

Drug treatments for Alzheimer's disease

There are no drug treatments available that can provide a cure for Alzheimer's disease. However, medicines have been developed that can improve symptoms, or temporarily slow down their progression, in some people. This factsheet explains how the main drug treatments for Alzheimer's disease work, where to access them, and when they can be prescribed and used effectively. For more information about Alzheimer's disease, see our factsheet [What is Alzheimer's disease? \(401\)](#).

All drugs have at least two names: a generic name, which identifies the substance and a proprietary (trade) name, which may vary depending upon the company that manufactures it. This factsheet uses generic names and gives the most common trade names in brackets.

What are the main drugs used?

There are two main types of medication used to treat Alzheimer's disease - cholinesterase inhibitors and NMDA receptor antagonists - which work in different ways. Cholinesterase inhibitors include donepezil hydrochloride (Aricept), rivastigmine (Exelon) and galantamine (Reminyl). The NMDA receptor antagonist is memantine (Ebixa).

How do they work?

Donepezil (Aricept), rivastigmine (Exelon) and galantamine (Reminyl)

Research has shown that the brains of people with Alzheimer's disease show a loss of nerve cells that use a chemical called acetylcholine as a chemical messenger. The loss of these nerve cells is related to the severity of symptoms that people experience.

Donepezil, rivastigmine and galantamine prevent an enzyme known as acetylcholinesterase from breaking down acetylcholine in the brain. Increased concentrations of acetylcholine lead to increased communication between the nerve cells that use acetylcholine as a chemical messenger, which may in turn temporarily improve or stabilise the symptoms of Alzheimer's disease.

All three cholinesterase inhibitors work in a similar way, but one might suit an individual better than another, particularly in terms of side-effects experienced. (Current guidance for NHS treatment is that

the cheapest of these drugs is generally tried first, see 'NICE guidance' below.)

Memantine (Ebixa)

The action of memantine is quite different from, and more complex than, that of donepezil, rivastigmine and galantamine. Memantine blocks a messenger chemical known as glutamate. Glutamate is released in excessive amounts when brain cells are damaged by Alzheimer's disease and this causes the brain cells to be damaged further. Memantine can protect brain cells by blocking these effects of excess glutamate.

Are these drugs effective for everyone with Alzheimer's disease?

The latest (2011) guidance from the National Institute for Health and Clinical Excellence (NICE) recommends that donepezil, rivastigmine and galantamine are available as part of NHS care for people with mild-to-moderate Alzheimer's disease. There are also now several studies - including work supported by Alzheimer's Society - which suggest that cholinesterase inhibitors may also help people with more severe Alzheimer's disease. However, these drugs are not licensed in the UK for the treatment of severe Alzheimer's disease.

Between 40 and 70 per cent of people with Alzheimer's disease benefit from cholinesterase inhibitor treatment, but it is not effective for everyone and may improve symptoms only temporarily, between six and 12 months in most cases. According to an Alzheimer's Society survey of 4,000 people, those using these treatments often experience improvements in motivation, anxiety levels and confidence, in addition to daily living, memory and thinking.

It is not clear whether the cholinesterase inhibitors bring benefits for behavioural symptoms such as agitation or aggression. Trials have given mixed results here. Research does suggest that these drugs (and memantine) bring some relief from the carer's perspective.

Memantine is licensed for the treatment of moderate-to-severe Alzheimer's disease. It can temporarily slow down the progression of symptoms, including everyday function, in people in the middle and later stages of the disease. There is evidence that memantine may also help behavioural symptoms such as aggression and agitation (see our factsheets 408, [Drugs used to relieve depression and behavioural symptoms](#) and 509, [Dealing with aggressive behaviour](#)).

The 2011 NICE guidance (see below) recommends use of memantine as part of NHS care for severe Alzheimer's disease and for patients with moderate disease who cannot take the cholinesterase inhibitor drugs.

Can memantine be taken at the same time as donepezil, rivastigmine or galantamine?

A few studies have looked, with a range of conclusions, at whether combining donepezil with memantine is more effective than taking donepezil alone in moderate-to-severe Alzheimer's disease. A recent trial provides strong evidence that, for people already on donepezil, there are important benefits for both patient and carer of the person remaining on donepezil when their Alzheimer's disease has become severe and treatment with memantine is started.

Memantine works in a completely different way from the acetylcholinesterase inhibitors and, if a person stopped taking donepezil in order to try memantine, their symptoms could become worse, which could then make it difficult to assess their suitability for memantine.

This latest research was not reflected in the 2011 guidance from NICE which does not recommend the combination treatment. Whether doctors will prescribe both medicines together, especially on the

NHS, is unclear.

Are there any side-effects?

Generally, cholinesterase inhibitors and memantine can be taken without too many side-effects. Not everyone experiences 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 donepezil, rivastigmine and galantamine are loss of appetite, nausea, vomiting and diarrhoea. Other side-effects include stomach cramps, headaches, dizziness, fatigue and insomnia. Side-effects can be less likely for people who start treatment by taking the lower prescribed dose for at least a month (see 'Taking the drugs' section).

The side-effects of memantine are less common and less severe than for the cholinesterase inhibitors. They include dizziness, headaches, tiredness, increased blood pressure and constipation.

It is important to discuss any side-effects with the doctor and/or the dispensing pharmacist.

None of these drugs are addictive.

How can these drugs be obtained?

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 wish to obtain these drugs privately. Private prescriptions can be obtained 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 each year. However, the UK patents for all these drugs are expiring during 2012 and prices will start to fall dramatically as competing 'generic' versions are introduced. Whether these drugs are obtained on the NHS or privately, the patient must be willing to take the treatment, and should discuss any possible benefits, risks or side-effects with the doctor.

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 dementia related to Parkinson's disease, for which rivastigmine is licensed. NICE guidelines allow acetylcholinesterase inhibitors to be offered to people with Lewy body or Parkinson's disease dementia if they have distressing symptoms or challenging behaviours. (See factsheet 403, [What is dementia with Lewy bodies?](#) and 442, [Rarer causes of dementia](#).)

There are several trials examining cholinesterase inhibitors for the treatment of vascular dementia, but the benefits are very modest, except in the individuals with a combination of both Alzheimer's disease and vascular dementia. Cholinesterase inhibitors are not licensed for the treatment of vascular dementia. (See factsheet 402, [What is vascular dementia?](#)) Research is continuing.

Taking the drugs

NICE guidelines (2011) recommend that the consultant seeks the views of the carer on the condition of the person with dementia before treatment and during follow-up appointments. They should also seek the patient's views. The person must take the drugs as prescribed and the consultant will need to be sure that this is the case.

Dosages vary. Usually a patient will start on a low dose, which will be increased later to maximise effectiveness. Some people may not be able to take the highest dose due to side-effects. The doctor will prescribe the best dose for each individual. Information about doses is given below.

- Donepezil (Aricept) is administered once a day at bedtime. It is available in 5mg or 10mg tablets. Treatment is started at 5mg a day and then increased to 10mg a day after one month if necessary. The maximum licensed total daily dose is 10mg.
- Rivastigmine (Exelon) capsules or oral solution is taken twice a day, normally in the morning and evening. People start with 3mg a day in two divided doses, which will usually increase to a dosage of between 6mg and 12mg a day. An Exelon patch is also available in two versions. These deliver daily dosages of 4.6mg or 9.5mg with fewer side-effects than the capsules. Patches are suited to patients who struggle with oral medication and they are popular with carers. The maximum licensed total daily dose for rivastigmine is 12mg.
- The recommended starting dose for galantamine (Reminyl) is 8mg each day for four weeks, increased to 16mg a day for another four weeks and then a maintenance dose of 16-24mg daily. Galantamine is made in a variety of forms including a 4mg/ml (twice-daily) oral solution. Tablets of 8mg and 12mg are taken twice daily for maintenance doses. Slow-release capsules (Reminyl XL) are available as 8mg, 16mg and 24mg. These are popular because they need to be taken only once a day. The maximum licensed total daily dose for galantamine is 24mg.
- Memantine (Ebixa) comes in two forms, as 10mg and 20mg tablets, and as 10mg oral drops. The 10mg 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. The maximum licensed total daily dose is 20mg. If the person misses a dose, they should take it as soon as they remember, if it is on the same day. If it is the next day, the person should not take two tablets but should simply continue with their normal dose.

Questions to 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 I get side-effects, should I stop taking the drug immediately?
- What will happen if I stop the drug suddenly?
- What other treatments (prescription and over-the-counter) might interact with these drugs?
- Can I drink alcohol while taking the drug?
- How might these drugs affect other medical conditions?
- What changes in health should I report immediately?
- How often will I need to visit the clinic or surgery?
- 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 have I been prescribed one drug rather than another?
- If one drug proves ineffective can I try another drug?

Stopping treatment

Medication should be reviewed regularly and continued so long as the drug benefits outweigh any side-effects. If the person with dementia decides to stop taking a drug, they should speak to the doctor first, if possible, or as soon as they can after stopping treatment.

If someone stops taking their prescribed drug, their condition is likely to deteriorate more rapidly for several weeks. It is important to contact your doctor as soon as possible after stopping the medication if you think it should be re-started.

NICE guidance

The National Institute for Health and Clinical Excellence (NICE) reviews drugs and decides whether they represent good enough value for money to be available as part of NHS treatment.

In March 2011, NICE issued new guidance recommending that people with Alzheimer's disease should now have increased access to the available drugs.

The latest NICE guidance on drug treatments for Alzheimer's disease recommends that people in the mild-to-moderate stages of the disease should be given treatment with donepezil (Aricept), galantamine (Reminyl) or rivastigmine (Exelon), including individuals with both Alzheimer's disease and learning disabilities.

This differs from the previous (2006) NICE guidance, which indicated these drugs could be prescribed only to people in the moderate stage of Alzheimer's disease.

The 2011 NICE guidance further recommends that memantine (Ebixa) should be prescribed as part of NHS care for patients with severe Alzheimer's disease, or for those with moderate disease who cannot take the cholinesterase inhibitor drugs. This differs from the previous NICE guidance, which stated that memantine should not be prescribed as part of NHS care, but emphasised further studies as an important research priority.

The clinical care guideline on the care and treatment of people with dementia, which NICE publishes alongside its guidance, stresses that the severity of a person's dementia should not be determined by cognition scores alone (eg Mini Mental State Examination), but by a more holistic view of the patient's condition.

NICE guidelines permit people with dementia with Lewy bodies or dementia associated with Parkinson's disease to be offered an acetylcholinesterase inhibitor if their non-cognitive symptoms (eg hallucinations, agitation) are causing distress or leading to challenging behaviour. The decision as to whether these treatments are appropriate for particular individuals lies with the specialist doctor.

In relation to the drugs for Alzheimer's disease, NICE recommends that:

- treatment is started by a doctor who specialises in the care of people with dementia
- patients who are started on one of the drugs are checked regularly, usually by a specialist team
- the check-up includes an assessment of the patient's cognition, behaviour and ability to cope with daily life

- the views of carers on the patient's condition are discussed at the start of drug treatment and at check-ups
- treatment is continued as long as it is judged to be having a worthwhile effect
- where a cholinesterase inhibitor is given, the least expensive of the three drugs is prescribed first. However, if it is not suitable for the patient another cholinesterase inhibitor could be chosen.

Printed copies of CG42 Dementia: supporting people with dementia and their carers, or of Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease, can be ordered from NICE by calling 0845 003 7780, or downloaded from www.nice.org.uk

Alzheimer's Society continues to campaign for drugs to be made freely available to anyone who may benefit from them. For more information, see alzheimers.org.uk/accesstodrugs

For details of Alzheimer's Society services in your area, visit alzheimers.org.uk/localinfo

For information about a wide range of dementia-related topics, visit alzheimers.org.uk/factsheets

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Reviewed by: Dr Rupert McShane, Department of Psychiatry, University of Oxford and Coordinating Editor, Cochrane Dementia and Cognitive Improvement Group, and Dr Denise Taylor, Senior Teaching Fellow in Clinical Pharmacy, Department of Pharmacy and Pharmacology, University of Bath

Alzheimer's Society National Dementia Helpline

England, Wales and Northern Ireland: 0300 222 11 22

9.00am-5.00pm Monday-Friday

10.00am-4.00pm Saturday-Sunday

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