

## Corporate Medical Policy

### Genetic Testing for Familial Alzheimer's Disease

<b>File Name:</b>	genetic_testing_for_familial_alzheimers_disease
<b>Origination:</b>	8/2010
<b>Last CAP Review:</b>	11/2011
<b>Next CAP Review:</b>	11/2012
<b>Last Review:</b>	11/2011

#### Description of Procedure or Service

---

Alzheimer's disease (AD) is commonly associated with a family history; 40% of patients with AD have a least one other afflicted first-degree relative. Numerous genes have been associated with late-onset AD, while mutations in chromosomes 1, 14, and 21 have been associated with early onset familial AD.

##### **Susceptibility Polymorphism at the Apolipoprotein E (APOE) Gene**

The APOE lipoprotein is a carrier of cholesterol produced in the liver and brain glial cells. The APOE gene has 3 alleles—epsilon 2, 3, and 4—with the epsilon 3 allele being the most common. Individuals carry 2 APOE alleles. The presence of at least 1 epsilon 4 allele is associated with a 1.2- to 3-fold increased risk of AD depending on the ethnic group. The epsilon 4 allele represents a risk factor for AD rather than a disease-causing mutation.

##### **Genetic Mutations**

Individuals with early onset familial AD (i.e., before age 65 but as early as 30 years) form a small subset of AD patients. AD within families of these patients may show an autosomal dominant pattern of inheritance. Pathogenic mutations in 3 genes have been identified in affected families: amyloid-beta precursor protein gene (APP), presenilin 1 (PSEN1) gene, and presenilin 2 (PSEN2) gene. These mutations have nearly 100% penetrance absent death from other causes, although rare cases of nonpenetrance in elderly individuals have been reported. A variety of mutations within these genes has been associated with AD; mutations in PSEN1 appear to be the most common. While only 3%–5% of all patients with AD have early onset disease, pathogenic mutations have been identified in up to 70% or more of these patients. Identifiable genetic mutations are, therefore, rare causes of AD.

Testing for the APOE 4 allele among patients with late-onset AD and for APP, PSEN1, or PSEN2 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. Mutations in PSEN1 and PSEN2 are specific for AD; APP mutations are also found in cerebral hemorrhagic amyloidosis of the Dutch type, a disease in which dementia and brain amyloid plaques are uncommon.

Currently, the clinical diagnosis of AD is established by the presence of a consistent history, and excluding treatable causes of dementia. In 1984, the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's and Related Disorders Association (ADRDA) developed clinical criteria for the diagnosis of AD. Three categories were defined: possible, probable, and definite AD. The diagnosis of definite AD requires a brain biopsy confirming the presence of characteristic neurofibrillary tangles. While definite AD is almost

# Genetic Testing for Familial Alzheimer's Disease

always diagnosed by autopsy, in approximately 85% of those with a diagnosis of probable AD, pathological findings are found to be consistent.

Other diagnostic tests for AD include cerebrospinal (CSF) fluid levels of Tau protein or beta-amyloid precursor protein. These CSF tests are considered separately in the policy titled, Biochemical Markers for Alzheimer's Disease. Genetic testing for Alzheimer's disease may be offered along with spinal fluid (CSF) levels of the Tau protein and AB-42 peptide. This group of tests may be collectively referred to as the ADmark™ Profile, offered by Athena Diagnostics (Worcester, Mass.).

## **Related Policy:**

Biochemical Markers of Alzheimer's Disease

*\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.*

## **Policy**

---

**Genetic testing for familial Alzheimer's disease is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.**

## **Benefits Application**

---

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## **When Genetic Testing for Familial Alzheimer's Disease is covered**

---

Not applicable.

## **When Genetic Testing for Familial Alzheimer's Disease is not covered**

---

Genetic testing for the diagnosis or risk assessment of Alzheimer's disease is considered investigational. Genetic testing includes, but is not limited to, testing for the apolipoprotein E epsilon 4 allele, presenilin genes, or amyloid precursor gene.

## **Policy Guidelines**

---

Predictive genetic testing for asymptomatic "at risk" individuals with an apparent autosomal dominant inheritance, and a family-specific mutation has been identified. However, evidence that

# Genetic Testing for Familial Alzheimer's Disease

testing for AD genetic markers can improve health outcomes is lacking.

Genetic screening with APOE genotype in asymptomatic individuals in the general population is not recommended because of the low specificity and sensitivity. Genetic testing with APOE genotype is not recommended for the purpose of diagnosing AD because the positive and negative predictive values are low.

## Billing/Coding/Physician Documentation Information

---

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: 81401, S3852, S3855*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

---

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.13

Medical Director – 8/2010

Specialty Matched Consultant Advisory Panel – 11/2010

## Policy Implementation/Update Information

---

9/14/10 New evidence based guideline. Reviewed by Medical Director 8/10/2010. “Genetic testing for the diagnosis or risk assessment of Alzheimer’s disease not recommended. Genetic testing includes, but is not limited to, testing for the apolipoprotein E epsilon 4 allele, presenilin genes, or amyloid precursor gene.” (btw)

12/21/10 Specialty Matched Consultant Advisory Panel review 11/29/2010. No change to guideline. (btw)

1/1/2012 Policy converted from Evidence Based Guideline to Corporate Medical Policy. Specialty Matched Consultant Advisory Panel review 11/30/2011. “Genetic testing for the diagnosis or risk assessment of Alzheimer’s disease is considered investigational. Genetic testing includes, but is not limited to, testing for the apolipoprotein E epsilon 4 allele, presenilin genes, or amyloid precursor gene.” Added new CPT code effective 1/1/2012, 81401, to “Billing/Coding” section. Notification given 1/1/2012. Policy effective 4/1/2012. (btw)

# Genetic Testing for Familial Alzheimer's Disease

---

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.