

## Treatments for Alzheimer's Disease

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Although there is no cure for Alzheimer's disease, certain treatments can help control or delay its symptoms, particularly in the early stages of the disease. Consult a physician before taking any medications.

### Anti-Amyloid Treatments

These newest treatments to fight Alzheimer's disease are immunotherapies targeting toxic amyloid-beta proteins that form plaques in the brain, a defining feature of the disease. Removing amyloid-beta from the brain reduces cognitive and functional decline in people living with early Alzheimer's.

#### ■ Kisunla™ (donanemab)

**How it works:** Targets a plaque-specific form of amyloid that is highly toxic and increases amyloid aggregation. In a phase 3 clinical trial, it slowed the progression of cognitive and functional decline by 35% in participants with early signs of Alzheimer's disease, with 76.4% of participants showing amyloid clearing with PET imaging.

**Delivery method:** Administered intravenously (through a vein); in clinical trials, treatment was administered every four weeks for up to 72 weeks.

**Side effects:** Amyloid-related imaging abnormalities (ARIA), headache, and infusion-related reactions.

#### ■ Leqembi® (lecanemab)

**Effective for:** Early cognitive impairment or mild dementia caused by Alzheimer's disease.

**How it works:** By clearing a small, especially toxic, soluble form of amyloid-beta from the brain, Leqembi can slow the cognitive decline associated with Alzheimer's disease by 25%.

**Delivery method:** Administered through a vein every two weeks at specialized centers, with each treatment lasting about an hour. How long patients should undergo the treatments is not clear; treatment lasted 18 months in clinical trials. An at-home injectable version is available for eligible patients who have completed the initial IV infusion phase.

**Side effects:** Headache, infusion-related reactions, and amyloid-related imaging abnormalities (also known as ARIA).

### ■ Aduhelm® (aducanumab)

This FDA-approved anti-amyloid treatment was discontinued by its manufacturer, Biogen, in January 2024 in order to redistribute company resources toward Leqembi, the first anti-amyloid Alzheimer's drug to receive traditional FDA approval.

## Not Yet FDA-Approved

### ■ Remternetug

**FDA status:** In phase 3 clinical trials, with results expected soon.

**How it works:** This immunotherapy drug targets the same plaque-specific form of amyloid as donanemab but may require lower doses and less invasive administration.

**Delivery method:** Administered intravenously or subcutaneously (injection under the skin).

**Side effects:** Early reports describe amyloid-related imaging abnormalities (ARIA) that track with dosage levels, but complete safety results are pending.

## Cholinesterase Inhibitors

These medications work by regulating levels of acetylcholine, an important brain chemical involved in nerve cell communication. Acetylcholine levels are reduced in the brains of people with Alzheimer's disease compared with unaffected brains. Cholinesterase inhibitors slow the breakdown of acetylcholine so that more of this chemical is available for nerve cell communication. The effects are slowed progression of cognitive impairment in some patients in the early to middle stages of Alzheimer's disease.

### ■ Zunveyl® (benzgalantamine)

**Effective for:** Early to moderate Alzheimer's disease.

**How it works:** Increases levels of acetylcholine, a brain chemical important for memory and thinking, by blocking the enzyme that breaks it down.

**Delivery method:** Oral medication available as tablets, in a liquid form, or in extended-release capsules.

**Side effects:** Nausea, vomiting, diarrhea, weight loss, dizziness, headache, and tiredness.

### ■ Razadyne® (galantamine)

**Effective for:** Early to moderate Alzheimer's disease.

**How it works:** Prevents the breakdown of acetylcholine and stimulates recognition proteins to respond more strongly to signals from acetylcholine and release more of it in the brain. Users may experience improvements in thinking and memory.

**Delivery method:** Oral medication available as tablets, in a liquid form, or in extended-

release capsules.

**Side effects:** Nausea, vomiting, diarrhea, weight loss, dizziness, headache, and tiredness.

#### ■ Exelon® (rivastigmine)

**Effective for:** Early to moderate Alzheimer's disease.

**How it works:** Prevents the breakdown of acetylcholine and butyrylcholine (a chemical similar to acetylcholine) in the brain. Users may experience improvements in memory and cognition.

**Delivery method:** Oral medication or skin patch, applied once daily and worn for 24 hours, with two dosage options.

**Side effects:** Nausea, diarrhea, increased frequency of bowel movements, vomiting, muscle weakness, loss of appetite, weight loss, dizziness, drowsiness, and upset stomach.

#### ■ Aricept® (donepezil)

**Effective for:** Early, moderate, and severe Alzheimer's disease.

**How it works:** Prevents the breakdown of acetylcholine in the brain, preserving its activity, which has been linked to slower progression of cognitive impairment. Users may experience improvements in awareness, memory, and daily functions.

**Delivery method:** Oral medication in the form of tablets to swallow or that can dissolve in the mouth.

**Side effects:** Diarrhea, dizziness, loss of appetite, muscle cramps, nausea, tiredness, trouble sleeping, vomiting, and weight loss.

**Other:** Aricept also may have a limited slowing effect on the progression from mild cognitive impairment to Alzheimer's disease. In 2006, Aricept was also approved by the FDA for the management of severe Alzheimer's symptoms.

## Glutamate Inhibitors

These medications protect brain cells by regulating an excitatory nerve communication chemical called glutamate, which Alzheimer's-damaged cells release in abnormally high amounts. Among its many roles, it promotes efficient learning and memory. Hyperactive or dying cells can release too much glutamate which leads to toxicity, additional cell damage, and ultimately cell death. Glutamate inhibitors interfere with this binding.

#### ■ Namenda® (memantine)

**Effective for:** Moderate to severe Alzheimer's disease

**How it works:** Namenda appears to protect the brain's nerve cells against excess glutamate by binding with glutamate's recognition proteins and inhibiting glutamate's access to them. Users may experience less forgetfulness or confusion.

**Delivery method:** Oral medication, available as tablets or an oral solution.

**Side effects:** Back pain, constipation, diarrhea, dizziness, drowsiness, headache, pain, and weight gain.

## Combination Drugs

One FDA-approved drug combines cholinesterase inhibitors and glutamate inhibitors. This combination prevents both the breakdown of acetylcholine in the brain and protects the brain's nerve cells against the effects of excess glutamate.

■ **Namzaric®** (combination drug containing both donepezil and memantine)

**Effective for:** Moderate to severe Alzheimer's disease.

**How it works:** Namzaric is a combination of two drugs that have already been on the market: memantine (Namenda) and donepezil (Aricept). Aricept prevents the breakdown of the signaling molecule acetylcholine in the brain. Namenda appears to protect the brain's nerve cells against the effects of excess glutamate, a signaling molecule that is overproduced by damaged nerve cells in the brain in some neurological conditions, including Alzheimer's disease. Users may experience improvements in cognition and overall daily functions, along with slowing of symptom progression.

**Delivery method:** Oral medication, taken once daily.

**Side effects:** Diarrhea, nausea, vomiting, loss of appetite, weight gain, loss of bladder control, back pain, headache, bruising, drowsiness, and dizziness.

## Treatment for Neuropsychiatric and Behavioral Symptoms

Often, as Alzheimer's disease progresses, people experience depression, agitation, and psychiatric symptoms, such as paranoid thoughts, delusions, or hallucinations. These conditions may manifest in different ways, including screaming, asking repetitive questions, hoarding, or pacing. They are also sometimes associated with aggression, hyperactivity, or combativeness.

■ **Auvelity®** (dextromethorphan - bupropion)

**Effective for:** Agitation associated with moderate to severe Alzheimer's.

**How it works:** Auvelity treats agitation associated with dementia by interacting with two signaling pathways in the brain to reduce toxicity and stress.

**Delivery method:** Tablets taken by mouth daily.

**Side effects:** Dizziness and stomach upset or pain.

■ **Rexulti®** (brexpiprazole)

**Effective for:** Moderate to severe Alzheimer's disease.

**How it works:** Rexulti was approved in 2015 for the treatment of schizophrenia and as an add-on treatment for major depressive disorder in adults. In 2023, the FDA approved its use for agitation associated with dementia resulting from Alzheimer's disease.

**Delivery method:** Tablets taken by mouth daily.

**Side effects:** Weight gain, sleepiness, dizziness, common cold symptoms, and restlessness or feeling the urgent need to move (akathisia).

■ **Belsomra®** (suvorexant)

**Effective for:** Moderate to severe Alzheimer's disease.

**How it works:** This drug blocks key proteins called orexin receptors, which are active in the sleep–wake cycle and associated with brain regions involved in cognition and Alzheimer's disease.

**Delivery method:** Tablets taken by mouth.

**Side effects:** Drowsiness, dizziness, diarrhea, dry mouth, headache, and respiratory issues.

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