GET THE FACTS:

Alzheimer's Disease Medications

Astral AT AUBURN

The process for developing new treatments that slow or halt the disease has been frustratingly slow. To expedite the development of more effective treatments, representatives from numerous organizations—including pharmaceutical companies, nonprofit patient advocate groups, academia, the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH), the National Institute on Aging (NIA), the National Institute of Neurological Disorders and Stroke (NINDS), and the European Medicines Agency (EMEA)—have joined together to share data from more than 6,500 study participants in Alzheimer's clinical trials and to develop data standards. Their goal is to transform the drug development paradigm for neurodegenerative diseases and serve as a model for other major diseases.

To date, the U.S. Food and Drug Administration (FDA) has approved five drugs to treat the symptoms of Alzheimer's disease—donepezil, rivastigmine, galantamine, memantine and memantine combined with donepezil. They do not deal with the changes in the brain or slow the progression of the disease.

Aducanumab, the only disease-modifying medication (targets the underlying cause of a disease) for Alzheimer's disease, received conditional FDA approval in June 2021 pending further studies to prove its benefit.

Treating symptoms: Mild to moderate[1]

Treating symptoms can give provide comfort, dignity, and independence over a longer period of time for those who suffer from Alzheimer's disease. Galantamine, rivastigmine, and donepezil are cholinesterase inhibitors that can be prescribed for mild to moderate symptoms. These drugs may help reduce or control some cognitive and behavioral symptoms.

Scientists do not yet fully understand how cholinesterase inhibitors work on Alzheimer's disease. Researchers believe that they may prevent the breakdown of acetylcholine, a brain chemical that may 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.

[1] "How is Alzheimer's Disease Treated?" https://www.nia.nih.gov/health/how-alzheimers-disease-treated, retrieved 09/02/2022.

Treating symptoms: Moderate to severe[2]

Memantine, an N-methyl D-aspartate (NMDA) antagonist, can be prescribed to treat moderate to severe Alzheimer's disease by decreasing 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 disease and his or her 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 memantine/donepezil medication for treating moderate to severe Alzheimer's disease.

Reversing or halting the disease[3]

Aducanumab may help slow the progression of Alzheimer's disease. It works by targeting beta-amyloid, a microscopic protein fragment that forms in the brain and accumulates into plaques. These plaques disrupt communication between nerve cells in the brain and may also activate immune system cells that trigger inflammation and devour disabled nerve cells.

While scientists aren't sure what causes cell death and tissue loss during the course of Alzheimer's, amyloid plaques, one of the hallmarks of the disease, are one of the potential contributors. Aducanumab is the first therapy to demonstrate that removing amyloid, one of the hallmarks of Alzheimer's disease, from the brain is reasonably likely to reduce cognitive and functional decline in people living with early Alzheimer's.

Clinical studies to determine the effectiveness of aducanumab were conducted on those with early-stage or mild cognitive impairment due to Alzheimer's disease, but it has not yet been shown to affect clinical symptoms or outcomes, such as progression of cognitive decline or dementia over time. This remains a topic of continuing research.

[2] "How is Alzheimer's Disease Treated?" https://www.nia.nih.gov/health/how-alzheimers-disease-treated, retrieved 09/02/2022.

[3] "Medications for Memory, Cognition, and Dementia-Related Behaviors," https://www.alz.org/alzheimers-dementia/treatments/medications-for-memory, retrieved 09/02/2022.

What the future holds[4]

The future looks hopeful. Like many cancers or HIV/AIDS, Alzheimer's disease treatments may eventually include a "cocktail" of drugs targeting different disease processes. These may include not only aducanumab, but also other immunotherapies.

- **Monoclonal antibodies** – These drugs may prevent plaques in the brain from clumping or remove them altogether.
- **Lecanemab and donanemab** – Both are showing promise and are moving into phase 3 clinical trials.
- **Solanezumab** – No benefit for mild or moderate stages of Alzheimer's disease, but may be beneficial in the pre-clinical stage.
- **Saracatinib** – Initially developed as a possible cancer treatment, saracatinib reversed some memory loss in mice and human trials are now underway.
- **Tau "detanglers"** – Tau aggregation inhibitors and tau vaccines, are currently in clinical trials to determine if they can prevent tangles, another common brain abnormality associated with Alzheimer's disease.
- **Sargramostim** – Sargramostim may stimulate the immune system to protect the brain from chronic, low-level brain cell inflammation.

Finally, studies are continuing on the effects of insulin on the brain and brain cell function, the link between heart and blood vessel health and brain health, and the relationship between estrogen and cognitive function.

Testing New Alzheimer's Drugs

Clinical trials to test the safety and efficacy of new treatments for Alzheimer's disease are ongoing around the U.S. and volunteers are needed for most. Talk with your doctor or visit alzheimers.gov/clinical-trials to learn more.

[4]"Alzheimer's Treatments: What's on the Horizon?" https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers-treatments/art-20047780, retrieved 09/02/2022.

DRUGS CURRENTLY APPROVED FOR USE IN ALZHEIMER'S DISEASE

	Type/Use	How It Works	Common Side Effects	Delivery Method	Prescribing Information
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	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	Prescribing information
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	Tablet: Once a day; dosage may be increased over time if well tolerated Orally disintegrating tablet: Same dosing regimen as above	Prescribing information
Rivastigmine	Cholinesterase inhibitor prescribed to treat symptoms of mild, moderate,	Prevents the breakdown of acetylcholine and butyrylcholine (a brain chemical similar to acetylcholine) in the brain	Nausea, vomiting, diarrhea, weight loss, indigestion, muscle weakness	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	Prescribing information

	Type/Use	How It Works	Common Side Effects	Delivery Method	Prescribing Information
Memantine	N-methyl D-aspartate (NMDA) antagonist prescribed to treat symptoms of moderate to severe Alzheimer's and severe Alzheimer's	Blocks the toxic effects associated with excess glutamate and regulates glutamate activation	Dizziness, headache, diarrhea, constipation, confusion	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	Prescribing information
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	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	Prescribing information
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	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	Prescribing information

Source: https://www.nia.nih.gov/health/how-alzheimers-disease-treated, retrieved 09/02/2022.

Resources

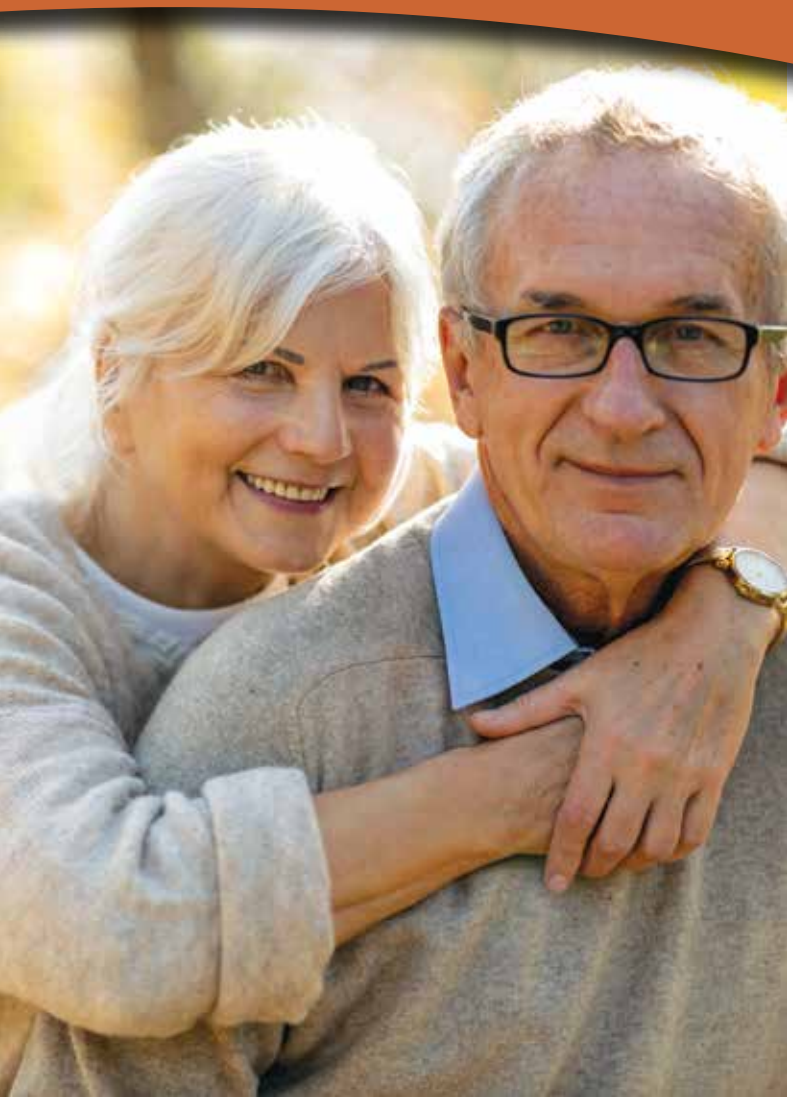
Alzheimer's and Related Dementias Education and Referral (ADEAR) Center
National Institutes of Health (NIH)
www.nia.nih.gov/health/alzheimers
Email: adear@nia.nih.gov
Phone: 1-800-438-4380

Alzheimers.gov
National Institute on Aging (NIA)
www.alzheimers.gov

Alzheimer's Association
www.alz.org
Phone: 1-800-272-3900 (24/7 helpline)

Alzheimer's Foundation of America
www.alzfdn.org
Phone: 1-866-232-8484

Astral At Auburn offers 24x7 memory care services and support in a secure environment that provides dignity and quality of life for a loved one with Alzheimer's disease and peace of mind for you. Visit *www.astralatauburn.com* to learn more.



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