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## FDA-approved treatments for Alzheimer's

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

Three of the five available medications — donepezil, galantamine and rivastigmine — are from a class of drugs called “cholinesterase inhibitors.” These drugs prevent the breakdown of a chemical messenger in the brain that is important for learning and memory. The fourth 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. The fifth medication is a combination of one of the cholinesterase inhibitors (donepezil) with memantine.

Understanding available treatment options can help individuals living with the disease and their caregivers to 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 (Razadyne®), approved for mild-to-moderate stages.
- Rivastigmine (Exelon®), approved for mild-to-moderate Alzheimer's.

### How do cholinesterase inhibitors work?

Cholinesterase inhibitors work by increasing levels of acetylcholine, a chemical messenger involved in memory, judgment and other thought processes. 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 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. However, the degree of improvement was small. 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 three 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 23 mg extended-release tablet of the medication 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. Ask your doctor whether the extended-release form may be a better option for the person with dementia.

### **What are the 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 is used to treat moderate-to-severe Alzheimer's. The FDA declined to approve memantine for mild Alzheimer's in 2005.

### **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 the 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 the 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 functioning and performing daily activities, while participants taking donepezil plus placebo continued to decline.

### **What are the side effects of memantine?**

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

### **What are the side effects of the memantine + donepezil combination therapy?**

Namzaric®, a combination of donepezil and memantine, was approved by the FDA for the treatment of moderate-to-severe Alzheimer's in people who are taking donepezil hydrochloride 10 mg.

Namzaric may cause serious side effects, including:

- Muscle problems in patients given anesthesia.
- Slow heartbeat and fainting: This happens more often in people with heart problems. Call the doctor right away if a person faints while taking Namzaric.
- Increased stomach acid: This raises the chance of ulcers and bleeding, especially when taking Namzaric. The risk is higher for those who have had ulcers or take aspirin or other NSAIDs.
- Nausea and vomiting.
- Difficulty passing urine.
- Seizures.
- Worsening of lung problems in people with asthma or other lung disease.

Individuals taking Namzaric may see an improvement in cognition and overall mental function, and a temporary slowdown in the worsening of symptoms. However, there is no evidence that Namzaric prevents or slows the underlying disease process in patients with Alzheimer's disease.

**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.
memantine + donepezil	Namzaric	Moderate to severe	Nausea, vomiting, loss of appetite, increased frequency of bowel movements, headache, constipation, confusion and dizziness.

**On the horizon**

Scientists have made remarkable progress in understanding how Alzheimer's disease 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. Visit [alz.org/trialmatch](http://alz.org/trialmatch) to learn about Alzheimer's Association TrialMatch®, a free clinical studies matching service, and how you can participate in vital Alzheimer's disease research.

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