Genetic and Biomarker Testing for Alzheimer Disease

Table of Contents
- Related Medical/Pharmacy Coverage Policies
- Related Documents
- Description
- Coverage Determination
- Coverage Limitations
- Coding Information
- References
- Appendix
- Change Summary

Disclaimer
The Coverage Summaries are reviewed by the iCare Medicare Utilization Management Committee. Policies in this document may be modified by a member’s coverage document. Clinical policy is not intended to preempt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test, or procedure over another. Clinical technology is constantly evolving, and we reserve the right to review and update this policy periodically. References to CPT® codes or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee of claims payment. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any shape or form or by any means, electronic, mechanical, photocopying or otherwise, without permission from iCare.

Related Medicare Advantage Medical/Pharmacy Coverage Policies

Aduhelm (aducanumab-avwa)
Genetic Testing
Genetic Testing for Diagnosis of Inherited Conditions

Related Documents

Please refer to CMS website for the most current applicable National Coverage Determination (NCD)/Local Coverage Determination (LCD)/Local Coverage Article (LCA)/CMS Online Manual System/Transmittals.

<table>
<thead>
<tr>
<th>Type</th>
<th>Title</th>
<th>ID Number</th>
<th>Jurisdiction Medicare</th>
<th>Applicable States/Territories</th>
</tr>
</thead>
</table>

**Effective Date:** 01/01/2024
**Revision Date:** Click or tap to enter a date.
**Review Date:** Click or tap to enter a date.
**Policy Number:** WI.PA-1095
**Line of Business:** Medicare
<table>
<thead>
<tr>
<th>NCD</th>
<th>Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (AD)</th>
<th>200.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCD</td>
<td>MolDX: Molecular Diagnostic Tests (MDT)</td>
<td>L36807</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: ApoE Genotype</td>
<td>A55141</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: Molecular Diagnostic Tests (MDT)</td>
<td>A57772</td>
</tr>
<tr>
<td>LCD</td>
<td>MolDX: Repeat Germline Testing</td>
<td>L38429</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: Repeat Germline Testing</td>
<td>A57100</td>
</tr>
<tr>
<td>LCD</td>
<td>MolDX: Molecular Diagnostic Tests (MDT)</td>
<td>L36021</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: ApoE Genotype</td>
<td>A54244</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: Molecular Diagnostic Tests (MDT)</td>
<td>A56973</td>
</tr>
<tr>
<td>LCD</td>
<td>MolDX: Repeat Germline Testing</td>
<td>L38288</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: Repeat Germline Testing</td>
<td>A57141</td>
</tr>
<tr>
<td>LCD</td>
<td>MolDX: Molecular Diagnostic Tests (MDT)</td>
<td>L35160</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: ApoE Genotype</td>
<td>A55094</td>
</tr>
<tr>
<td>LCA</td>
<td>Billing and coding: MolDX: Molecular Diagnostic Tests (MDT)</td>
<td>A57526</td>
</tr>
</tbody>
</table>

Administrative Contractors (MACs):
- J5, J8 - Wisconsin Physicians Service Insurance Corporation: IA, IN, KS, MI, MO, NE
- J15 - CGS Administrators, LLC: KY, OH
- JE - Noridian Healthcare Solutions, LLC: CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
### Description

Alzheimer disease (AD) is the most common form of dementia. It is a neurologic condition characterized by loss of mental ability severe enough to interfere with normal activities of daily living, lasting at least 6 months and not present from birth. AD usually occurs in adulthood and is marked by a decline in cognitive functions such as remembering, reasoning and planning.
Molecular biomarkers such as beta-amyloid (Aβ) and Tau proteins may be detected through cerebrospinal fluid (CSF). Other proposed methods for collecting biomarkers for AD diagnosis and screening include plasma and skin biopsy.

Genetic testing has also been proposed to aid in the diagnosis of a type of AD known as early-onset familial AD (EOFAD). EOFAD is a rare form of AD in which onset occurs at 30 to 60 years of age. Most cases are caused by a pathogenic variant in one of three known genes: APP, PSEN1, PSEN2.

Coverage Determination

iCare follows the CMS requirement that only allows coverage and payment for services that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

Genetic tests must demonstrate clinical utility, analytical and clinical validity and fulfill the CMS “reasonable and necessary” criteria. Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas. The test must be ordered by a physician who is treating the beneficiary and the results will be used in the management of a beneficiary’s specific medical problem.

For jurisdictions with no Medicare guidance, iCare will utilize the MolDX program and Technical Assessments for molecular assays as the standard to evaluate clinical utility, analytical and clinical validity in conjunction with adhering to Medicare’s reasonable and necessary requirement.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the following criteria:

CSF testing for Aβ and Tau proteins will be considered medically reasonable and necessary when treatment with an US Food & Drug Administration (FDA) approved Aβ monoclonal antibody drug (eg, lecanemab [Leqembi]) is being considered.35

DNA analysis for APOE epsilon 4 allele (APOE ε4) for AD will be considered medically reasonable and necessary when treatment with an FDA approved Aβ monoclonal antibody drug (eg, lecanemab [Leqembi]) is being considered.35

The use of the criteria in this Medicare Advantage Medical Coverage Policy provides clinical benefits highly likely to outweigh any clinical harms. Services that do not meet the criteria above are not medically necessary and thus do not provide a clinical benefit. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.
Coverage Limitations

US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage

The following test types are examples of testing services that may not be considered a benefit (statutory excluded) and denied as Medicare excluded tests:\textsuperscript{45}

- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law; OR
- Tests that confirm a diagnosis or known information; OR
- Tests to determine risk for developing a disease or condition; OR
- Tests performed to measure the quality of a process; OR
- Tests without diagnosis specific indications; OR
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial

These treatments and services fall within the Medicare program’s statutory exclusion that prohibits payment for items and services that have not been demonstrated to be reasonable and necessary for the diagnosis and treatment of illness or injury (§1862(a)(1) of the Act). Other services/items fall within the Medicare program’s statutory exclusion at 1862(a)(12), which prohibits payment.

Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the MolDX Program will not be considered medically reasonable and necessary. A review of the current medical literature shows that the evidence is insufficient to determine that these services are standard medical treatments. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

**Biomarker testing for AD** is considered not medically reasonable or necessary for any indications other than those listed above including, but may not be limited to:

- CSF testing for alpha-Synuclein (eg, SYNTap biomarker test); OR

- Plasma testing for any of the following:
  - A\textbeta\textsuperscript{2} and/or Tau proteins
    - A\textbeta\textsuperscript{2} peptide testing (eg, SOBA-AD assay)
    - A\textbeta\textsuperscript{42}/40 ratio and APOE proteotype assay (eg, PrecivityAD [0412U])
    - A\textbeta\textsuperscript{42}/40 ratio and p-Tau217 ratio (eg, PrecivityAD2)
    - A\textbeta\textsuperscript{42}/40 ratio testing (eg, Quest AD-Detect [0346U])
    - P-Tau181 and APOE ε4 assay (eg, Elecsys Amyloid Plasma Panel)
- p-Tau181 testing (eg, LucentAD)
  - U-p53AZ (AZ 284) biomarker testing (eg, AlzoSure Predict test); OR

- Skin biopsy (eg, DISCERN test [0206U and 0207U], Syn-One test)

A review of the current medical literature shows that the evidence is insufficient to determine that these tests are standard medical treatment for these indications. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of this service in clinical management for these indications.

**Genetic testing for AD** is considered not medically reasonable or necessary for any indications other than those listed above including but may not be limited to, APOE genotyping.\textsuperscript{11,12,13,14,15} A review of the current medical literature shows that the evidence is insufficient to determine that this service is standard medical treatment for these indications. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of this service in clinical management for these indications.

**Summary of Evidence**

**Genetic Testing for AD**

Effective April 7, 2022, CMS provides national coverage for FDA approved *monoclonal antibodies directed against amyloid for the treatment of Alzheimer’s disease (AD)* when furnished in accordance with Section B under coverage with evidence development (CED) for an individual who has a clinical diagnosis of mild cognitive impairment (MCI) due to AD or mild AD dementia, both with confirmed presence of amyloid beta pathology consistent with AD.\textsuperscript{35}

There are several widely investigated biomarkers for the molecular and degenerative process of AD that can be supportive of a diagnosis of AD but are not yet recommended for routine diagnostic purposes. Plasma biomarkers (eg, SOBA-AD assay, Quest AD-Detect) show promise but do not currently have an established role in clinical practice; more studies are needed. Decreased APOE and APOE €4 plasma levels (eg, Elecsys amyloid plasma panel, PrecivityAD) as well as a variety of other plasma/serum and CSF proteins (eg, AlzoSure Predict test, LucentAD, PrecivityAD2, SYNTap biomarker test) have been assessed for predictive value for AD in persons without dementia and in patients with MCI. Ongoing research is investigating the role of such biomarkers that may help distinguish AD from other forms of dementia.\textsuperscript{47}

**Coding Information**

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

<table>
<thead>
<tr>
<th>CPT® Code(s)</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
</table>


### Genetic and Biomarker Testing for Alzheimer Disease

<table>
<thead>
<tr>
<th>CPT® Category III Code(s)</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>No code(s) identified</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### HCPCS Code(s)

<table>
<thead>
<tr>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
References


Change Summary

- Click or tap to enter a date. New Policy.