Medical Policy
Biochemical Markers of Alzheimer’s Disease

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Policy Number: 581
BCBSA Reference Number: 2.04.14

Related Policies
- Genetic Testing for Familial Alzheimer’s Disease, #580
- Beta Amyloid Imaging with Positron Emission Tomography (PET) for Alzheimer’s Disease, #903

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO BlueSM and Medicare PPO BlueSM Members

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

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

Prior Authorization Information

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CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. 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
A variety of biochemical changes have been associated with Alzheimer’s disease pathology and are being evaluated to aid in the diagnosis of Alzheimer’s disease (AD). Some of the most commonly studied biomarkers are amyloid beta peptide 1-42 (AB-42), and total or phosphorylated tau protein (T-tau or P-tau) in cerebrospinal fluid (CSF).

Background
The diagnosis of Alzheimer’s disease (AD) is divided into 3 categories: possible, probable, and definite AD. (1) A diagnosis of definite AD requires post-mortem confirmation of AD pathology, including the presence of extracellular beta amyloid plaques and intraneuronal neurofibrillary tangles in the cerebral cortex. (2) 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 non-amnestic, e.g., language, visuospatial, or executive function deficits, and a history of progressively worsening cognition over time. A diagnosis of possible AD dementia is made when the patient meets the 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 not sufficient impairment for the diagnosis of dementia. (3) Features of MCI are evidence of impairment in one or more cognitive domains and preservation of independence in functional abilities. In some patients, MCI may be a predementia phase of AD. Patients with MCI or suspected AD may undergo ancillary testing (e.g., neuroimaging, laboratory studies, and 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. There are several potential biomarkers of AD that are associated with Alzheimer’s disease pathology (i.e., beta amyloid plaques and neurofibrillary tangles).

Elevated CSF levels of P-tau or T-tau or an amyloid beta peptide such as AB-42 have been found in patients with AD. Other potential CSF peptide markers have also been explored. (4, 5) The tau protein is a microtubule-associated molecule that is found in the neurofibrillary tangles that are typical of AD. This protein is thought to be related to degenerating and dying neurons, and high levels of tau proteins in the CSF have been associated with AD. AB-42 is a subtype of amyloid beta peptide that is produced following the metabolism of amyloid precursor protein. AB-42 is the key peptide deposited in the amyloid plaques characteristic of AD. Low levels of AB-42 in the CSF have been associated with AD, perhaps because AB-42 is deposited in amyloid plaques instead of remaining in solution. Finally, investigators have suggested a Tau/AB-42 ratio, a potentially more accurate diagnostic marker than either alone. (6) A variety of kits are commercially available to measure AB-42 and tau proteins, and there is large between-laboratory variability in cerebrospinal fluid (CSF) biomarker measurement. (7)

Neural thread protein is associated with the 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, as developed by Nymox Pharmaceutical Corporation.

Summary
Evidence that testing for Alzheimer’s disease (AD)-related biomarkers in patients with dementia can improve health outcomes is lacking. A majority of studies derive from select samples and define optimal test cutoffs without validation, thus generalizability of results is unclear. For the diagnosis of AD, evidence does not demonstrate incremental improvement in diagnostic accuracy over clinical testing. For predicting conversion from mild cognitive impairment to AD, limited evidence, including that from the Alzheimer’s Disease Neuroimaging Initiative, suggests testing might define increased risk. Whether earlier diagnosis leads to improved health outcomes through delay of AD onset or quality of life is lacking. Guidelines are consistent with these conclusions. Therefore, this testing is considered investigational.
Policy History

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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