

SHARED CARE GUIDELINES

Galantamine for the treatment of mild to moderate 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:

Galantamine is licensed for the treatment of mild to moderate Alzheimer's dementia.

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:

Please follow the Cheshire & Wirral Partnership NHS Foundation Trust, Mental Health Medicines Formulary;

First line

Donepezil

Second line

Rivastigmine capsules

Third line

Galantamine tablets, orally, 4mg twice daily for 4 weeks; maintenance 8 to 12mg twice daily.

This is available as a twice daily tablet and a MR once daily capsule.

N.B The MR capsule should be reserved for those with difficulty taking the medicine twice daily.

- If donepezil is not prescribed the rationale for prescribing one of the alternative acetylcholinesterase inhibitors must be documented and details shared with the GP.**

Galantamine should be taken with food and ensure adequate fluid intake during treatment. There is no rebound effect after abrupt discontinuation of treatment.

Plasma levels may be increased in patients with moderate to severe hepatic or renal impairment. In patients with moderately impaired hepatic function it is recommended that dosing should begin with 4mg once daily, preferably taken in the morning, for at least a week then 4mg twice daily for at least four weeks. In these patients, daily doses should not exceed 8mg twice a day. In patients with severe hepatic impairment the use of galantamine is contraindicated. No dosage adjustment is required for patients with mild hepatic impairment.

For patients with a creatinine clearance greater than 9 ml/min no dosage adjustment is required. In patients with severe renal impairment (creatinine clearance less than 9 ml/min), the use of galantamine is contraindicated. Not recommended for use in children and adolescents below 18 years of age.

Contra-indications: Hypersensitivity to the active substance or to any of the excipients. Patients with severe hepatic (Child-Pugh score greater than 9), severe renal (creatinine clearance less than 9 ml/min) impairment and in patients who have both significant renal and hepatic dysfunction.

Cautions: Cholinomimetics may have vagotonic effects on heart rate (e.g. bradycardia). The potential for this action may be particularly important to patients with 'sick sinus syndrome' or other supraventricular cardiac conduction disturbances or in those who use medicinal products that significantly reduce heart rate concomitantly, such as digoxin and beta blockers or for patients with an uncorrected electrolyte disturbance (e.g. hyperkalaemia, hypokalaemia).

Caution should therefore be exercised when administering galantamine to patients with cardiovascular diseases, e.g. immediate post-myocardial infarction period, new-onset atrial fibrillation, second degree heart block or greater, unstable angina pectoris, or congestive heart failure, especially NYHA group III – IV.

Patients with Alzheimer's dementia treated with galantamine have shown an increased incidence of certain cardiovascular adverse events.

Patients at increased risk of developing peptic ulcers, e.g. those with a history of ulcer disease or those predisposed to these conditions, including those receiving concurrent non-steroidal anti-inflammatory drugs (NSAIDs), should be monitored for symptoms. The use of galantamine is not recommended in patients with gastrointestinal obstruction or recovering from gastrointestinal surgery.

Although cholinomimetics are believed to have some potential to cause seizures, seizure activity may also be a manifestation of Alzheimer's disease. In rare cases an increase in cholinergic tone may worsen Parkinsonian symptoms.

Care should be taken when administering galantamine to patients with cerebrovascular disease – monitor patients.

Cholinomimetics should be prescribed with care for patients with a history of severe asthma or obstructive pulmonary disease or active pulmonary infections (e.g. pneumonia).

The use of galantamine is not recommended in patients with urinary outflow obstruction or recovering from bladder surgery.

Galantamine, as a cholinomimetic is likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia, especially in cases of pseudocholinesterase deficiency.

Some forms of galantamine contain sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

The administration of galantamine concomitantly with other inhibitors of acetylcholinesterase, agonists or antagonists of the cholinergic system should be avoided.

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

Adverse effects:

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

Common diarrhoea, abdominal pain, nausea, vomiting, dyspepsia, syncope, depression, headache, fatigue, anorexia, tremor, fever and weight loss.

Less Common arrhythmias, palpitations, hypotension, blurred vision, myocardial infarction, paraesthesia, tinnitus and leg cramps.

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

Monitoring requirements: Because of the risk of bradycardia, the pulse must be monitored regularly, and discontinued immediately if the pulse falls below 50 beats per minute, or if there is evidence of developing heart block. 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 (MoCA, www.mocatest.org), Mini-Addenbrooke's cognitive Examination (mini-ACE) and the Global Deterioration Scale (GDS).

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 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: Galantamine should not be given concomitantly with other cholinomimetics (such as ambenonium, donepezil, neostigmine, pyridostigmine, rivastigmine or systemically administered pilocarpine). Galantamine has the potential to antagonise the effect of anticholinergic medication. Should anticholinergic medication such as atropine be abruptly stopped there is a potential risk that galantamine's effect could be exacerbated. As expected with cholinomimetics, a pharmacodynamic interaction is possible with medicinal products that significantly reduce the heart rate such as digoxin, beta-blockers, certain calcium-channel blocking agents and amiodarone. Caution should be taken with medicinal products that have potential to cause torsades de pointes. In such cases an ECG should be considered.

Galantamine, as a cholinomimetic, is likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia, especially in cases of pseudocholinesterase deficiency.

Galantamine bioavailability is increased when given with paroxetine (a potent CYP2D6 inhibitor) and ketoconazole and erythromycin (both CYP3A4 inhibitors). Therefore, during initiation of treatment with potent inhibitors of CYP2D6 (e.g. quinidine, paroxetine or fluoxetine) or CYP3A4 (e.g. ketoconazole or ritonavir) patients may experience an increased incidence of cholinergic adverse reactions, predominantly nausea and vomiting. Under these circumstances, based on tolerability, a reduction of the galantamine maintenance dose can be considered.

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 galantamine 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.
6. Review patients referred back to secondary mental health services through Single Point of Access due to deterioration in behaviours or significant risks that cannot be safely managed in the community by their GP.

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 stabilization. Allow 48hrs for to generate prescription.

3. Review the patient every six months, including their pulse, 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.
8. Refer patient back to consultant through single point of access if patient's condition deteriorates.

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.

References:

Summary of Product characteristics for Reminyl®
 NICE Technology Appraisal – Donepezil, galantamine, rivastigmine & memantine for the treatment of Alzheimer's disease, issued March 2011 (TA217)
 Mims March 2016
 Drug Tariff Online, March 2016

Availability:

Galantamine 8mg tablets, 56 tablet pack
 Galantamine 12mg tablets, 56 tablet pack
 Galantamine 8mg modified-release capsules, 28 capsule pack
 Galantamine 16mg modified-release capsules, 28 capsule pack
 Galantamine 24mg modified-release capsules, 28 capsule pack
N.B Reminyl 4mg/ml sugar-free oral solution, 100ml bottle with pipette
Primary Care – see Scriptswitch for the most cost effective choice to prescribe

Back up advice and support	Specialist	Telephone/Fax	Email address
Dr Andrew Ellis	Consultant Psychiatrist	0151 488 8155	Andrew.Ellis@cwpc.nhs.uk
Written By Dr Andrew Ellis, Consultant Psychiatrist		Abigail Cowan, Prescribing Adviser, Wirral Medicines Management Team, MLCSU	