

# Medications for Memory, Cognition and Dementia-Related Behaviors

Although current medications cannot cure Alzheimer's, two U.S. Food and Drug Administration (FDA)-approved treatments address the underlying biology. Other medications may help lessen symptoms, such as memory loss and confusion.

- [FDA-approved drugs for Alzheimer's](#)
- [Participate in clinical studies](#)
- [Treatments at a glance](#)

## FDA-approved drugs for Alzheimer's

The FDA has approved medications that fall into two categories: drugs that change disease progression in people living with early Alzheimer's disease, and drugs that may temporarily mitigate some symptoms of Alzheimer's dementia.

When considering any treatment, it is important to have a conversation with a health care professional to determine whether it is appropriate. A clinician who is experienced in using these types of medications should monitor people who are taking them and ensure that the recommended guidelines are strictly observed.

## Drugs that change disease progression

Drugs in this category slow disease progression by going after the underlying biology of the disease process. They aim to slow the decline of memory and thinking, as well as function, in people living with Alzheimer's disease.

## Amyloid-targeting approaches

Anti-amyloid treatments work by removing beta-amyloid, a protein that accumulates into plaques, from the brain. Each works differently and targets beta-amyloid at a different stage of plaque formation.

These treatments change the course of the disease in a meaningful way for people in the early stages, giving them more time to participate in daily life and live independently. Clinical trial participants who received anti-amyloid treatments experienced reduction in cognitive decline observed through measures of cognition and function.

Examples of cognition measures include:

- Memory.
- Orientation.

Examples of functional measures include:

- Conducting personal finances.
- Performing household chores such as cleaning.

Anti-amyloid treatments do have side effects. These treatments can cause serious allergic reactions. Side effects can also include amyloid-related imaging abnormalities (ARIA), infusion-related reactions, headaches and falls.

ARIA is a common side effect that does not usually cause symptoms but can be serious. It is typically a temporary swelling in areas of the brain that usually resolves over time. Some people may also have small spots of bleeding in or on the surface of the brain with the swelling, although most people with swelling in areas of the brain do not have symptoms. Some may have symptoms of ARIA such as headache, dizziness, nausea, confusion and vision changes.

Some people have a genetic risk factor (ApoE  $\epsilon$ 4 gene carriers) that may cause an increased risk for ARIA. The FDA encourages that testing for ApoE  $\epsilon$ 4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, doctors should discuss with patients the

risk of ARIA and the implications of [genetic testing](#) results.

These are not all the possible side effects, and individuals should talk with their doctors to develop a treatment plan that is right for them, including weighing the benefits and risks of all approved therapies.

Donanemab (Kisunla™)

[Donanemab \(Kisunla\)](#) is an anti-amyloid antibody intravenous (IV) infusion therapy delivered every four weeks. It has received traditional approval from the FDA to treat early Alzheimer's disease, including people living with mild cognitive impairment (MCI) or mild dementia due to Alzheimer's disease who have confirmation of elevated beta-amyloid in the brain. There is no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied.

Donanemab was the third therapy to demonstrate that removing beta-amyloid from the brain reduces cognitive and functional decline in people living with early Alzheimer's.

Lecanemab (Leqembi®)

[Lecanemab \(Leqembi\)](#) is an anti-amyloid antibody intravenous (IV) infusion therapy that is delivered every two weeks. It has received traditional approval from the FDA to treat early Alzheimer's disease, including people living with [mild cognitive impairment \(MCI\)](#) or mild dementia due to Alzheimer's disease who have confirmation of elevated beta-amyloid in the brain. There is no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied.

Lecanemab was the second therapy to demonstrate that removing beta-amyloid from the brain reduces cognitive and functional decline in people living with early Alzheimer's.

## **Drugs that treat symptoms**

### **Cognitive symptoms (memory and thinking)**

As Alzheimer's progresses, brain cells die and connections among cells are lost, causing cognitive symptoms to worsen. While these medications do not stop the damage Alzheimer's causes to brain cells, they may help lessen or stabilize symptoms for a limited time by affecting certain chemicals involved in carrying messages among and between the brain's nerve cells.

The following medications are prescribed to treat symptoms related to memory and thinking.

#### Cholinesterase inhibitors

Cholinesterase (KOH-luh-NES-ter-ays) inhibitors are prescribed to treat symptoms related to memory, thinking, language, judgment and other thought processes. These medications prevent the breakdown of acetylcholine (a-SEA-til-KOHlean), a chemical messenger important for memory and learning. These drugs support communication between nerve cells.

The cholinesterase inhibitors most commonly prescribed are:

- Benzgalantamine (Zunveyl®): approved for mild-to-moderate dementia due to Alzheimer's disease.
- Donepezil (Aricept®): approved for mild-to-severe dementia due to Alzheimer's disease.
- Galantamine (Razadyne®): approved for mild-to-moderate dementia due to Alzheimer's disease.
- Rivastigmine (Exelon®): approved for mild-to-moderate dementia due to Alzheimer's disease as well as mild-to-moderate dementia due to Parkinson's disease.

Though generally well-tolerated, if side effects occur, they commonly include diarrhea, dizziness, headache, nausea, vomiting, loss of appetite and increased frequency of bowel movements.

#### Glutamate regulators

Glutamate regulators are prescribed to improve memory, attention, reason, language and the ability to perform simple tasks. This type of drug works by

regulating the activity of glutamate, a different chemical messenger that helps the brain process information. This drug is known as:

- Memantine (Namenda®): approved for moderate-to-severe Alzheimer's disease. Can cause side effects, including headache, constipation, confusion and dizziness.

Cholinesterase inhibitor + glutamate regulator

This type of drug is a combination of a cholinesterase inhibitor and a glutamate regulator.

- Donepezil and memantine (Namzaric®): approved for moderate-to-severe Alzheimer's disease. Possible side effects include nausea, vomiting, loss of appetite, increased frequency of bowel movements, headache, constipation, confusion and dizziness.

### **Non-cognitive symptoms (behavioral and psychological symptoms)**

Alzheimer's affects more than just memory and thinking. A person's quality of life may be impacted by a variety of behavioral and psychological symptoms that accompany dementia, such as [sleep disturbances](#), [agitation](#), [hallucinations and delusions](#). Some medications focus on treating these non-cognitive symptoms for a time, though it is important to try [non-drug strategies to manage behaviors](#) before adding medications.

The FDA has approved one drug to address symptoms of insomnia that has been tested in people living with dementia and one that treats agitation.

Orexin receptor antagonist

Prescribed to treat insomnia, this drug inhibits the activity of orexin, a type of neurotransmitter involved in the sleep-wake cycle:

- Suvorexant (Belsomra®): approved for treatment of insomnia and has been shown in clinical trials to be effective for people living with mild to moderate Alzheimer's disease. Possible side effects include, but are not limited to: risk of impaired alertness and motor coordination (including impaired driving), worsening of depression or suicidal thinking, complex

sleep behaviors (such as sleep-walking and sleep-driving), sleep paralysis and compromised respiratory function.

### Atypical antipsychotics

Atypical antipsychotics are a group of antipsychotic drugs that target the serotonin and dopamine chemical pathways in the brain. These drugs are largely used to treat schizophrenia and bipolar disorder and as add-on therapies for major depressive disorder. The FDA requires that all atypical antipsychotics carry a safety warning that the medication has been associated with an increased risk of death in older patients with dementia-related psychosis.

Many atypical antipsychotic medications are used "off-label" to treat dementia-related behaviors, and there is currently only one FDA-approved atypical antipsychotic to treat agitation associated with dementia due to Alzheimer's. It is important to try non-drug strategies to manage non-cognitive symptoms — like agitation — before adding medications.

- Brexpiprazole (Rexulti®): approved for the treatment of agitation associated with dementia due to Alzheimer's disease. Possible side effects include, but are not limited to: weight gain, sleepiness, dizziness, common cold symptoms, and restlessness or feeling like you need to move. Warning for serious side effects: increased risk of death in older adults with dementia-related psychosis. Rexulti is not approved for the treatment of people with dementia-related psychosis without agitation that may happen with dementia due to Alzheimer's disease.

## Medication safety

Before beginning a new medication, make sure your physician and pharmacist are aware of all medications, dietary supplements or other products currently being taken (including over-the-counter and alternative preparations). This is important to make certain medications will not interact with one another, causing side effects.

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# Participate in clinical studies

Scientists have made remarkable progress in understanding how Alzheimer’s disease affects the brain.

Ultimately, the path to effective therapies is through clinical studies. Learn more about [Alzheimer’s Association TrialMatch®](#), a free clinical studies matching service, and how you can participate in vital Alzheimer’s disease research. Recruiting and retaining trial participants is now the greatest obstacle, other than funding, to developing the next generation of Alzheimer’s treatments. Individuals living with dementia, caregivers and healthy volunteers are all needed to participate in clinical studies focused on Alzheimer’s and other dementias.

## Treatments at a glance

Change disease progression

Name (Generic/Brand)	Indicated For	Common Side Effects
Donanemab Kisunla™	Alzheimer's disease (MCI or mild dementia).	ARIA and headache.
Lecanemab Leqembi®	Alzheimer's disease (MCI or mild dementia).	Infusion-related reactions, ARIA and headache.

Treats cognitive symptoms (memory and thinking)

Name (Generic/Brand )	Indicated For	Common Side Effects
Benzgalantamine Zunveyl®	Mild-to-moderate dementia due to Alzheimer's disease.	Nausea, vomiting, diarrhea, dizziness, headache and loss of appetite.
Donepezil Aricept®	Mild-to-severe dementia due to Alzheimer's disease.	Nausea, vomiting, loss of appetite, muscle cramps and increased frequency of bowel movements.
Galantamine Razadyne®	Mild-to-moderate dementia due to Alzheimer's disease.	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.
Rivastigmine Exelon®	Mild-to-moderate dementia due to Alzheimer's disease or Parkinson's disease.	Nausea, vomiting, loss of appetite and increased frequency of bowel movements.



Memantine Namenda®	Moderate-to-severe dementia due to Alzheimer's disease.	Headache, constipation, confusion and dizziness.
Memantine + Donepezil Namzaric®	Moderate-to-severe dementia due to Alzheimer's disease.	Nausea, vomiting, loss of appetite, increased frequency of bowel movements, headache, constipation, confusion and dizziness.

Treats non-cognitive symptoms (behavioral and psychological)

Name (Generic/Brand)	Indicated For	Common Side Effects
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Brexpiprazole Rexulti®	Agitation associated with dementia due to Alzheimer's disease.	Weight gain, sleepiness, dizziness, common cold symptoms, and restlessness or feeling like you need to move.  Warning for serious side effects: increased risk of death in older adults with dementia-related psychosis. Rexulti is not approved for the treatment of people with dementia-related psychosis without agitation that may happen with dementia due to Alzheimer's disease.
Suvorexant Belsomra®	Insomnia, has been shown to be effective in people living with mild to moderate Alzheimer's disease.	Impaired alertness and motor coordination, worsening of depression or suicidal thinking, complex sleep behaviors, sleep paralysis, compromised respiratory function.

[Back to Top](#)

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