



Guidance on initiating the Prescribing of Donepezil in Primary Care

Introduction

This guidance has been commissioned by the Strategic Clinical Network for Mental Health, Dementia, and Neurological Conditions (South West) as a resource for prescribers to support and inform prescribing of anti-dementia drugs, and to inform the design of dementia diagnosis and post-diagnosis pathways.

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Assumptions

This guidance assumes that:

- Donepezil will only be initiated in primary care within its licenced indication i.e. for the symptomatic treatment of mild to moderately severe Alzheimer's dementia.
- The diagnosis of Alzheimer's disease has been adequately confirmed according to current clinical guidelines or locally agreed pathways.
- The initiating clinician is competent in the application and interpretation of appropriate assessments of cognitive, functional and behavioural symptoms.
- A recent assessment of the patient's dementia is available as a treatment baseline.

BEFORE INITIATING

- Discuss views, expectations and treatment goals with patient and/or carer (if patient consents) as part of shared decision making process.
- Patients and carers should be advised:
- That Donepezil may help to maintain current skills and abilities, thereby helping to improve quality of life.
- Not to expect a dramatic reversal of cognitive decline or prevention of progression.
- Not all patients will obtain clinical benefit.
- Of the possibility of discontinuation of treatment after review, or if the dementia progresses to a more severe stage.

Consider co-morbidities (Table, page 5) and potential drug interactions (Table 2, page 6).

Check pulse at baseline (and at initial 4 week and 3 month reviews and then at routine 6 monthly reviews thereafter). If the pulse rate is below 50 bpm, or between 50-60 bpm with symptoms of syncope, withhold Donepezil and review the patient to identify the underlying cause of the bradycardia.

INITIATE DONEZEPIL

at 5mg nocte for 4 weeks

If patient has swallowing difficulties prescribe as orodispersible tablets.

Side effects (see Table 3, page 7) commonly include diarrhoea, muscle cramps, fatigue, nausea, vomiting, insomnia and are possible in up to 20% of patients, particularly on initiation or dosage increase, but often diminish after a few days.

AFTER 4 WEEKS

review patient response and tolerance and recheck pulse

- If well tolerated - consider increasing the dose to the maximum of 10mg nocte.
- If treatment with a dose of 10mg daily is interrupted for longer than several days due to side effects or compliance, treatment should be re-initiated on the lower 5mg dose.
- Many patients can be adequately maintained at 5mg daily to minimise side effects.

AFTER 3 MONTHS

review treatment effect using clinical judgement and if required, functional and/or cognitive assessments and recheck pulse

- Consider patient and carers opinion on any improvement.
- Consider physical, sensory and communication difficulties that could affect the result.
- If no benefit demonstrated at 3 months but well tolerated – reassess at 6 month review before considering discontinuing.

AFTER 6 MONTHS

review clinical benefit being obtained

- Prescribing should only be continued if having a worthwhile effect on cognitive, global, functional or behavioural symptoms.
- If the patient is not responding to treatment, or side effects are intolerable, discontinue prescribing and consider seeking specialist advice.
- After discontinuation, drug effects can wear off anytime in between 2 days to 4 weeks. Consider restarting if there is a decline in symptoms within this period.
- The benefits of acetyl cholinesterase inhibitors (ACIs) appear to last for 2 to 3 years in some patients. None of the ACIs are licenced for severe dementia.

Table 1: Donepezil - Cautions in use

(if any doubt – seek specialist advice)

Concurrent condition	Effect
Cardiac disease, sick sinus syndrome, supraventricular conduction abnormalities	↑ Risk of bradycardia
Gastro or duodenal ulcers or susceptibility to ulcers	↑ Risk of ulcers
Asthma / COPD	↑ Risk of bronchospasm
History of convulsions	↑ Risk of generalised convulsions
Bladder outflow obstruction	may ↑ bladder outflow obstruction
Mild to moderate hepatic impairment	Perform dose escalation according to individual tolerability.
Severe hepatic impairment	Contraindicated
Renal impairment	No dosage adjustment required.

Table 2: Donepezil - Potential drug interactions

Drug	Adverse Effect
Amiodarone, Beta blockers, Diltiazem,	↑ Risk of bradycardia, arrhythmias or syncope
Verapamil	Potential antagonistic effect; monitor for ↑ efficacy of either drug
Antimuscarinics	↑ Risk of movement disorders and neuroleptic malignant syndrome
Olanzapine, Risperidone	↑ Plasma concentration of Donepezil
Carbamazepine, Dexametasone,	↑ Plasma concentration of Donepezil
Phenobarbital, Phenytoin, Rifampicin	Potential additive effect

Table 3: Donepezil - Potential side effects

Frequency	Side effects
Very Common (>1/10)	Diarrhoea, headache, nausea
Common (>1/100, <1/10)	Abdominal disturbance, abnormal dreams and Nightmares*, accident, aggressive behaviour*, agitation*, anorexia, common cold, dizziness, fatigue, hallucinations*, insomnia, muscle cramps, pain, pruritis, rash, syncope**, urinary incontinence, vomiting
Uncommon (>1/1000, <1/100)	Bradycardia, gastric and duodenal ulcers, gastrointestinal haemorrhage, minor increase in serum concentration of muscle creatine kinase, seizure**
Rare (>1/10000, <1/1000)	Atrioventricular block, extrapyramidal symptoms, liver dysfunction including hepatitis***, sino-atrial block

* Reports of hallucinations, abnormal dreams, nightmares, agitation and aggressive behaviour have resolved on dose-reduction or discontinuation of treatment

** In investigating patients for syncope or seizure, the possibility of heart block or long sinus pauses should be considered

*** In cases of unexplained liver dysfunction, withdrawal of Donepezil should be considered

More detailed prescribing information is available in the Donepezil SPC at:

[http://www.medicines.org.uk/EMC/searchresults.aspx?
term=Donepezil&searchtype=QuickSearch](http://www.medicines.org.uk/EMC/searchresults.aspx?term=Donepezil&searchtype=QuickSearch)