

Drug treatments for Alzheimer's disease – Aricept, Exelon, Reminyl and Ebixa

No drug treatments can provide a cure for Alzheimer's disease. However, drug treatments have been developed that can temporarily slow down the progression of symptoms in some people. Aricept, Exelon and Reminyl all work in a similar way and are known as acetylcholinesterase inhibitors. There is also a newer drug, Ebixa, which works in a different way to the other three.

How do the drugs work?

Aricept, Exelon and Reminyl

Research has shown that there is not enough of a chemical called acetylcholine in the brains of people with Alzheimer's disease. Acetylcholine is one of the chemicals that nerve cells use to communicate.

Aricept, Exelon and Reminyl prevent an enzyme known as acetylcholinesterase from breaking down acetylcholine in the brain. Increased concentrations of acetylcholine lead to increased communication between nerve cells, which may in turn temporarily improve or stabilise the symptoms of Alzheimer's disease.

Aricept, Exelon and Reminyl work in similar ways. However, Reminyl also appears to act on the nicotinic neuronal receptors in the body, making them release more acetylcholine.

It is possible that one of these drugs might suit an individual better than another. The specialist should be able to advise whether there is any advantage associated with a particular drug.

Ebixa

The action of Ebixa is quite different to, and more complex than, that of Aricept, Exelon and Reminyl. Ebixa blocks a messenger chemical, known as a neurotransmitter glutamate. Glutamate is released in excessive amounts when brain cells are damaged by Alzheimer's disease, which causes the brain cells to be damaged further. Ebixa can protect brain cells by blocking this release of excess glutamate.

Can Ebixa be taken at the same time as Aricept, Exelon or Reminyl?

US research has suggested that a combination of Aricept and Ebixa is more effective than Aricept alone. Although this research is not conclusive, there is little evidence to support a contrary view. Ebixa works in a completely different way from the acetylcholinesterase inhibitors. Furthermore, a

person's symptoms could become worse if they stopped taking Aricept, which could then make it difficult to assess their suitability for Ebixa. However, whether doctors will prescribe both drugs together, especially on the NHS, is unclear.

Are these drugs effective for all people with Alzheimer's disease?

At present Aricept, Exelon and Reminyl are only used in people with mild to moderate Alzheimer's disease. They are not effective for everyone and may only temporarily improve memory or delay memory loss. Research is being undertaken to find out whether any of these drugs may be effective in the later stages of Alzheimer's disease.

Ebixa, however, can temporarily slow down the progression of symptoms in people in the middle and later stages of the disease. This is the first time a drug has been available for this group of people. There is also a suggestion that Ebixa may slow down the disease process itself.

Are there any side-effects?

Not everyone has the same side-effects or has them for the same length of time, if they have them at all. The most frequent side-effects of Aricept, Exelon and Reminyl include nausea and vomiting, diarrhoea, stomach cramps and headaches, dizziness, fatigue, insomnia and loss of appetite.

Side-effects of Ebixa include hallucinations, confusion, dizziness, headaches and tiredness. Ebixa is not recommended for people with severe kidney problems, but only because there has been no safety test for this group of people as yet. Caution is recommended for people with epilepsy and heart problems.

Side-effects can be less likely for people who start treatment by taking the lower prescribed dose for at least a month. Sometimes 'splitting' the dose and

taking half in the morning and half later in the day can help – but make sure you maintain the correct full daily dose.

If side-effects are experienced, discuss them with the doctor.

None of these drugs are addictive.

How and where can these drugs be obtained?

Aricept, Exelon and Reminyl

A government advisory committee, the National Institute for Clinical Excellence (NICE), has recommended that Aricept, Exelon and Reminyl should be available on NHS prescription for anyone with a diagnosis of Alzheimer's disease who could benefit from the drug treatment.

In the first instance, these drugs can only be prescribed by a consultant. A GP will need to refer the person to a hospital for a specialist assessment. A consultant will carry out a series of tests to assess whether the person is suitable for treatment and will write the first prescription if appropriate. Subsequent prescriptions may be written by the GP or the consultant.

Some people may still wish to obtain these drugs privately. Private prescriptions can be obtained either through a consultant, a GP or a private hospital. Private prescriptions are subject to consultation fees, prescription charges and dispensing fees, which vary. The current cost of these drugs to the NHS ranges from £800 to £1,000 per patient per annum.

Whether these drugs are obtained on the NHS or privately, the patient must be willing to take the treatment. It is also important to discuss any possible benefits, risks or side-effects with the doctor.

Ebixa

Ebixa is the most recent of the Alzheimer's drugs. It was launched in the UK in October 2002. The immediate availability of Ebixa on the NHS will depend on individual health authorities, as was the case with the three previous drugs. It may be available in some areas and not in others.

NICE was due to consider Ebixa in December 2003. However, this is now postponed until 2004 and NICE is not due to issue guidelines until May 2005. If NICE finds in favour of Ebixa, it should be available free of charge to all who meet NICE's criteria. Because NICE has yet to issue guidelines on Ebixa, it is currently unclear whether GPs will be able to prescribe. In theory, any suitably qualified doctor should be able to prescribe Ebixa. However,

guidelines and rules at local health authority levels may prohibit this in some areas.

Are these drugs effective for other types of dementia?

The acetylcholinesterase inhibitors were developed specifically to treat Alzheimer's disease. We do not yet know whether they can be helpful for people with other forms of dementia, although there is evidence that they may be effective in dementia with Lewy bodies and even in vascular dementia. Research is continuing.

Merz, the manufacturer of Ebixa, has released data showing that Ebixa is also effective for people in the later stages of vascular dementia. However, the drug has only been licensed for Alzheimer's disease. It is likely that Merz will eventually apply for a licence to market Ebixa as a treatment for people with vascular dementia.

What are the benefits of the drugs?

It is impossible to predict the potential benefits of using any of these drugs. Some people will improve, some will not, while others will continue to deteriorate.

In cases where these drugs prove effective they appear to slow down the progression of symptoms, including memory loss. They can also improve mood, reduce anxiety and restore confidence.

People who do not show an improvement or slowing down of symptoms in the first few months are unlikely to show any benefit later on. In these cases the drugs will be stopped.

If the person with dementia decides to stop taking a drug, they should speak to the doctor first if possible. If this is not possible, they should discuss it with the doctor as soon as possible after stopping treatment.

When someone stops taking a drug, their condition will deteriorate over a period of about four to six weeks until they are no better than someone who has not taken the drug.

Taking the drugs

It may be helpful if the consultant seeks the carer's views of the person's condition before treatment and during follow-up appointments. The patient's views should also be sought. It is important that these drugs are taken as prescribed and the consultant will need to be sure that the patient takes their medication regularly.

Dosages vary. Usually a patient will start on a low dose, which will be increased later to maximise

effectiveness. It is important to be on the highest tolerable dose to get the maximum effect.

- Aricept is administered once a day and can be taken with or without food. It is available in 5mg or 10mg tablets.
- Exelon is taken twice a day, normally in the morning and evening. People start with 3mg a day, which will usually increase to a dosage of between 6mg and 12mg.
- Reminyl is taken twice daily with food and is available in 4mg, 8mg and 12mg tablets. The recommended starting dose is 8mg to be taken daily for at least four weeks.
- Ebixa comes in two forms, as 10mg tablets and as 10mg oral drops. The tablets can be broken in half into 5mg doses, and taken with or without food. The recommended starting dose is 5mg a day, increasing after four weeks to up to 20mg a day.

If a dose is missed, it should be taken as soon as the person remembers, if it is the same day. If it is the next day, the person should not take two tablets but should simply continue with their normal dose.

What questions should you ask the doctor?

- What are the potential benefits of taking these drugs?
- How long will it be before I see a result?
- How often do these drugs need to be taken?
- If there are side-effects should the drug be stopped immediately?
- What happens if the drug is stopped suddenly?
- What other treatments (prescription and over-the-counter) might interact with these drugs?
- Can alcohol be consumed while taking the drug?
- How might these drugs affect other medical conditions?
- What changes in health should be reported immediately?
- How often will visits to the clinic/surgery be needed?
- Can someone with Alzheimer's disease living in a residential or nursing home take these drugs?

- Are there any costs associated with taking these drugs?
- Why is one drug prescribed rather than another?
- If one drug proves ineffective can another drug be tried?

Notes on drugs

Aricept (donepezil hydrochloride), produced by Eisai and co-marketed with Pfizer, was the first drug to be licensed in the UK specifically for Alzheimer's disease.

Exelon (rivastigmine), produced by Novartis Pharmaceuticals, was the second drug licensed in the UK specifically for Alzheimer's disease.

Reminyl (galantamine) was co-developed by Shire Pharmaceuticals and the Janssen Research Foundation. Originally derived from the bulbs of snowdrops and narcissi, Reminyl was the third drug licensed in the UK specifically for Alzheimer's disease.

Ebixa (memantine) is produced by Merz and marketed in Europe by Lundbeck. It is the newest of the Alzheimer's drugs.

