How Is Alzheimer's Disease Treated?

Alzheimer's disease is complex, and it is therefore unlikely that any one drug or other intervention will ever successfully treat it in all people living with the disease. Still, in recent years, scientists have made tremendous progress in better understanding Alzheimer's and in developing and testing new treatments, including several medications that are in late-stage clinical trials.

Several prescription drugs are already approved by the U.S. Food and Drug Administration (FDA) to help managesymptoms in people with Alzheimer's disease. And, on June 7, 2021, FDA provided accelerated approval for the newest medication, aducanumab, which helps to reduce amyloid deposits in the brain and may help slow the progression of Alzheimer's, although it has not yet been



shown to affect clinical symptoms or outcomes, such as progression of cognitive decline or dementia.

Most medicines work best for people in the early or middle stages of Alzheimer's. However, it is important to understand that none of the medications available at this time will cure Alzheimer's.

Treatment For Mild To Moderate Alzheimer's

Treating the symptoms of Alzheimer's can provide people with comfort, dignity, and independence for a longer period of time and can encourage and assist their caregivers as well. Galantamine, rivastigmine, and donepezil are cholinesterase inhibitors that are prescribed for mild to moderate Alzheimer's symptoms. These drugs may help reduce or control some cognitive and behavioral symptoms.

Scientists do not yet fully understand how cholinesterase inhibitors work to treat Alzheimer's disease, but research indicates that they prevent the breakdown of acetylcholine, a brain chemical believed to be important for memory and thinking. As Alzheimer's progresses, the brain produces less and less acetylcholine, so these medicines may eventually lose their effect. Because cholinesterase inhibitors work in a similar way, switching from one to another may not produce significantly different results, but a person living with Alzheimer's may respond better to one drug versus another.

Treatment For Mild To Moderate Alzheimer's (cont'd)

Medications that target the underlying causes of a disease are called disease-modifying drugs or therapies. Aducanumab is the only disease-modifying medication currently approved to treat Alzheimer's. This medication is a human antibody, or immunotherapy, that targets the protein beta-amyloid and helps to reduce amyloid plaques, which are brain lesions associated with Alzheimer's. Clinical studies to determine the effectiveness of aducanumab were conducted only in people with early-stage Alzheimer's or mild cognitive impairment. Researchers are continuing to study whether this medication works to affect a person's rate of cognitive decline over time.

Before prescribing aducanumab, doctors may require PET scans or an analysis of cerebrospinal fluid to evaluate whether amyloid deposits are present in the brain. This can help doctors make an accurate diagnosis of Alzheimer's before prescribing the medication. Once a person is on aducanumab, their doctor or specialist

may require routine MRIs to monitor for side effects such as brain swelling or bleeding in the brain.

Several other disease-modifying medications are being tested in people with mild cognitive impairment or early Alzheimer's as potential treatments.

FDA's Accelerated Approval Program

Aducanumab was approved through the FDA's Accelerated Approval Program, which provides a path for earlier approval of drugs that treat certain serious conditions. This helps people living with the disease gain earlier access to the treatment. The approval of aducanumab was based on the ability of the drug to reduce amyloid in the brain. When using the accelerated approval pathway, drug companies are required to conduct additional studies to determine whether there is in fact clinical benefit after the drug is approved. If the follow-up trial fails to verify clinical benefit, the FDA may withdraw approval of the drug. Results of the phase 4 clinical trial for aducanumab are expected to be available by early 2030.

Treatment For Moderate To Severe Alzheimer's

A medication known as memantine, an N-methyl D-aspartate (NMDA) antagonist, is prescribed to treat moderate to severe Alzheimer's disease. This drug's main effect is to decrease symptoms, which could enable some people to maintain certain daily functions a little longer than they would without the medication. For example, memantine may help a person in the later stages of the disease maintain his or her ability to use the bathroom independently for several more months, a benefit for both the person with Alzheimer's and caregivers.

Memantine is believed to work by regulating glutamate, an important brain chemical. When produced in excessive amounts, glutamate may lead to brain cell death. Because NMDA antagonists work differently from cholinesterase inhibitors, the two types of drugs can be prescribed in combination.

The FDA has also approved donepezil, the rivastigmine patch, and a combination medication of memantine and donepezil for the treatment of moderate to severe Alzheimer's.

Drug Name	Drug Type and Use	How It Works	Common Side Effects
Aducanumab	Disease-modifying immunotherapy prescribed to treat mild cognitive impairment or mild Alzheimer's	Removes abnormal beta-amyloid to help reduce the number of plaques in the brain	Amyloid-related imaging abnormalities (ARIA), which can lead to fluid buildup or bleeding in the brain; also headache, dizziness, falls, diarrhea, confusion
Donepezil	Cholinesterase inhibitor prescribed to treat symptoms of mild, moderate, and severe Alzheimer's	Prevents the breakdown of acetylcholine in the brain	Nausea, vomiting, diarrhea, muscle cramps, fatigue, weight loss
Rivastigmine	Cholinesterase inhibitor prescribed to treat symptoms of mild, moderate, and severe Alzheimer's	Prevents the breakdown of acetylcholine and butyrylcholine (a brain chemical similar to acetylcholine) in the brain	Nausea, vomiting, diarrhea, weight loss, indigestion, muscle weakness
Memantine	N-methyl D-aspartate (NMDA) antagonist prescribed to treat symptoms of moderate to severe Alzheimer's	Blocks the toxic effects associated with excess glutamate and regulates glutamate activation	Dizziness, headache, diarrhea, constipation, confusion
Manufactured combination of memantine and donepezil	NMDA antagonist and cholinesterase inhibitor prescribed to treat symptoms of moderate to severe Alzheimer's	Blocks the toxic effects associated with excess glutamate and prevents the breakdown of acetylcholine in the brain	Headache, nausea, vomiting, diarrhea, dizziness, anorexia
Galantamine	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate Alzheimer's	Prevents the breakdown of acetylcholine and stimulates nicotinic receptors to release more acetylcholine in the brain	Nausea, vomiting, diarrhea, decreased appetite, dizziness, headache

Treatment For Moderate To Severe Alzheimer's (cont'd)

Drug Name	Delivery Method	
Aducanumab	Intravenous: Dose is determined by a person's weight; given over one hour every four weeks; most people will start with a lower dose and over a period of time increase the amount of medicine to reach the full prescription dose	
Donepezil	Tablet: Once a day; dosage may be increased over time if well tolerated. Orally disintegrating tablet: Same dosing regimen as above	
Rivastigmine	Capsule: Twice a day; dosage may be increased over time, at minimum two-week intervals, if well tolerated. Patch: Once a day; dosage amount may be increased over time, at minimum four-week intervals, if well tolerated	
Memantine	Tablet: Once a day; dosage may be increased in amount and frequency (up to twice a day) if well tolerated. Oral solution: Same dosage as tablet. Extended-release capsule: Once a day; dosage may increase in amount over time, at minimum one-week intervals, if well tolerated	
Manufactured combination of memantine and donepezil	Extended-release capsule: Once a day; initial dosage depends on whether the person is already on a stable dose of memantine and/or donepezil; dosage may increase over time, at minimum one-week intervals, if well tolerated	
Galantamine	Tablet: Twice a day; dosing may increase over time, at minimum four-week intervals, if well tolerated. Extended-release capsule: Same dosage as tablet but taken once a day	

Dosage And Side Effects Of Alzheimer's Disease Medications

Doctors usually start patients at low drug doses and gradually increase the dosage based on how well a patient tolerates the drug. There is some evidence that certain people may benefit from higher doses of Alzheimer's medications. However, the higher the dose, the more likely side effects will occur.

Patients should be monitored when a drug is started. All of these medicines have possible side effects, including nausea, vomiting, diarrhea, allergic reactions, and loss of appetite. Report any unusual symptoms to the prescribing doctor right away. It is important to follow the doctor's instructions when taking any medication, including vitamins and herbal supplements. Also, let the doctor know before adding or changing any medications.

Managing Behavioral Symptoms Of Alzheimer's Disease

Common behavioral symptoms of Alzheimer's include sleeplessness, wandering, agitation, anxiety, aggression, restlessness, and depression. Scientists are learning why these symptoms occur and are studying new treatments — drug and nondrug — to manage them. Research has shown that treating behavioral symptoms can make people with Alzheimer's more comfortable and makes things easier for caregivers.

Experts agree that medicines to treat these behavior problems should be used only after other strategies that don't use medicine have been tried. Learn more about behavioral changes in people with Alzheimer's disease and ways to cope.

Medicines To Be Used With Caution In People With Alzheimer's Disease

There are some medicines, such as sleep aids, anti-anxiety drugs, anti-convulsants, and antipsychotics, that a person with Alzheimer's disease should take only:

- After the doctor has explained all the risks and side effects of the medicine
- After other, safer nonmedication options have not helped treat the problem

People living with Alzheimer's and their caregivers must watch closely for side effects from these medications.

Sleep aids are used to help people get to sleep and stay asleep. People with Alzheimer's should NOT use these drugs regularly because they make the person more confused and more likely to fall. There are lifestyle changes people can make to improve their sleep. Learn more about getting a good night's sleep.

Anti-anxiety drugs are used to treat agitation. These drugs can cause sleepiness, dizziness, <u>falls</u>, and confusion. For this reason, doctors recommend they should only be used for short periods of time.

Anti-convulsants are drugs sometimes used to treat severe aggression. Side effects may cause sleepiness, dizziness, mood swings, and confusion.

Antipsychotics are drugs used to treat <u>paranoia</u>, <u>hallucinations</u>, <u>agitation</u>, and <u>aggression</u>. Side effects of using these drugs can be serious, including increased risk of death in some older people with dementia. They should only be given to people with Alzheimer's when the doctor agrees that the symptoms are severe.

The Future Of Alzheimer's Disease Treatments



Alzheimer's disease research has developed to a point where scientists are exploring a variety of avenues to not only treat symptoms but also address underlying disease processes. In ongoing clinical trials, scientists are developing and testing several possible interventions, including immunization therapy, drug therapies, cognitive training, physical activity, and treatments for cardiovascular disease and diabetes.

We Can Help!

Alzheimer's Orange County

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For more caregiver tips

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Information taken from the National Institute on Aging, part of the National Institutes of Health https://www.nia.nih.gov/health | NIH July 2021 | Reviewed by AlzOC July 2022