DRUGS FOR DEMENTIA: Memantine
INFORMATION FOR PRIMARY CARE

Who will diagnose and decide who is suitable for which drug?
Specialists will diagnose and communicate to primary care the recommended dementia drug for the patient which may include instructions on any necessary titration. Specialists will counsel and inform patients of their diagnosis and treatment options.

Who will increase the dose?
Primary care may be asked to oversee the titration of medication to the recommended dose, whilst monitoring for any adverse effects or tolerability issues.

Who will follow up the patients?
Once the patient is stable on the maximum tolerated dose of medication, specialists usually discharge the patient back to primary care. During the assessment period, specialists will identify patients with complex needs and would be expected to refer onto other services or if they are not able to do so, may request that primary care assist in making onward referrals e.g., to occupational therapy, speech and language, Adult Social Care.

RAG List Status
Memantine is classified as a GREEN (following specialist advice – see local guidance) drug by the Greater Manchester Medicines Management Group.

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

NICE Guidance
NICE TA217 recommends memantine monotherapy as an option for managing moderate Alzheimer's disease in patients who are intolerant of or have a contraindication to AChE inhibitors or who have severe Alzheimer's disease.

NICE NG97 recommends memantine 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 or severe Alzheimer's disease. It may also be offered as an adjunct to existing AChE therapy in patients with moderate to severe Alzheimer's disease.

Preparations available
Initiation packs containing 5mg, 10mg, 15mg and 20mg tablets
10mg and 20mg film coated tablets OR 10mg and 20mg orodispersible tablets
10mg/ml (or 5mg per pump actuation) oral solution

Dosage and Administration
- Initially 5mg daily for a minimum of seven days.
- Dose increased by 5mg in weekly intervals to a maximum daily dose of 20mg.

Memantine should be administered orally once a day and should be taken at the same time every day.
All memantine formulations can be taken with or without food.

Dose Modifications

Renal Impairment		**Hepatic Impairment**
eGFR >49	No dose adjustment required	Mild to moderate (Child Pugh A or B) – no dose adjustment required. Severe – avoid.
eGFR 30-49	10-20mg daily depending on tolerability	
eGFR 5-29	10mg daily	
eGFR <5	Avoid	

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Contraindications
Known hypersensitivity to memantine or any listed excipient

Cautions
History of seizures or predisposing factors for epilepsy
Recent MI, uncompensated congestive heart failure or uncontrolled hypertension.
Oral solution contains sorbitol – avoid in rare hereditary problems of fructose intolerance.

What are the main side-effects?
Common side effects (may affect up to 1 in 10 people):

- Drug hypersensitivity
- Somnolence
- Dizziness
- Balance disorders
- Hypertension
- Dyspnoea
- Constipation
- Elevated liver function test
- Headache

Alzheimer's disease has been associated with depression, suicidal ideation and suicide. In post-marketing experience these reactions have been reported in patients treated with memantine.

Drug Interactions

- Avoid concomitant use of ketamine, dextromethorphan and amantadine.
- Memantine possibly enhances the anticoagulant effect of warfarin so if these drugs are to be used concurrently additional INR monitoring should be carried out and dose adjusted accordingly.
- Drugs that increase the pH of the urine (e.g. sodium bicarbonate, carbonic anhydrase inhibitors or drastic dietary changes) may reduce the elimination of memantine.
- Memantine is predicted to enhance the effects of antimuscarinics, levodopa and dopaminergic (dopamine agonist) drugs
- Memantine might modify the effects of antispasmodic drugs such as dantrolene or baclofen and dosage adjustment might be required
- Effects of barbiturates and antipsychotics may be reduced.
- Increased memantine plasma levels possible with concomitant use of cimetidine, ranitidine, procainamide, quinidine, quinine and nicotine.

Advice for patients having a general anaesthetic
Concurrent use of memantine and esketamine / ketamine should be avoided. Both medicines are N-methyl-D-aspartate (NMDA) antagonists and potentially concurrent use could increase the frequency and severity of central nervous system adverse drug reactions including psychosis.

Deterioration in cognitive function if memantine omitted.

Situation	Advice
Planned & Emergency Operations	Continue

Monitoring -

1. **Adverse effects:** Most common side effects are gastrointestinal disturbance (nausea, vomiting, and diarrhoea).
2. **Concurrent medication:** Medication should be reviewed at each visit in order to identify potential drug interactions.
3. **Renal and hepatic function:** Baseline creatinine and LFTs should be measured; patients with renal or hepatic impairment should have doses titrated slowly and be monitored closely for adverse effects. Dose limitations exist for certain degrees of decreased renal function (see above)

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4. **Cognitive, global functional and behavioural assessment:** Patients who continue on treatment should be reviewed at least annually by the GP. A cognition test may be done but, especially in more advanced dementia where benefits of cholinesterase inhibitors may cease to outweigh risks of continued treatment, an assessment of well-being and functioning is more important. Carers' views on the patient's condition at follow-up should be sought.

When should the drug be stopped?

Drugs should be stopped if a patient developed an allergy or contra-indication to the medication. If a patient is not apparently gaining any benefit from the drug that may be an indication for stopping, however in addition to treating the cognitive aspects of dementia, cholinesterase inhibitors and memantine have a role in behavioural and psychiatric changes in dementia and therefore, patients who are scoring low on cognitive testing may still benefit. Specialist advice should be sought on this decision from the locality memory treatment services.

What happens if my patient's needs change or become more complex following discharge?

They can be re-referred back to the appropriate memory service via the normal referral pathway.
You may wish to seek advice in the following circumstances:

- Emergent concerns regarding tolerability
- To consider whether to discontinue treatment

Patient Counselling Points

Oral solution: patient/carer should be shown how to use the dosing pump.
Oral solution must not be poured or pumped into the mouth directly from the bottle/pump but should given via a spoon/oral syringe or into a glass of water.

Guidance for GPs prescribing

The GP will monitor for ongoing side effects and discuss with Memory Service if any arise for advice on dose reduction, discontinuation etc.

- Provide regular prescriptions for memantine as per local guidance.
- Be aware of side effects and common drug interactions as documented in this guideline.
- Provide regular health checks including where relevant the review of clients with vascular dementia or mixed dementia and provision of advice about lifestyle.
- Inform specialist services of any relevant physical health problems at the earliest opportunity for those still open to specialist services or re-refer if necessary.
- If patient suffers any adverse reaction, GP should liaise with secondary care/specialist services.