Galantamine

Traffic light classification- Amber 2
Information sheet for Primary Care Prescribers

Licensed Indications
Galantamine is indicated for the symptomatic treatment of mild to moderately severe dementia in Alzheimer's disease.

Therapeutic Summary
According to NICE, galantamine is recommended as an option for managing mild to moderate Alzheimer's disease[1].
Galantamine is an acetylcholinesterase inhibitor which works by increasing the concentration of acetylcholine at sites of neurotransmission and also modulates activity at nicotinic receptors[2].

Medicines Initiation and Continuation
Treatment with galantamine must 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].

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

Products available[3]
Prolonged-release capsules: 8mg, 16mg and 24mg (refer to Preferred Prescribing List for brand)

Oral solution 4mg/ml (100ml bottle) - prescribe as Galzemic® brand.

Dosages and route of administration[2, 4]
Adequate fluid intake should be ensured during treatment.
There is no evidence of a rebound effect after abrupt discontinuation of therapy.
When switching from oral solution to the prolonged-release capsules, the last dose of oral solution should be taken in the evening, and the prolonged-release capsules started once-daily in the morning. It is recommended that the same total daily dose of galantamine is administered to patients.

Prolonged-Release Capsules

- Administer once-a-day in the morning, preferably with food. Do not chew or crush.
- Starting dose is 8mg/day for 4 weeks.
- Following review at one month, the dose can be increased to 16mg/day for at least 4 weeks.
- Maintenance dose is 16-24mg/day dependent upon tolerability and response.
- The minimum effective dose is 16mg/day.
- In individual patients not showing an increased response or not tolerating 24 mg/day, a dose reduction to 16 mg/day should be considered.
- Hepatic impairment
  Mild hepatic impairment: no dosage adjustment is required.
  Moderate hepatic impairment: dosing should begin with 8mg once every other day (morning) for at least one week, followed by 8mg once-a-day for at least 4 weeks. Doses should not exceed 16mg once-a-day.
  Severe hepatic impairment: the use of galantamine is contraindicated.
- Renal impairment
  In patients with a creatinine clearance greater than 9mls/minute no dosage adjustment is required. The use of galantamine is contraindicated in patients with severe renal impairment (creatinine clearance less than 9mls/minute).

Oral Solution

- Treatment should be initiated at 4mg twice a day, preferably with morning and evening meals to minimise nausea.
- Following review at one month, the dose can be increased to 8mg twice daily for at least 4 weeks.
- Maintenance dose is 8-12mg twice daily.
- The minimum effective dose is 8mg twice daily
- In individual patients not showing an increased response or not tolerating 12mg twice daily, a dose reduction to 8mg twice daily should be considered.
- Hepatic impairment
  Mild hepatic impairment: no dosage adjustment is required.
  Moderate hepatic impairment: dosing should begin with 4mg once daily (morning) for at least one week, followed by 4mg twice daily for at least 4 weeks. Doses should not exceed 8mg twice daily.
  Severe hepatic impairment: the use of galantamine is contraindicated.
- Renal impairment
  In patients with a creatinine clearance greater than 9mls/minute no dosage adjustment is required. The use of galantamine is contraindicated in patients with severe renal impairment (creatinine clearance less than 9mls/minute).

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.

Do not stop Acetylcholinesterase inhibitors in people with Alzheimer's disease because of disease severity alone. When assessing the severity of Alzheimer's disease and the need for treatment, healthcare professionals should not rely solely on cognition scores in circumstances in which it would be inappropriate to do so[1].

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

For patients with existing or suspected cardiac disease or bradycardia (including those with cardiac arrhythmias or valve problems, and patients with hypertension who are being treated with anti-hypertensives that have a rate-limiting affect e.g. beta-blockers), an ECG should be carried out by the GP, as part of the baseline investigations prior to referral. Other patients should be referred with the GP confirming the absence of these conditions.

No routine plasma monitoring is required during galantamine treatment.

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

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, 6].

Contraindications[2]

- Severe hepatic impairment (Child-Pugh score greater than 9)
- Severe renal impairment (creatinine clearance less than 9mls/minute)
- Known hypersensitivity to any ingredient
- Pregnancy and breastfeeding – no clinical data available (animals studies show reproductive toxicity)

Precautions[2]

- Cardiovascular conditions: galantamine 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 conditions, such as sinoatrial or atrioventricular block, or those with an uncorrected electrolyte disturbance e.g. hyperkalaemia, hypokalaemia.
  Caution should be exercised in 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.

  Galantamine should be used with caution in patients with prolongation of the QTc interval, in patients treated with drugs affecting the QTc interval or in patients with pre-existing cardiac disease or electrolyte disturbances. There have been reports of QTc prolongation in patients using therapeutic doses of galantamine.
- Gastrointestinal conditions: patients with a history of ulcer disease or those receiving concurrent non-steroidal anti-inflammatory medication (NSAIDs) may be at risk for developing ulcers and should be monitored for symptoms. Use is not recommended in patients with gastrointestinal obstruction or those recovering from gastrointestinal surgery.
- Genitourinary: use is not recommended in patients with urinary outflow obstruction or those recovering from bladder surgery.
- Neurological conditions: galantamine has the potential to cause generalised convulsions, however seizure activity may also be manifestation of Alzheimer's disease. Galantamine may also have the potential to exacerbate or induce extrapyramidal symptoms.
- Pulmonary conditions: prescribe with care to patients with a history of severe asthma, obstructive pulmonary disease or active pulmonary infections (e.g. pneumonia) due to cholinomimetic actions.
- Serious skin reactions**:** galantamine has been reported to cause Stevens-Johnson syndrome and acute generalised exanthematous pustulosis. Patients should be informed of the signs of serious skin reactions and to discontinue galantamine at the first appearance of skin rash
- Severe dementia in Alzheimer's disease and other types of dementia – benefit has not been demonstrated.

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

ADVERSE EFFECT	ACTION
Very Common (≥ 1/10)	
Nausea and vomiting	Advise patient to take with or after food. If severe consider an antiemetic. Please note if any symptoms are persistent & problematic consider a reduction in the dose of galantamine to a previously well tolerated dose.
Common (≥ 1/100 to < 1/10)	
Diarrhoea Abdominal pain Dyspepsia	• Ensure patient takes plenty of fluids. • Discuss with psychiatrist. • If severe consider prescribing an antacid.
Weight decrease / anorexia	• Monitor weight on a regular basis.
Headache	• Treat with a simple analgesic e.g. paracetamol.
Syncope / Dizziness / Fall	• Advise patient to take time to stand up. May subside during continued therapy. • Consider a dose reduction. • If syncope consider possibility of heart block
Tremor	• Withhold & discuss with psychiatrist.
Bradycardia	• Withhold & discuss with psychiatrist.
Hypertension	• Consider a dose reduction.
Hyperhydrosis	• Discuss with psychiatrist.
Muscle Spasms	• Discuss with psychiatrist.
Somnolence /Fatigue / Lethargy / Malaise	• Consider a dose reduction.
Insomnia, Confusion, Hallucinations, Depression	• Consider a dose reduction. • Discuss with psychiatrist.

Uncommon (≥ 1/1000 to < 1/100)
Dehydration, Paraesthesia, Dysgeusia, Hypersomnia**,** Blurred Vision, Tinnitis, Supraventricular Extrasystoles, Atrioventricular Block First Degree, Sinus Bradycardia, Palpitations, Hypotension, Flushing, Retching, Muscular Weakness, Hepatic Enzymes Increased, Hepatitis (Rare).

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]

- Potent inhibitors of CYP2D6 (e.g. quinidine, paroxetine and fluoxetine) and CYP3A4 (e.g. ketoconazole, erythromycin and ritonavir) may increase the bioavailability of galantamine. Therefore, during initiation of such treatments there may be an increase in cholinergic side effects such as nausea and vomiting. A dose reduction of galantamine should be considered in these circumstances.
- Galantamine may antagonise the effect of anticholinergic medication (e.g. procyclidine)
- Caution when used in combination with other medications that significantly reduce the heart rate e.g. digoxin, beta-blockers, certain calcium-channel blocking agents and amiodarone due to synergistic effects.
- Caution with medications that have the potential to cause torsades de pointes – consider an ECG in these cases
- Galantamine is not to be used with other cholinergic agonists / cholinomimetics (e.g. donepezil, rivastigmine, neostigmine, pyridostigmine, ambenonium) due to synergistic effects.
- Caution with Succinylcholine and other muscle relaxants. Galantamine is likely to exaggerate succinylcholine-type muscle relaxation during anaesthesia.
- Food - concomitant administration with food slows the absorption rate of galantamine but does not affect the extent of absorption. It is recommended to be taken with food in order to minimise cholinergic side effects.
- Non-steroidal anti-inflammatory medication (NSAIDs) - galantamine has the potential to increase the risk for developing ulcers as well as NSAIDs.

Information Given To Patient

Further written information sheets on galantamine can be accessed via the following sites:
- https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/alzheimers-drug-treatments
- https://www.alzheimers.org.uk/about-dementia/treatments/drugs/drug-treatments-alzheimers-disease

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 30th November 2023].

2. Electronic Medicines Compendium (EMC). *Reminyl XL (galantamine hydrobromide) 8mg prolonged release capsules SmPC.* Available from https://www.medicines.org.uk/emc/product/3934/smpc [Accessed 30th November 2023].

3. The Electronic Drug Tariff. http://www.drugtariff.nhsbsa.nhs.uk/#/00786378-DD/DD00786373/Home [Accessed 30th November 2023].

4. Joint Formulary Committee. *British National Formulary*. 2023. Available at: http://www.medicinescomplete.com [Accessed: 30th November 2023

5. Nottinghamshire Area Prescribing Committee (NAPC). Managing Behaviour and Psychological Problems in Patients with Diagnosed or Suspected Dementia in Primary and Secondary care. (2023). Available from: https://www.nottsapc.nhs.uk/media/p0jlee5o/bpsd-guideline.pdf?UNLID=913286040202311231242 2 [Accessed 30th November 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 30th November 2023].