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Waitemata District Health Board
Best Care for Everyone

DONEPEZIL - SAFE PRESCRIBING - DON'T FORGET

- DISCUSS TREATMENT GOALS WITH PATIENT AND CAREGIVERS
- ENCOURAGE ONGOING ASSESSMENTS AND GOOD ADHERENCE
- START LOW AND GO SLOW
- CHECK PULSE BEFORE PRESCRIBING, AND AT EACH VISIT
- CONSIDER RISK/BENEFIT WHEN CHANGING MEDICINE REGIMES

In New Zealand donepezil is registered for the treatment of mild, moderate and severe Alzheimer's disease and vascular dementia.[1,2] Treatment should always be initiated and supervised by a prescriber with appropriate knowledge of diagnosis and management of these conditions[3] such as a psychogeriatrician, geriatrician, neurologist, or general practitioner with experience in the treatment of dementia. Make sure you have a clear diagnosis, having ruled out other treatable causes of dementia.[3]

Note: Prescribers within the Auckland region are encouraged to use the Auckland Regional Cognitive Impairment Pathway.[4]

http://aucklandregion.healthpathways.org.nz

DISCUSS TREATMENT GOALS WITH PATIENT AND CAREGIVERS

Dementia

Clear and realistic goals should be clarified with the patient and their caregivers prior to starting treatment.[3] Family and caregivers are well placed to observe for treatment response and adverse effects.[3]

The management of dementia is primarily supportive and symptomatic.[3] Donepezil may help to maintain current skills and abilities; improving quality of life temporarily.[3] There is no evidence that any current treatment can prevent the onset or progression of Alzheimer's disease.

BPSD

There may be some benefit in using donepezil to manage the behavioural and psychological symptoms of dementia (BPSD), although the evidence is weak.[5] Much more important is to determine likely causes or triggers of the behaviours and attempt to correct reversible factors. For example, pain, anxiety, infection or depression should be treated with appropriate medication.[6] Psychosocial interventions should be used throughout treatment.[7]

Delirium

Donepezil is not recommended for the treatment of delirium. Donepezil provides no significant improvement in delirium, but more adverse effects.[8]

ENCOURAGE ONGOING ASSESSMENTS AND GOOD ADHERENCE

To establish whether the patient is suitable for donepezil, consider whether they are able to participate in ongoing assessments of response, and be adherent with their treatment. Family and caregivers are an important part of this process.[3]

Rating scales to assess cognitive function can be useful, but other factors must also be taken into account to provide a complete assessment. Any benefit in cognition, global, functional or behavioural symptoms should be seen as a good response and considered as a reason to continue treatment. Individual response cannot be predicted.

Rating scales that are useful for assessments of cognitive function are the Montreal Cognitive Assessment (MoCA)[9], or Addenbrooke's Cognitive Examination, version 3 (ACE-3).[10] Use of the Mini Mental State Examination (MMSE) is discouraged due to unresolved copyright claims.

Assess for side effects, treatment efficacy and disease progression at baseline, and again at 1, 3 and 6 months[11] Assessments should be made in consultation with the family, patient, and carers to determine if treatment goals are being met.[1,3]

Note: Good adherence is essential; the benefits of donepezil are rapidly lost when treatment is interrupted and may not be fully regained on re-initiation. If treatment has been interrupted for more than several days, re-initiate with the lowest daily dose.[12]

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DONEPEZIL

START LOW AND GO SLOW

The recommended starting dose is 5mg at night. After one month, if tolerated, increase to 10mg,[1] and assess at 3 and 6 months. Further assessments should continue on a 6-monthly basis to determine ongoing efficacy and response with the predetermined treatment goals.

Adverse effects are dose-dependent, and the rate of titration may affect their frequency.[1] Although usually mild and transient, the most common reasons for discontinuing therapy are gastrointestinal effects such as nausea, vomiting and diarrhoea. These occur more frequently when the dose is rapidly escalated from 5mg to 10mg, and can be minimised by using gradual dose increments, taking the tablets with food and ensuring adequate hydration.[12]

Donepezil can also cause muscle cramps, dizziness and fatigue; driving ability should be regularly evaluated if the patient is driving.[1] Dizziness is usually mild and transient and not related to cardiovascular problems.[6]

Unusual dreams and nightmares are commonly reported; these may resolve by reducing the dose. Moving the dose to morning, rather than evening may not be helpful because donepezil has a long half-life, and once steady state has been reached, plasma concentrations show little variability over the course of the day.[1] Other adverse effects include aggressive behaviour, agitation, hallucinations and fatigue.[11]

If the patient cannot tolerate adverse effects, reduce the dose back to 5mg or discontinue.[3]

Note: Doses of 23mg per day have been used in the trial setting for moderate to severe Alzheimer's disease. Although higher doses may have some benefit, many participants experienced unacceptable side effects.[13]

Interactions

Donepezil is a cholinesterase inhibitor. Medicines with *anticholinergic* actions or side effects including tricyclic antidepressants, sedating antipsychotics, medicines for overactive bladder, and over the counter medicines such as sedating antihistamines and some antiemetics will compete for the same receptors, negating the action of donepezil. Co-prescription with these medicines should be avoided.

Other potential interactions include medicines that could increase the risk of bradycardia such as amiodarone, beta blockers, digoxin or diltiazem.[3,11,14,15]

Note: Other precautions with donepezil include the presence of asthma, obstructive pulmonary disease, urinary retention, or a history of peptic ulcer.[1]

CHECK PULSE BEFORE PRESCRIBING, AND AT EACH VISIT

Donepezil is associated with rare incidences of heart block and sinus bradycardia.[1,14] Check heart rate before initiation; if it is under 60 per minute, an ECG is recommended prior to starting treatment. Check the pulse at monthly intervals during titration and 6-monthly thereafter.

If there are any symptoms of dizziness or syncope, organise a clinical review to measure heart rate, blood pressure and arrange an ECG.

Note: There is a detailed flowchart for the management of bradycardia for people prescribed donepezil via the Auckland regional clinical pathway:

http://aucklandregion.healthpathways.org.nz

CONSIDER RISK/BENEFIT WHEN CHANGING MEDICINE REGIMES

Health professionals may be asked about transferring patients from a non-subsidised acetylcholinesterase inhibitor to donepezil. Although there may be cost advantages, the changeover may cause destabilisation and loss of treatment efficacy. Specialist advice should be sought prior to any changes being made.[3]

Rivastigmine is an alternative acetylcholinesterase inhibitor that is available as a transdermal patch.[3] This may be preferable for patients who experience adverse gastrointestinal effects with donepezil.[3] Rivastigmine is available on Special Authority under these circumstances.[3]

When to stop treatment

There is very limited evidence to guide decisions about whether to continue treatment as the condition progresses.[16]

If the following issues occur, consider discontinuing cholinesterase inhibitors such as donepezil[3]

- significant adverse effects
- poor adherence to treatment or monitoring requirements
- treatment goals not achieved

Note: Treatment goals should be set before initiating

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therapy and used to assess response and help guide decisions about continuation or discontinuation of treatment.

Although some recommendations suggest discontinuation of donepezil when there is no longer evidence of a therapeutic effect,[1] there is emerging evidence to suggest that patients with moderate or severe Alzheimer's disease do receive cognitive and functional benefits with continued treatment.[16]

If a decision is made to stop donepezil, it should be reduced over 2-3 weeks if possible. Beneficial effects usually abate gradually, however in some cases there may be a rebound effect after abrupt cessation.[3] If this occurs then consideration should be given to restarting.

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