Donepezil to be funded on pharmaceutical schedule

PHARMAC recently announced that donepezil, a medicine used in the treatment of Alzheimer's disease, is to be funded on the pharmaceutical schedule. Donepezil (brand name Donepezil-Rex) will be available for prescription by any prescriber, and will not require Special Authority approval or specialist recommendation. The exact date of funding has not yet been determined.

Donepezil is a specific and reversible inhibitor of acetylcholinesterase, registered in New Zealand for the treatment of mild, moderate and severe Alzheimer's disease and vascular dementia (dementia associated with cardiovascular disease). However most international guidelines recommend that donepezil is used only for the symptomatic treatment of moderate Alzheimer's disease (rated by a MMSE* score of 10 – 20).

Efficacy of donepezil in Alzheimer's disease

Donepezil has been shown to have a modest beneficial effect in some people with mild to moderate Alzheimer's disease. Minor improvements in daily activity scores and cognition test results have been observed (e.g. an improvement of two to three points on the 70 point ADAS-cog† score and one to two points on the MMSE).

Trials that have compared donepezil with placebo have generally been of short duration (12 – 60 weeks) and long term benefits have not been shown. However, it is clear that in some patients donepezil provides modest improvements or delays in progression of Alzheimer's disease for up to six months or more.

Although not a requirement for funding, it is recommended that donepezil is only prescribed by practitioners experienced in the treatment of patients with dementia. It is important to obtain a baseline evaluation of cognition using ADAS-cog or MMSE and continue monitoring during treatment.

Dose

The starting dose of donepezil is 5 mg daily for the first month, increasing to 10 mg daily if necessary. The higher dose may be slightly more effective in some patients but dose related adverse effects may increase.

Adverse effects and drug interactions

In clinical trials, dropout rates for patients taking donepezil were significantly higher (about 30%) than those taking placebo. The most common adverse effects are nausea, vomiting and diarrhoea.

The hepatic metabolism of donepezil involves the enzymes CYP3A4 and possibly CYP2D6. Drugs that inhibit CYP3A4 such as erythromycin and fluoxetine may increase the plasma concentration of donepezil but the clinical significance of this is unknown. Donepezil may interfere with actions of anticholinergic drugs.

For more information refer to the medicine safety data sheet, available from: www.medsafe.govt.nz/Profs/Datasheet/DSForm.asp

Further information about donepezil and the pharmacological management of Alzheimer's disease will be covered in a future edition of Best Practice Journal.

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* Mini Mental State Examination

† Alzheimer's Disease Assessment Scale-cognitive subscale

Dextropropoxyphene - finding alternatives

From August 1, 2010 dextropropoxyphene (combined with paracetamol in Paradex and Capadex) will no longer be approved for use in New Zealand. Patients who continue to require treatment will need to be prescribed an alternative analgesic.

There is no robust evidence that dextropropoxyphene combined with paracetamol is any more effective than paracetamol alone, for either acute or chronic pain.

Review analgesic requirements

Review the patient's medical history and ascertain the type and severity of pain they are experiencing. If a recent review has not taken place, symptoms may have resolved or ameliorated. Most people taking dextropropoxyphene are likely to have mild to moderate pain which responds well to paracetamol, a weak opioid or low dose NSAIDs.

A recent time series analysis looked at the impact of the discontinuation of dextropropoxyphene containing products in the UK.[1] Over the two years following discontinuation, there was a significant increase in the number of prescriptions for paracetamol, codeine and paracetamol/codeine products, but not tramadol. These observations indicate that most patients can be successfully switched to regular full dose paracetamol (1 g, four times daily).

If paracetamol alone is not sufficient, a low dose NSAID (e.g. Ibuprofen 200 – 400 mg three times daily) can be added to, or used instead of paracetamol.[2] NSAIDs should be used at the lowest possible dose for the shortest possible time. If an NSAID is contraindicated or if there are safety concerns, a weak opioid such as codeine can be added to full dose paracetamol.[2] Preparations containing a combination of paracetamol with codeine can be tried initially, but the amount of codeine may be insufficient to add to the analgesic effects of paracetamol alone. A full dose of 30 – 60 mg codeine, up to four times daily, may be required.

It is not necessary to calculate opioid analgesic dose equivalents when switching from dextropropoxyphene.

For more information on the use of weak opioids for pain see "WHO analgesic ladder: which weak opioid to use at step two", BPJ 18 (Dec, 2008).

If these combinations are not effective in controlling pain, a strong opioid may be indicated. The strong opioid of choice is morphine. However, it is very unlikely that morphine will be required for anyone previously taking dextropropoxyphene.

A relatively small number of patients may need referral; to a pain clinic for complex pain syndromes, or to a drug and alcohol centre if dextropropoxyphene is being misused.

Tramadol and oxycodone - not logical alternatives

Tramadol and oxycodone should not be considered as first line alternatives to dextropropoxyphene. Although tramadol has recently been funded on the pharmaceutical schedule, it is NOT because it is intended to replace dextropropoxyphene. Tramadol is an alternative to first line weak opioids, such as codeine, if these are not tolerated or are contraindicated. Oxycodone is a strong opioid and is only recommended as an alternative to morphine for severe pain.

References

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