Interface Prescribing Subgroup
DRUGS FOR DEMENTIA: Donepezil
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

Donepezil is licensed for the symptomatic treatment of patients with mild to moderately severe Alzheimer's disease. Donepezil is the 1st choice acetylcholinesterase inhibitors.

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

5mg and 10mg film coated tablets OR 5mg and 10mg orodispersible tablets
1mg/ml oral solution

Dosage and Administration

It is given initially at 5 mg once daily. After 1 month the treatment should be assessed, and the dose can be increased to a maximum of 10 mg once daily if necessary. It is recommended that the dose is given at bedtime to minimise likelihood of gastrointestinal (GI) symptoms. However if sleep disturbances are noted, particularly vivid nightmares, then a shift to morning dosing can resolve this.

Dose Modifications

Renal Impairment	Hepatic Impairment
No dose adjustment required	Mild to moderate – dose escalation depending on individual tolerability. Severe – avoid.

Contraindications

Known hypersensitivity to donepezil or any excipient.

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?

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.

Approved: 19.3.15
Reviewed: 18.8.2017
Review date: 18.8.2019

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

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:

- Potent inhibitors of CYP3A4 (including ritonavir, clarithromycin and itraconazole) may raise donepezil levels.
- Inducers of CYP3A4 (including carbamazepine, phenytoin, and rifampicin) may lower donepezil levels.

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

Drug	Situation	Advice
Donepezil	Planned operations	Stop 2 – 3 weeks before operation for complete wash out.
	Emergency operations	Inform the anaesthetist of potential of prolonged muscle relaxation.
	Post-operative	Re-introduce during post-surgical rehabilitation.

Approved: 19.3.15
Reviewed: 18.8.2017
Review date: 18.8.2019