Interface Prescribing Subgroup
DRUGS FOR DEMENTIA: Rivastigmine
INFORMATION FOR PRIMARY CARE

RAG List Status

Cholinesterase inhibitors are classified as GREEN (following specialist initiation) drugs by the Greater Manchester Medicines Management Group.

Licensed Indications

Rivastigmine is licensed for the symptomatic treatment of patients with mild to moderately severe Alzheimer's disease.

NICE Guidance

NICE TA217 recommends that Acetylcholinesterase inhibitors are clinically cost effective and has recommended their use in mild to moderate Alzheimer's Disease.
NICE CG42 also recommends they be considered for people with dementia with Lewy bodies and patients with Alzheimer's Disease irrespective of severity who have non cognitive symptoms and/or behavioural challenges causing significant distress or potential harm to the individual.

Who will diagnose and decide who is suitable for which drug?

Specialists will continue to diagnose, assess suitability and safety of drug treatment for patients referred to Memory Services. Specialists will counsel and inform patients of their diagnosis and treatment options. Specialists will then follow up the patients until the patient is stable on the maximum tolerated dose of medication, this is usually for a period of one to three months.

Preparations available

1.5mg, 3mg, 4.5mg and 6mg capsules; 2mg/ml oral solution; 4.6mg/24hour, 9.5mg/24 hour and 13.3mg/24 hour patches.

Dosage and Administration

The dose is initially 1.5 mg twice daily and may be increased in steps of 1.5 mg twice daily at intervals of at least 2 weeks according to tolerance up to a maximum dose of 6 mg twice daily.
Rivastigmine increases gastric acid secretion and should be taken with food to minimise the effects of this.
Alternatively rivastigmine patches are available, initially using a 4.6-mg patch per day. This can be increased to a 9.5-mg patch per day for at least 4 weeks. 9.5 mg/24 h is the recommended daily effective dose which should be continued for as long as the patient continues to demonstrate therapeutic benefit. If well tolerated and only after a minimum of six months of treatment at 9.5 mg/24 h, the treating physician may consider increasing the dose to 13.3 mg/24 h in patients who have demonstrated a meaningful cognitive deterioration (e.g. decrease in the MMSE) and/or functional decline (based on physician judgement) while on the recommended daily effective dose of 9.5 mg/24 h.
See SPC for further information on using patches.

Dose Modifications

Renal Impairment	Hepatic Impairment
Use with caution	Use with caution

Contraindications

Known hypersensitivity to rivastigmine or any excipient.
Severe hepatic impairment

Cautions

History of seizures
Pre-existing cardiac disease
Asthma or COPD
History of peptic ulcers or recovering from gastrointestinal surgery.
Urinary retention/bladder outflow obstruction

What are the main side-effects?

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The most common side-effects of cholinesterase inhibitors are nausea, mild anorexia, fatigue, diarrhoea, muscle cramps and sometimes poor sleep. Weight loss can also occur with donepezil. Patients should be advised to take the medicine with food to minimise side effects. Please refer to the BNF for further details.

Drug Interactions

There are no specific dose changes which need to be made in relation to acetylcholinesterase inhibitors however it would be useful for prescribers to be aware of the following:

- Smoking tobacco increases the clearance of rivastigmine.

The risk of adverse effects, including bradycardia, may be increased if an acetylcholinesterase inhibitor is given with amiodarone or other antihypertensive/antiarrhythmic drugs. Acetylcholinesterase inhibitors may antagonise effects of anticholinergic drugs and worsen Parkinsonian symptoms; this may induce or exacerbate extrapyramidal side effects.

Monitoring -

1. **Adverse effects:** Most common side effects are gastrointestinal disturbance (nausea, vomiting, and diarrhoea).
2. **Weight/BMI:** weight loss is associated with Alzheimer's disease but can also occur with acetylcholinesterase inhibitors.
3. **Concurrent medication:** Medication should be reviewed at each visit in order to identify potential drug interactions.
4. **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.
5. **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 develops an allergy or contra-indication to the medication.
If treatment is considered to be no longer having a worthwhile effect on cognitive, global, functional or behavioural symptoms contact specialist for advice.
Where withdrawal of the treatment is advised this should be done gradually over a 4 week period.

When to seek Specialist advice / review

You can get advice regarding patients taking drug treatments for dementia from the locality memory treatment services in addition to CCG community pharmacy support
Tolerability may change over time consequent upon the ageing process and the emergence of medical co-morbidities and frailty. In this situation it may appropriate to reduce the dose or discontinue treatment &/or consider an alternative drug. It may be appropriate to make such decisions in consultation with the specialist who initiated treatment.
You may wish to seek advice in the following circumstances:
• Emergent concerns regarding tolerability
• To consider whether to discontinue treatment at an advanced stage of the illness

Advice for patients having a general anaesthetic

Rivastigmine can enhance the effects of suxamethonium and the duration of the block may be prolonged. Rivastigmine can antagonise the effects of non-depolarising muscle relaxants such as atracurium, cisatracurium, mivacurium, pancuronium, rocuronium, vecuronium.

Drug	Situation	Advice
Rivastigmine	Planned Operations	Miss the last dose prior to surgery, i.e., if the operation is in the morning miss the previous night-time dose.
	Emergency operations	Inform the anaesthetist of potential of prolonged muscle relaxation.
	Post-operative	Re-introduce during post-surgical rehabilitation.

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