

Licensed Drug Treatments for Alzheimer's Disease in Australia: Acetylcholinesterase Inhibitors

There are several drug treatments for Alzheimer's disease that have been approved for marketing and use in Australia. This sheet provides information on the three drugs called acetylcholinesterase inhibitors. For information on another drug for Alzheimer's disease, Ebixa (Memantine), see Update Sheet No 6.

Acetylcholinesterase inhibitors offer some relief from the symptoms of Alzheimer's disease for some people for a limited period of time. These drugs are available on the Pharmaceutical Benefits Schedule (PBS) subject to certain conditions being met. There are currently no approved drug treatments for other forms of dementia.

This sheet provides information about how acetylcholinesterase inhibitors work, who might benefit, how they are prescribed and what questions people with dementia, their families and carers should ask their doctor before being prescribed any of these drugs.

Acetylcholine

Nerve cells talk to each other by releasing chemicals; these chemicals are called neurotransmitters. A considerable amount of research has concentrated on the neurotransmitter called acetylcholine, the major neurotransmitter for memory. People with Alzheimer's disease have low levels of acetylcholine in their brain. An enzyme called acetylcholinesterase breaks down acetylcholine in the brain.

it being passed on to the next nerve cell.

Acetylcholinesterase inhibitors may result in higher concentrations of acetylcholine, leading to increased communication between nerve cells, which in turn, may temporarily improve or stabilise the symptoms of dementia.

How acetylcholinesterase inhibitor drugs work

Acetylcholinesterase inhibitor drugs stop or inhibit acetylcholinesterase from destroying acetylcholine when it travels from one cell to another. This means that the acetylcholine, which is in short supply in people with Alzheimer's disease, is not destroyed so quickly and there is more chance of

The use of acetylcholinesterase inhibitors is only one possible pharmaceutical approach to treating the symptoms of Alzheimer's disease. Many other neurotransmitters are involved and may in future be shown to be more important.

What do the drugs do?

The effect of these drugs varies for different people. Some will not notice any effect, while others may find that their condition improves slightly, or that they stay the same when they

would have expected to become gradually less able.

The areas in which some people with Alzheimer's disease may find improvement are:

- ability to think clearly
- function in daily activities, eg. manage bank account, talk, dress
- behaviour, eg. help with apathy, hallucinations, delusions, etc.

How long do the drugs work?

Trials indicate that these drugs on average delay the progression of symptoms for about nine to twelve months. This does not mean that the drugs should be stopped after nine months, otherwise the nine months delay in progression of symptoms will be lost. Some people with dementia report benefits for longer periods and some recent research has shown benefits can be sustained for up to five years.

Acetylcholinesterase inhibitor drugs registered in Australia

The following is general information about these medications, which can only be prescribed by a medical practitioner. Comprehensive product information should be consulted before taking these medications.

Donepezil Hydrochloride (Aricept)

This drug's generic name is donepezil. Its trade name, the name used for marketing, is **Aricept**. Pfizer Pty Ltd markets the drug in Australia.

- **Daily dosage required**

Aricept is administered once a day and can be taken with or without food. It is available in 5mg or 10mg tablets; the lower dosage is prescribed initially. The dose is increased to one 10mg tablet per day usually after one month.

Rivastigmine (Exelon)

Rivastigmine is this drug's generic name and the name used for marketing is **Exelon**. Novartis Pharmaceuticals markets the drug in Australia.

- **Daily dosage required**

Tablets

Exelon is taken twice a day, normally in the morning and evening. The dose is gradually increased from 1.5mg twice per day in steps to a maximum of 6mg twice per day.

Patch

An Exelon patch has recently been approved for use in Australia. As of 1st July 2008, the Exelon patch will be listed on the Pharmaceutical Benefits Schedule and available on prescription at subsidised costs. The patch delivers the same drug via the skin rather than orally and may reduce gastrointestinal side effects.

Galantamine Hydrobromide (Reminyl)

The generic name for this drug is galantamine. It is marketed in Australia under the name of **Reminyl** by Janssen-Cilag Pty Ltd.

- **Daily dosage required**

Prolonged release capsules

Reminyl is available in 8, 16 and 24mg prolonged release capsules, taken once a day, preferably with food. Usually the lower dose is prescribed initially and then gradually increased to the most suitable dose.

Are there side effects?

Side effects from these drugs are more common when someone first takes them, and they often settle down with time. The most likely side effects are diarrhoea, nausea, vomiting, muscle cramps, lowered blood pressure, insomnia, fatigue and loss of

appetite. Other reported side effects include dizziness and nightmares. If the dose is increased gradually the likelihood of side effects is lower.

Caution is required in people with a history of peptic ulcers, asthma or abnormally slow heart rates.

The type and rate of side effects vary depending on the drug prescribed. It is recommended that this issue be discussed with your doctor.

Are these drugs effective for all people with dementia?

Currently in Australia, Aricept is approved for use for people with mild, moderate and severe Alzheimer's disease, while Exelon and Reminyl are approved for use for people with mild to moderate Alzheimer's disease.

There is some evidence that the earlier these drugs are started the better. Clinical trials with acetylcholinesterase inhibitors for the treatment of people in the later stages of Alzheimer's disease and of people with other forms of dementia are currently under way. People who have a less common form of dementia called dementia with Lewy bodies have been shown to benefit and there is emerging evidence that people with mixed vascular dementia and Alzheimer's disease may also benefit.

There are also clinical trials underway for using alternative forms of the acetylcholinesterase inhibitors, such as slow release and injectable forms, that may help people who don't respond to or cannot tolerate the side effects of the currently available forms.

Clinical trials showed no difference in the effectiveness of acetylcholinesterase inhibitors in relation to age, sex or ethnic origin.

These drugs treat the symptoms of Alzheimer's disease only and are not a cure - there is no evidence that they can halt or reverse the process of cell damage that causes the disease. It is also important to realise that these drugs will not help everyone who tries them.

How to get treatment

It is important that the person has a proper diagnosis and assessment to determine that he/she has Alzheimer's disease and not another form of dementia and to determine if the person is in the mild to moderate stages of the illness and therefore eligible for the PBS subsidy of the drugs.

A specialist, such as a psychogeriatrician, geriatrician, neurologist or psychiatrist will usually be involved in this assessment and the prescription of the drug. For further information about the commonly used tests and assessments, see Update Sheet 8: *Tests Used in Diagnosing Dementia*.

Whenever a person begins taking a new drug, the doctor, patient and family members should discuss the potential side effects and how the drug may interact with any other medicines being taken.

Is there any subsidy available for these drugs?

Aricept, Exelon and Reminyl are approved for listing on the Pharmaceutical Benefits Schedule (PBS) and so the cost is subsidised by the Australian Government. At the time of writing, the subsidy is only available to people with a diagnosis of mild to moderate Alzheimer's disease. For more information about the conditions that need to be met in order

to receive these medications at the subsidised rate, please see Update Sheet 2: *Subsidies for Aricept, Exelon and Reminyl: What are the conditions?*

People who meet the conditions required by the PBS are able to purchase the prescription at the subsidised rates of \$31.30 or \$5.00 for concession card holders. Special concessions may be available to veterans.

People who do not meet the criteria for the subsidy may choose to purchase the prescribed drug at full cost. Depending on the pharmacy and the dosage prescribed, the full cost for any one of these drugs can range from \$160 a month to more than \$220 a month. People are able to shop around to obtain a more competitive price.

PBS criteria are reviewed regularly and a new schedule is updated monthly to include new listings and the latest changes. The latest schedule can be viewed on line at www.pbs.gov.au

What questions should you ask your doctor about any drug being prescribed?

- What are the potential benefits of taking this drug?
- How long before improvement may be noticed?
- What action should be taken if a dose is missed?
- What are the known side effects?
- If there are side effects, should the dosage be reduced or should the drug be stopped?
- If the drug is stopped suddenly, what happens?
- What drugs (prescription and over-the-counter) might interact with the medication?
- How might this drug affect other medical conditions?

- Are there any changes that should be reported immediately?
- How often will a visit to the doctor who prescribed the drug be needed?
- Is the drug available at a subsidised rate?

Alzheimer's Australia recognises that the currently licensed Alzheimer's drugs are not a cure. It is evident however that these drugs improve the quality of life for **some** individuals with Alzheimer's disease.

Parts of this Update Sheet are based on information produced by the US Alzheimer's Association and the UK Alzheimer's Society.

Thanks to Dr Mark Yates for reviewing this material.

This Update Sheet is provided for your information only, and does not represent an endorsement of any drug by Alzheimer's Australia.

Further Information

A range of books and videos, Help Sheets and Update Sheets are available through Alzheimer's Australia in your State or Territory by contacting the National Dementia Helpline on 1800 100 500.

Help Sheets and Update Sheets, including any more recent information, can also be obtained on the internet at www.alzheimers.org.au