

# Medical Coverage Policy



## Genetic Testing for Alzheimer's Disease

Device/Equipment  Drug  Medical  Surgery  Test  Other

Effective Date:	12/14/2000	Policy Last Updated:	5/1/2012
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**Prospective review is recommended/required. Please check the member agreement for preauthorization guidelines.**

**Prospective review is not required.**

### Description:

Alzheimer's disease (AD) is a progressive neurological disorder that slowly destroys the patient's memory. As time progresses, the patient becomes unable to learn, reason, communicate, and participate in daily activities of living. Patients often experience changes in personality and behavior. Forty percent of Alzheimer's patients have a family history of Alzheimer's Disease with at least one other first-degree relative affected.

There are two types of Alzheimer's, Familial AD (FAD) and Sporadic. Affecting less than 10 percent of Alzheimer's Disease patients, FAD is a rare form of AD. FAD is associated with gene mutations on chromosome 1, 14, or 21. In this case, all offspring of the same generation have a 50/50 chance of developing AD if one of their parents have the disease.

It is more common for patients to develop late-onset (after the age of 65) or sporadic AD. Although some families may develop clusters of cases, there is no obvious family pattern. There are no known causes of late-onset AD, although it is thought that Sporadic AD is related to the Apolipoprotein E (APOE) gene found on chromosome 19.

### Susceptibility polymorphism at the Apolipoprotein (APOE) gene:

The APOE lipoprotein is a carrier of cholesterol and is produced in the liver and brain glial cells. The APOE gene has three alleles—epsilon 2, 3, and 4—with the epsilon 3 allele being the most common. Every person carries two APOE alleles. The presence of at least one epsilon 4 allele is associated with an increased risk of AD in the range of 1.2 to 3 fold, depending on the ethnic group. For those homozygous for epsilon 4 (about 2 percent of the population), the risk of AD is higher than for those heterozygous for epsilon 4. The mean age of onset of AD is about 68 years for epsilon 4 homozygotes, about 77 years for heterozygotes, and about 85 years for those with no epsilon 4 allele. It should be noted that the epsilon 4 allele represents a risk factor for AD rather than a disease-causing mutation.

### Genetic mutations:

Patients with early onset (Familial AD) are a small subset of patients. The families of these patients may show an autosomal dominant pattern of inheritance. Three genes have been identified by linkage analysis of affected families: amyloid AB precursor gene (APP), presenilin 1 gene, and presenilin 2 gene. A variety of mutations within these genes have been associated with AD; mutations in presenilin-1 appear to be the most common. However only 2 to 10 percent of all patients with AD have early onset AD, and genetic mutations have only been identified in 30 to 50 percent of these patients. Therefore, overall identifiable genetic mutations are rare causes of AD.

Genetic testing for the APOE allele in patients with late onset AD and testing for APP, PS1, or PS2 mutations in the rare patient with early onset AD have been investigated as an aid in diagnosis in patients presenting with symptoms suggestive of AD, or a technique for risk assessment in asymptomatic patients with a family history of AD.

Currently, the clinical diagnosis of AD is primarily one of exclusion, focusing on eliminating treatable causes of dementia. In 1988, the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's and Related Disorders Association (ADRDA) published clinical criteria for the diagnosis of Alzheimer's disease. These organizations defined three categories: possible, probable, and definite Alzheimer's disease. The only difference between probable and definite Alzheimer's disease is that the definite category requires a brain biopsy confirming the presence of characteristic neurofibrillary tangles. Thus, definite AD is typically identified only with an autopsy.

### **Medical Criteria:**

Genetic testing for the diagnosis or risk assessment of Alzheimer's disease is considered **not covered** due to inadequate data on the reliability of such testing and that testing affects the outcomes of treatment. Genetic testing includes, but is not limited to, testing for the Apolipoprotein E epsilon 4 allele, Presenilin 1 and 2 genes, or amyloid precursor gene.

Genetic testing related to signs and symptoms of Alzheimer's disease is considered **not medically necessary**.

### **Policy:**

Genetic testing for the diagnosis or risk assessment of Alzheimer's disease is **not covered** as genetic screening is a contract exclusion.

Genetic testing related to signs and symptoms of Alzheimer's disease is considered **not medically necessary** due to lack of peer-reviewed medical literature that supports its use.

**Coverage:**

Benefits may vary between groups/contracts. Please refer to the appropriate Evidence of Coverage, Subscriber Agreement, Benefit Booklet, for the applicable benefits/coverage.

Medicare excludes all screening (not just genetic screening) with certain statutory exceptions. Blue CHIP for Medicare provides no additional benefits for genetic screening. Only if the patient exhibits signs or symptoms of the disease, would the test not be considered screening.

**Coding:**

**S3852** DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease  
**S3855** Genetic testing for detection of mutations in the presenilin - 1 gene  
**81401**

**Also known as:**

Not applicable

**Related topics:**

Genetic testing and counseling

**Published:**

*Policy Update*, Feb 2001  
*Policy Update*, Aug 2006  
*Policy Update*, Jan 2008  
*Provider Update*, Oct 2008  
*Provider Update*, Nov 2009  
Provider Update, Mar 2011  
Provider Update, Jan 2012  
Provider Update, Jul 2012

**References:**

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Daw EW, Payami H, Nemens EJ, et al. The Number of Trait Loci in Late-Onset Alzheimer Disease. American Journal Human Genetics 2000;66:196-204.

Hirono N, Hashimoto M, Yasuda M, Kazui H, Mori E,. Accelerated Memory Decline in Alzheimer's Disease with Apolipoprotein e4 Allele. Journal Neuropsychiatry Clinical Neuroscience;15:3: Summer 2003:354-358.

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