

About FDA-approved cholinesterase inhibitors

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The U.S. Food and Drug Administration (FDA) has approved two classes of drugs to treat cognitive symptoms of Alzheimer's disease. The first Alzheimer medications to be approved were cholinesterase (*KOH luh NES ter ays*) inhibitors. Three of these drugs are commonly prescribed—donepezil (Aricept®), approved in 1996; rivastigmine (Exelon®), approved in 2000; and galantamine (Reminyl®), approved in 2001. Tacrine (Cognex®), the first cholinesterase inhibitor, was approved in 1993 but is rarely prescribed today because of associated side effects, including possible liver damage.

What is a cholinesterase inhibitor designed to do?

Cholinesterase inhibitors are designed to enhance memory and other cognitive functions by influencing certain chemical activities in the brain. Acetylcholine is a chemical messenger in the brain that scientists believe is important for the function of brain cells involved in memory, thought, and judgment. Acetylcholine is released by one brain cell to transmit a message to another. Once a message is received, various enzymes, including one called acetylcholinesterase, break down the chemical messenger for reuse.

In the Alzheimer-afflicted brain, the cells that use acetylcholine are damaged or destroyed, resulting in lower levels of the chemical messenger. A cholinesterase inhibitor is designed to stop the activity of acetylcholinesterase, thereby slowing the breakdown of acetylcholine. By maintaining levels of acetylcholine, the drug may help compensate for the loss of functioning brain cells.

Galantamine also appears to stimulate the release of acetylcholine and to strengthen the way that certain receptors on message-receiving nerve cells respond to it.

What effects did cholinesterase inhibitors have on the memories of persons who took them in clinical trials?

Donepezil and rivastigmine were associated with better performance in memory and thinking tests in patients who were on the active medication compared with patients taking a placebo (an inactive substance). It should be stressed that the degree of improvement was modest, and more than half of the patients showed no improvement at all.

Galantamine also resulted in modest improvements in clinical trials. Additional research will help scientists determine how many individuals are likely to benefit from the drug.

How are cholinesterase inhibitors used?

Donepezil (Aricept®) is a tablet and can be administered once daily. Generally, the initial dose is 5 mg a day (usually given at night). After four to six weeks, if it is well tolerated, the dose is often increased to the therapeutic goal of 10 mg a day.

Rivastigmine (Exelon®) is available as a capsule or as a liquid. The dosage is gradually increased to minimize side effects. Usually the medication is started at 1.5 mg daily. After two weeks the dosage is increased to 1.5 mg twice a day. The therapeutic goal is to increase the dosage gradually every two weeks to reach 6 to 12 mg a day. There is a greater frequency of side effects at these higher doses; however, taking drugs with meals may be helpful in reducing the occurrence of side effects.

Galantamine (Reminyl®) is supplied in the form of tablets in strengths of 4, 8 and 12 mg. The recommended starting dose is 4 mg twice a day. If well-tolerated after four weeks or more of treatment, the dose is increased to 8 mg twice a day. There was no statistical benefit in clinical trials for 12 mg twice a day over the dose of 8 mg twice a day, but if 8 mg twice a day is well-tolerated after four weeks, the dose can be increased to 12 mg twice a day by the physician.

What are the side effects of cholinesterase inhibitors?

Generally, cholinesterase inhibitors are well tolerated. Symptoms such as nausea, vomiting, loss of appetite, and increased frequency of bowel movements might be expected. It is strongly recommended that a physician who is comfortable and experienced in using these medications monitor patients treated with any of these compounds and that the recommended guidelines be strictly observed. There is no evidence or reason to believe that combining the drugs would be any more beneficial than taking either one alone, and it is likely that combining the drugs would result in greater side effects.

The Alzheimer's Association is fighting on your behalf to give everyone a reason to hope. For other more information about Alzheimer research, treatment and care, please contact the Alzheimer's Association.

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