MASSACHUSETTS

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Medical Policy

# Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer Disease

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## Policy Number: 581

BCBSA Reference Number: 2.04.14
NCD/LCD: N/A

## Related Policies

None

## Policy

### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue[SM] and Medicare PPO Blue[SM] Members

Measurement of cerebrospinal fluid biomarkers of Alzheimer disease, including but not limited to tau protein, amyloid beta peptides, or neural thread proteins, is considered **INVESTIGATIONAL**.

Measurement of urinary biomarkers of Alzheimer disease is considered **INVESTIGATIONAL**, including but not limited to neural thread proteins.

## Prior Authorization Information

**Inpatient**

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

**Outpatient**

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

| | Outpatient |
|---|---|
| **Commercial Managed Care (HMO and POS)** | This is **not** a covered service. |
| **Commercial PPO and Indemnity** | This is **not** a covered service. |
| **Medicare HMO Blue[SM]** | This is **not** a covered service. |
| **Medicare PPO Blue[SM]** | This is **not** a covered service. |

## CPT Codes / HCPCS Codes / ICD Codes

*Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.*

*Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.*

**CPT Codes**

There are no specific CPT codes for this testing.

## Description

**Biomarkers**

Several potential biomarkers of Alzheimer disease (AD) are associated with AD pathophysiology (eg, β-amyloid plaques, neurofibrillary tangles).

Elevated cerebrospinal fluid (CSF) levels of specific proteins have been found in patients with AD. They include tau protein, phosphorylated at AD-specific epitopes such as phosphorylated threonine 181 or total tau protein, or an amyloid-β peptide such as 1-42 (Aβ42). Other potential CSF[1,2,] and serum[3,] peptide markers have been explored. Tau protein is a microtubule-associated molecule found in neurofibrillary tangles that are typical of AD. Tau protein is thought to be related to degenerating and dying neurons and high levels of tau protein in the CSF have been associated with AD. Aβ42 is a subtype of amyloid-β peptide produced from the metabolism of the amyloid precursor protein. Aβ42 is the key peptide deposited in amyloid plaques characteristic of AD. Low levels of Aβ42 in the CSF have been associated with AD, perhaps because Aβ42 is deposited in amyloid plaques instead of remaining in the fluid. Investigators have suggested the tau/Aβ42 ratio may be a more accurate diagnostic marker than either alone.[4,] A variety of kits are commercially available to measure Aβ42 and tau proteins. Between-laboratory variability in CSF biomarker measurement is large.[5,6]

Neural thread protein is associated with neurofibrillary tangles of AD. Both CSF and urine levels of this protein have been investigated as a potential marker of AD. Urine and CSF tests for neural thread protein may be referred to as the AD7C test.

## Summary

Biochemical changes associated with the pathophysiology of Alzheimer disease (AD) are being evaluated to aid in the diagnosis of AD. Some common biomarkers studied are amyloid-b peptide 1-42 and total or phosphorylated tau protein in cerebrospinal fluid.

For individuals who have AD or mild cognitive impairment (MCI) who receive cerebrospinal fluid biomarker testing for AD, the evidence includes systematic reviews, meta-analyses, and case series. These studies assess using cerebrospinal fluid biomarkers for diagnosis of AD or for the prognosis of progression of MCI to AD. The relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life (QOL), medication use, and resource utilization. Most clinical validity studies have been derived from select patient samples and defined optimal test cutoffs without validation; thus, the generalizability of results is uncertain. For predicting conversion from MCI to AD, limited evidence has suggested that testing may define increased risk. Whether an earlier diagnosis leads to improved health outcomes through a delay of AD onset due to medical therapy or other interventions or improved QOL is unknown. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have AD or MCI who receive urinary biomarker testing for AD, the evidence includes a systematic review and observational studies. The relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, QOL, medication use, and resource utilization. Clinical validity studies have included normal healthy controls and defined optimal test cutoffs without validation; thus, clinical validity is uncertain. Whether an earlier diagnosis leads to improved health outcomes

through a delay of AD onset or improved QOL is unknown. The evidence is insufficient to determine the effects of the technology on health outcomes.

## Policy History

| Date | Action |
|---|---|
| 1/2020 | BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged. |
| 2/2019 | BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged. |
| 3/2018 | New references added from BCBSA National medical policy. |
| 2/2017 | BCBSA National medical policy review.<br>Title changed to "Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer Disease."<br>New references added. 2/1/2017 |
| 10/2014 | New references added from BCBSA National medical policy. |
| 3/2014 | New medical policy describing ongoing investigational indications. |

## Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

## References


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