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

- Positron Emission Tomography (PET) Brain Imaging, #903

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 **INVESTIGATIONAL**.

Measurement of urinary biomarkers of Alzheimer disease is **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

Alzheimer Disease

The diagnosis of Alzheimer disease (AD) is divided into 3 categories: possible, probable, and definite AD. A diagnosis of possible AD dementia is made when the patient meets core clinical criteria for AD dementia but has an atypical course or an etiologically mixed presentation. Probable AD dementia is diagnosed clinically when the patient meets core clinical criteria for dementia and has a typical clinical course for AD. A typical clinical course is defined as an insidious onset, with the initial and most prominent cognitive deficits being either amnestic or nonamnestic (eg, language, visuospatial, or executive function deficits), and a progressively worsening cognition over time. A diagnosis of definite AD requires postmortem confirmation of AD pathology, including the presence of extracellular β-amyloid plaques and intraneuronal neurofibrillary tangles in the cerebral cortex.[1]

Mild Cognitive Impairment

Mild cognitive impairment (MCI) may be diagnosed when a dementia diagnosis cannot be made yet there is a significant change in cognition.[2] MCI is characterized by impairment in one or more cognitive domains yet there remains preserved functional independence. In some patients, MCI may be a predementia phase of AD. Patients with MCI or suspected AD may undergo ancillary testing (eg, neuroimaging, laboratory tests, neuropsychological assessment) to rule out vascular, traumatic, and medical causes of cognitive decline and to evaluate genetic factors. Because clinical diagnosis can be difficult, particularly early in the course of disease, there has been considerable interest in developing an accurate laboratory test for AD.

Biomarkers

Several potential biomarkers of 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[3,4] and serum[5] 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 metabolism of 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 fluid. Investigators have suggested that the tau/Aβ42 ratio may be a more accurate diagnostic marker than either alone.[6] A variety of kits are commercially available to measure Aβ42 and tau proteins. Between-laboratory variability in CSF biomarker measurement is large.[7,8]

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 who receive cerebrospinal fluid biomarker testing for AD, the evidence includes systematic reviews, meta-analyses, and case series. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and resource utilization. The technical reliability of cerebrospinal fluid biomarker measurement in AD is limited by variability between laboratories and assay methods. 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 mild cognitive impairment to AD, limited evidence has suggested that testing may define increased risk. Whether an earlier diagnosis leads to improved health outcomes through delay of AD onset due to medical therapy or other interventions or improved quality of life is unknown. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have AD or mild cognitive impairment who receive urinary biomarker testing for AD, the evidence includes a systematic review and observational studies. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and resource utilization. Limited data are available on the technical reliability of urinary biomarker measurement in AD. 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 delay of AD onset or improved quality of life is unknown. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

Date	Action
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. Title changed to “Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer Disease.” 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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