: https://www.nice.org.uk/guidance/ta217 [Accessed 6th December 2023].