



Alzheimer's Disease Treatment Clinic: Genetic Testing

The Alzheimer's Disease Treatment Clinic is designed to support patients eligible for new medications such as lecanemab, approved by the U.S. Food and Drug Administration in 2023. New therapies like lecanemab are given through IV infusions to treat the presence of a protein in your brain called amyloid.

As part of your evaluation in the Alzheimer's Disease Treatment Clinic, it is recommended that you have genetic testing. The genetic test will look for the apolipoprotein E gene, also called the *APOE* gene. Results from the genetic test may affect how likely you are to experience benefits and side effects from treatment.

FORMS OF *APOE*

Everyone has two copies of the *APOE* gene. Each of your biological parents gives you one copy. Each copy of *APOE* can have 3 different forms, known as $\epsilon 2$, $\epsilon 3$, or $\epsilon 4$.

- $\epsilon 2$: This is the least common form of the gene. The $\epsilon 2$ form may modestly protect against risk of developing Alzheimer's disease.
- $\epsilon 3$: This is the most common form of the gene. There is no increased risk between the $\epsilon 3$ form and risk of Alzheimer's disease.
- $\epsilon 4$: This form is found in approximately 25% of people. People with one copy of the $\epsilon 4$ form have a higher risk of developing Alzheimer's disease. People with two copies of the $\epsilon 4$ form of the *APOE* gene have an even higher risk of developing Alzheimer's disease.

The *APOE* gene is one of many factors that affect the risk of developing Alzheimer's disease. Lifestyle and the

environment are other factors that affect risk. We are still learning about these and other risk factors.

An *APOE* result cannot predict for sure whether a person will – or won't – develop dementia. Many people with the $\epsilon 4$ form of *APOE* never develop Alzheimer's disease. Others develop Alzheimer's disease or other causes of dementia without having the $\epsilon 4$ form of *APOE*.

CONSIDERING THE BENEFITS AND RISKS OF TREATMENT IN RELATION TO THE *APOE* GENE

Treatment that removes amyloid from your brain has risks. One risk is brain swelling, also called edema. Another risk is brain bleeding. These risks are known as ARIA, or amyloid-related imaging abnormalities. In the clinical trial for lecanemab, the risk of ARIA was higher in patients who had one copy of the $\epsilon 4$ form of *APOE*. The risk was much higher in patients who had two copies of the $\epsilon 4$ form of *APOE*.

Some data but not all also suggested that patients who had the $\epsilon 4$ form of *APOE* (especially those with two copies of the $\epsilon 4$ form) may be less likely to benefit from treatment.

TESTING FOR *APOE* IN THE ALZHEIMER'S DISEASE TREATMENT CLINIC

It is strongly recommended that all patients considering treatment with lecanemab or other similar drugs be tested for the *APOE* gene in order to determine the risks and benefits of treatment.

This genetic test is completed through a blood draw and results will be shared with you to help decide whether treatment is the best fit for you. The cost of this test may or may not be covered by your insurance.

If it is determined very early in the course of your evaluation that you are not a candidate for lecanemab or similar drugs, *APOE* gene testing may be cancelled.

RISKS OF *APOE* TESTING

Genetic testing may affect you and your loved ones beyond your treatment plan.

If you are found to have at least one copy of the $\epsilon 4$ form of the *APOE* gene, your children, siblings, parents, and possibly later generations of your family would be considered at risk of having the $\epsilon 4$ form of the *APOE* gene themselves. Knowing your *APOE* result might lead to anxiety about risk for your family members, or might affect relationships between you and your loved ones.

Also, it is possible that results of *APOE* testing could affect your eligibility and/or premiums for life, disability, or long-term care insurance.

Currently, *APOE* testing is not recommended in clinical care outside of the context of treatment decisions (related to lecanemab and similar drugs) for patients with early symptomatic Alzheimer's disease.

Learn more online at [mayoclinic.org](https://www.mayoclinic.org)