

FDA-Approved Treatments for Alzheimer's

While there is no cure for Alzheimer's disease, there are five prescription drugs approved by the U.S. Food and Drug Administration (FDA) to treat its symptoms.

Donepezil, galantamine, rivastigmine and tacrine are called "cholinesterase inhibitors." These drugs prevent the breakdown of a chemical messenger in the brain important for learning and memory. The fifth drug, memantine, regulates the activity of a different chemical messenger in the brain that is also important for learning and memory. Both types of drugs help manage symptoms but work in different ways.

Understanding available treatment options can help you and the person with the disease cope with symptoms and improve quality of life.

What are cholinesterase inhibitors?

Cholinesterase inhibitors are prescribed to treat symptoms related to memory, thinking, language, judgment and other thought processes. Three different cholinesterase inhibitors are commonly prescribed:

- Donepezil (marketed under the brand name Aricept), which is approved to treat all stages of Alzheimer's disease
- Galantamine (marketed under the brand name Razadyne), approved for mild to moderate stages.
- Rivastigmine (marketed under the brand name Exelon), approved for mild to moderate Alzheimer's.

Tacrine (Cognex), the first cholinesterase inhibitor, was approved in 1993 but is rarely prescribed today because of associated side effects, including possible liver damage.

How do cholinesterase inhibitors work?

Cholinesterase inhibitors work by increasing levels of acetylcholine, a chemical messenger involved in memory, judgment and other thought processes. Here's how: Certain brain cells release acetylcholine, which helps deliver messages to other cells. After a message reaches the receiving cell, various other chemicals, including an enzyme called acetylcholinesterase, break acetylcholine down so it can be recycled.

Alzheimer's disease damages or destroys cells that produce and use acetylcholine, thereby reducing the amount available to carry messages. A cholinesterase inhibitor slows the breakdown of acetylcholine by blocking the activity of acetylcholinesterase. By maintaining acetylcholine levels, the drug may help compensate for the loss of functioning brain cells.

Cholinesterase inhibitors seem to offer other benefits, as well. For example, galantamine appears to stimulate the release of acetylcholine and to strengthen the way certain message-receiving nerve cells respond to it. Rivastigmine may block the activity of another enzyme involved in breaking down acetylcholine.

Cholinesterase inhibitors can't reverse Alzheimer's and won't stop the underlying destruction of nerve cells. Consequently, their ability to improve symptoms eventually declines as brain cell damage progresses.

What are the benefits of cholinesterase inhibitors?

In clinical trials of all three cholinesterase inhibitors, people taking the medications performed better on memory and thinking tests than those taking a placebo, or inactive substance. The degree of benefit was small, however. In terms of overall effect, cholinesterase inhibitors may delay or slow worsening of symptoms. The effectiveness of cholinesterase inhibitors, as well as how long they are effective, varies from person to person.

There is no evidence that combining the drugs would be more helpful than taking any one of them. In fact, combining them would likely result in greater frequency of side effects. There is some evidence that individuals with moderate to severe Alzheimer's who are taking a cholinesterase inhibitor might benefit by also taking memantine.

The makers of Aricept (donepezil) released a higher-dose (23 mg), extended-release tablet of Aricept intended for individuals with moderate to severe Alzheimer's who have been taking the more common (10 mg) dose for at least three months. These individuals may have a better result with the extended-release form of Aricept, although both the extended-release and original forms can cause similar side effects. The person's doctor can provide advice about whether the extended-release form may be a better option for the person with dementia.

What are common side effects of cholinesterase inhibitors?

Cholinesterase inhibitors are generally well tolerated. If side effects occur, they commonly include nausea, vomiting, loss of appetite and increased frequency of bowel movements. It is strongly recommended that a physician who is experienced in using these medications monitor patients who are taking them, and that the recommended guidelines be strictly observed.

What is memantine?

Memantine (Namenda) is prescribed to improve memory, attention, reason, language and the ability to perform simple tasks. It was the first Alzheimer's drug of the NMDA receptor antagonist type approved in the United States. It's used to treat moderate to severe Alzheimer's. In 2005, the FDA declined to approve memantine for mild Alzheimer's.

How does memantine work?

Memantine appears to work by regulating the activity of glutamate, a chemical involved in information processing, storage and retrieval. Glutamate plays an essential role in learning and memory by triggering NMDA receptors to let a controlled amount of calcium into a nerve cell. The calcium helps create the chemical environment required for information storage. Excess glutamate, on the other hand, overstimulates NMDA receptors so that they allow too much calcium into nerve cells. That leads to disruption and death of cells. Memantine may protect cells against excess glutamate by partially blocking NMDA receptors.

What are the benefits of memantine?

One clinical study showed that people taking memantine showed a small but statistically significant improvement in their mental function and ability to perform daily activities. But study participants with lowest cognitive functioning showed no improvement on either daily activities or overall function.

Another study randomly assigned participants to receive either 10 mg of memantine twice a day or a placebo in addition to donepezil (Aricept), a cholinesterase inhibitor. Those receiving memantine showed a statistically significant benefit in mental function and performing daily activities, while participants taking donepezil plus placebo continued to decline.

What are common side effects of memantine?

Adverse side effects include headache, constipation, confusion and dizziness.

At-a-glance treatment chart

Generic	Brand	Approved For	Side Effects
donepezil	Aricept	All stages	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
galantamine	Razadyne	Mild to moderate	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
memantine	Namenda	Moderate to severe	Headache, constipation, confusion and dizziness.
rivastigmine	Exelon	Mild to moderate	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
tacrine	Cognex	Mild to moderate	Possible liver damage, nausea, and vomiting.

On the horizon

Scientists have made remarkable progress in understanding how Alzheimer’s affects the brain. Their insights point toward promising new treatments to slow or stop the disease. Ultimately, the path to effective therapies is through clinical studies.

If you or someone you know is interested in participating in a clinical study, visit www.alz.org/trialmatch.

The Alzheimer’s Association is the world’s leading voluntary health organization in Alzheimer’s care, support and research. Our mission is to eliminate Alzheimer’s disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health.

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