Medical Coverage Policy | Cerebrospinal Fluid and Urinary Biomarkers of Alzheimer Disease

EFFECTIVE DATE: 01|01|2017
POLICY LAST UPDATED: 02|06|2020

OVERVIEW
Biochemical changes associated with the pathophysiology of Alzheimer disease (AD) are being evaluated to aid in the diagnosis of AD. Some of the most commonly studied biomarkers are amyloid-β peptide 1-42 and total or phosphorylated tau protein in cerebrospinal fluid (CSF). This policy documents whether testing cerebrospinal fluid and urinary biomarkers improves outcomes in individuals with mild cognitive impairment or Alzheimer disease

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
BlueCHiP for Medicare
Measurement of cerebrospinal fluid biomarkers of Alzheimer disease, including but not limited to tau protein, amyloid-β peptides, or neural thread proteins, is considered not covered as whether 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.

Measurement of urinary biomarkers of Alzheimer disease is considered not covered, including but not limited to neural thread proteins as whether 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.

Commercial
Measurement of cerebrospinal fluid biomarkers of Alzheimer disease, including but not limited to tau protein, amyloid-β peptides, or neural thread proteins, is considered not medically necessary as whether 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.

Measurement of urinary biomarkers of Alzheimer disease is considered not medically necessary, including but not limited to neural thread proteins as whether 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.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for not medically necessary/not covered services.

BACKGROUND
The diagnosis of Alzheimer disease (AD) is divided into 3 categories: possible, probable, and definite AD. 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 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 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.

Mild cognitive impairment (MCI) may be diagnosed when there is a change in cognition but insufficient impairment for the diagnosis of dementia.2 MCI is characterized by impairment in 1 or more cognitive domains but 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. 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 CSF3,4 and serum5 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.

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

For individuals who have AD or mild cognitive impairment (MCI) who receive CSF biomarker testing for AD, the evidence includes systematic reviews, meta-analyses, and case series. Relevant outcomes are test accuracy and validity, symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and resource utilization. The analytic validity of CSF 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 MCI to AD, limited evidence has suggested that testing may define increased risk. Whether 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.

For individuals who have AD or MCI who receive urinary biomarker testing for AD, the evidence includes a systematic review and observational studies. Relevant outcomes are test accuracy and validity, symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and resource utilization. Limited data are available on the analytic validity 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 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

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). AlzheimAlert™ and AdMark® CSF analysis are available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

CODING

BlueCHiP for Medicare and Commercial

There are no specific codes for these tests. Claims should be filed with code 81099 when performed in urine and the unlisted immunology code 86849 when performed in CSF.

CPT code 83520 (Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative; not otherwise specified) may be used to report testing for tau protein and amyloid-β peptides. Claims filed with this code for this service will be denied as not medically necessary.

RELATED POLICIES

None

PUBLISHED

Provider Update, April 2020
Provider Update, January 2020
Provider Update, November/December 2018
Provider Update, June 2017

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