

Subject:	Testing for Biochemical Markers for Alzheimer's Disease	Publish Date:	12/18/2025
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Description/Scope

This document addresses the use of testing for biochemical markers (for example, tau protein, long-form amyloid beta, and neural thread protein) as a diagnostic or screening technique for Alzheimer's disease.

Long-form amyloid beta, also referred to as A β , A β 1-42, Beta-amyloid [1-42], and Abeta42, is one of the primary components of amyloid plaques. These amyloid β containing plaques are one of the neuropathological hallmarks of Alzheimer's disease.

Notes:

- This document does not address imaging tests, including MRI and PET. For criteria related to MRI and PET, refer to applicable guidelines used by the plan.

Position Statement

Medically Necessary:

Measurement of long-form amyloid beta is considered **medically necessary** when criteria A, B and C are met:

- A cerebrospinal fluid test is used; **and**
- Treatment with [amyloid beta targeting therapy](#) is being considered; **and**
- Any of the following tests are used:
 - Total A β 42; **or**
 - A β 42:A β 40 ratio; **or**
 - A β 42: phospho-tau.

Investigational and Not Medically Necessary:

Measurements of biochemical markers (including but not limited to tau protein, long-form amyloid beta, neural thread protein) is considered **investigational and not medically necessary** as a diagnostic technique for individuals with symptoms suggestive of Alzheimer's disease when the criteria above have not been met.

Measurements of biochemical markers as a screening technique in asymptomatic individuals with or without a family history of Alzheimer's disease is considered **investigational and not medically necessary**.

Rationale

Summary

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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Testing for Biochemical Markers for Alzheimer's Disease

At this time, there are inadequate data regarding the role of biochemical testing for Alzheimer's disease in *asymptomatic* individuals or whether test results might alter the medical management, treatment, or clinical outcomes in individuals with Alzheimer's disease. With regard to *symptomatic* individuals, testing for the presence of A β in cerebrospinal fluid (CSF) or on PET imaging is required for the selection of appropriate candidates for treatment with amyloid beta targeting therapy (for example, lecanemab-irmb [LeqembiTM]).

Testing for other biochemical markers has not been demonstrated to improve the accuracy of a clinical diagnosis of Alzheimer's disease. The majority of available studies focus on those with probable Alzheimer's disease, for whom the clinical diagnosis has a sensitivity of 85%. Additionally, there are inadequate data to suggest that the use of biomarker tests (other than A β in CSF) is likely to impact clinical management in terms of either altering the diagnostic work up or therapy, or informing appropriateness for therapy, in a manner that improves net health outcomes.

Discussion

Diagnosis of Alzheimer's disease

Alzheimer's disease is an age-related disease caused by unrelenting neurodegeneration and brain atrophy. Behaviorally, Alzheimer's disease is characterized by progressive memory loss and cognitive decline. Pathologically, Alzheimer's disease is characterized by local accumulations of amyloid β (A β) peptide and neurofibrillary tangles (NFTs) comprised of tau protein in the brain. At present, a definitive diagnosis of Alzheimer's disease requires postmortem verification of A β deposits (plaques) and NFTs in the brain. In current clinical practice, a diagnosis of Alzheimer's disease is based on clinical presentations, a detailed clinical history, cognitive screening tools and clinical diagnostic criteria (for example, the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association [NINCDS-ADRDA] guidelines and the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition [DSM-IV]). However, the diagnostic accuracy of these Alzheimer's disease criteria is not perfect. Diagnosis of Alzheimer's disease is often a diagnosis of exclusion and is challenging for both physicians and patients.

Based on the 2011 guidelines from the National Institute on Aging (NIAA) and the Alzheimer's Association (AA), the diagnosis of Alzheimer's disease is a clinical diagnosis, focusing on the exclusion of other causes of senile dementia. Ancillary imaging studies such as computed tomography [CT], magnetic resonance imaging [MRI], single-photon emission CT [SPECT], or positron emission tomography [PET]) and laboratory tests may be used to aid in the diagnosis. These tests help rule out other possible causes for dementia (for example, cerebrovascular disease, cobalamin [vitamin B12] deficiency, syphilis, and thyroid disease). According to the NIA-AA, the core clinical criteria for Alzheimer's disease dementia will continue to be the foundation of the diagnosis in clinical practice, however, "further studies are needed to prioritize biomarkers and to determine their value and validity in practice and research settings" (McKahn, 2011).

In 2018, the NIA-AA published an updated biological definition of Alzheimer's disease that focuses on the underlying pathological activities of the disease, which can be identified either in living individuals (via biomarkers) or during autopsy. The NIA-AA framework proposes using three groups of biomarkers (A β deposition, pathologic tau, and neurodegeneration) that can be measured by obtaining spinal fluid and/or special radiological imaging tests. The new definition is intended for research purposes only (to identify and stage research participants)

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and is meant to provide a flexible framework amenable to new (yet to be discovered) biomarker tests. The definition is not intended to be used in routine clinical care, and further investigation is required to establish the role and utility of biomarkers (Jack, 2018).

In 2024, Jack and associates published an update to the 2018 research framework for diagnosing and staging Alzheimer's disease. The framework integrates research and clinical care, categorizing biomarkers into Core 1 (early detection) and Core 2 (later detection) types. It emphasizes the need for high accuracy in biomarkers and incorporating clinical judgments with biomarker results. The document provides guidance for the utilization of biomarkers in clinical trials and therapeutic decision-making. Although blood-based testing is progressively approaching the diagnostic accuracy of CSF testing, it currently exhibits less clinical robustness compared to CSF assays and has a with limited diagnostic range. The guideline notes:

Only biomarkers that have been proven to be accurate with respect to an accepted reference standard should be used for clinical diagnostic purposes, and the same criteria apply to PET, CSF, or blood-based biomarkers. We recommend, as a minimum requirement, an accuracy of 90% for the identification of moderate/frequent neuritic plaques at autopsy (or an approved surrogate, which, at this point, would be amyloid PET or CSF) in the intended-use population.

The Global CEI Initiative on Alzheimer's Disease published a consensus statement outlining recommendations for the minimum acceptable performance metrics for blood biomarker (BBM) testing of amyloid pathology in clinical practice (Schindler, 2024). Amyloid PET and CSF biomarker testing have long been the standards in diagnosing Alzheimer's disease. To maintain diagnostic accuracy and timeliness, the committee recommends that blood-based biomarker tests demonstrate sensitivity and specificity comparable to CSF tests. With the approval of FDA-sanctioned treatments, there has been a shift towards developing more accessible blood-based biomarker testing methodologies.

The committee did not evaluate any specific tests but instead provided general performance standards. The group recommends that BBM tests used in primary care settings achieve a minimum of 90% sensitivity and 85% specificity. In secondary care settings, these tests should exhibit sensitivity and specificity in the range of 75% to 85% when employed as triaging tools. For confirmatory testing without the need for follow-up procedures, BBM tests should demonstrate sensitivity and specificity approximating 90%, similar to CSF tests.

Biomarkers for Alzheimer's Disease

Fluid biomarkers (found in the CSF or blood) have the potential to be easily implemented in clinical trials, and several biomarkers linked to different pathophysiological mechanisms can be analyzed in a single sample. Furthermore, fluid biomarkers may provide a window for identifying some biomarkers that cannot be detected via brain imaging.

Several CSF biomarkers, including but not limited to A β 42, tau protein (T-tau) and neurofilament light chain (NF-L) are detectable in the blood and have been investigated as a means to screen for and diagnose Alzheimer's disease. However, a major challenge in measuring these blood-based proteins is that their concentrations are lower in serum or plasma than in CSF. Currently, these tests are not considered standard of care in the evaluation of individuals with mild cognitive impairment (MCI) in the clinical setting (Petersen, 2018).

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Amyloid Beta (A β) Peptide

A β accumulation in the brain is proposed to be an early toxic event in the pathogenesis of Alzheimer's disease, which is the most common form of dementia associated with plaques and tangles in the brain. Currently, it is unclear what the physiological and pathological forms of A β are and by what mechanism A β causes dementia.

A β in Plasma

In May 2025, the FDA granted 510(k) premarket notification clearance for Lumipulse G pTau217/ β -Amyloid 1-42 Plasma Ratio (Fujirebio Diagnostics Inc., Malvern, Pennsylvania) as the first blood test to assist in diagnosing Alzheimer's disease. The Lumipulse is designed to detect signs of Alzheimer's disease by identifying amyloid plaques in the plasma. According to the FDA 510(k) premarket notification, the test is cleared for use in adults 50 years and older who are being evaluated for Alzheimer's disease and other causes of cognitive decline. The test measures the ratio of two pTau 217 and β -Amyloid 1-42 proteins in plasma. This ratio correlates with the presence of amyloid plaques in the brain. The FDA emphasizes that the test is not 100% accurate and cannot be used alone to confirm a diagnosis. Results must be interpreted in conjunction with other clinical information and are not for general screening of healthy individuals. Additional testing, such as PET brain scans or CSF analysis, is often required to verify the presence of Alzheimer's-related changes in the brain. The test serves as a preliminary testing option to indicate whether other tests may be necessary.

The FDA clearance of the Lumipulse test (K242706) was based on a study involving 499 adults with cognitive impairment. Researchers compared the Lumipulse blood test results with PET scan and CSF findings. The study found that approximately 92 % of individuals who tested positive on the Lumipulse test had confirmed amyloid plaque buildup, while more than 97% of those with negative results demonstrated negative findings on the confirmatory tests. Less than 20% of participants received inconclusive results. This study demonstrated that while Lumipulse test is highly reliable for both positive and negative results, it is not definitive and may require follow-up testing for clarification.

Monane and colleagues (2025) conducted a single-arm, multisite, prospective cohort study to evaluate how the PrecivityAD2 (C2N Diagnostics, St. Louis, MO) BBM test impacted clinical decision-making for 203 individuals (median age, 74 years; 53% women) who displayed signs of dementia or mild cognitive impairment consistent with AD. The test measures plasma A β 42/A β 40 and p-tau217/np-tau217 ratios to generate an Amyloid Probability Score 2 (APS2), which estimates the likelihood of brain amyloid plaque presence. Clinicians completed surveys on patient management before and after receiving the BBM test results to assess its clinical utility. The study's primary outcome focused on two key aspects: patient selection and test result interpretation. Patient selection was measured by determining how closely clinicians' decisions to order the PrecivityAD2 blood test aligned with its intended use criteria. Test interpretation was evaluated by examining changes in clinical decision-making after receiving the Amyloid Probability Score 2 (APS2) results. Specifically, researchers measured shifts in clinicians' estimated probability of Alzheimer's disease (rated from 0–100%), as well as changes in prescribing Alzheimer's-related medications and in ordering additional amyloid brain imaging before and after the BBM test.

With regards to the primary outcome, concordance with the intended use of the BBM test was 99% (200/203). Reasons for non-concordance were test use outside of the intended use, including participants below the age of 55 (n=1) and participants without symptoms of MCI or dementia (n=2). The study found that the composite primary endpoint, defined as any change in diagnostic certainty, drug therapy, or the need for additional brain amyloid

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evaluation pre- and post-BBM testing, was 75% (153/203, $p < 0.0001$ vs. a pre-specified threshold of 20% clinically meaningful change). Among participants with negative APS2 results, use of anti-Alzheimer's medications and further amyloid imaging decreased, while both increased among participants with positive APS2 results ($p < 0.0001$). The findings indicate that the PrecivityAD2 blood test effectively refines diagnostic confidence, reduces unnecessary confirmatory testing, and helps guide the initiation or discontinuation of Alzheimer's-specific treatments, ultimately improving decision-making in memory care settings.

There are some limitations related to this study's design and scope. First, it assessed clinicians' intended changes in clinical management after receiving the BBM test results, rather than confirming whether those changes were actually implemented. This was due to the study's real-world, survey-based design conducted under an IRB exemption, which relied on clinician-reported data. Second, the study's outcomes were limited to clinician-reported measures, such as changes in diagnostic confidence, treatment decisions, and use of additional amyloid testing. It did not directly evaluate patient-level outcomes like cognitive function, daily living performance, or quality of life improvements.

A β in CSF

Researchers are investigating the use of CSF biomarkers to predict the conversion from MCI to dementia and to diagnose Alzheimer's disease. The most explored CSF biomarkers include tau protein or phosphorylated tau protein and A β 42 peptide, which may be represented by a low ratio of A β 42 to A β 40 levels, or a low ratio of A β 42 to tau levels or elevated levels of tau or tau protein phosphorylated at threonine 181.

Schmand and colleagues (2010) reported the results of a meta-analysis that sought to determine if biomarkers can detect preclinical Alzheimer's disease prior to the onset of behavioral (for example, memory) symptoms. The researchers included relevant longitudinal studies of CSF and MRI biomarkers published between January 2003 and November 2008. Study participants were not demented at baseline, but some declined to MCI or to Alzheimer's disease. A total of 21 MRI studies and 14 CSF studies were included in the analysis. The effect sizes of A β 42, total tau (t-tau), and phosphorylated tau (p-tau) ranged from 0.91 to 1.11. The effect size of medial temporal lobe (MTL) atrophy was 0.75. Memory performance had an effect size of 1.06. Memory impairment and MTL atrophy tended to increase when measured closer to the time of diagnosis, whereas effect sizes of CSF biomarkers tended to increase when measured longer before the diagnosis. The researchers concluded that memory impairment is a more accurate predictor of early Alzheimer's disease than atrophy of MTL on MRI, whereas CSF abnormalities and memory impairment are about equally predictive. Therefore, the MRI and CSF biomarkers are not very sensitive to preclinical Alzheimer's disease. While CSF markers have shown promise, additional studies with long follow-up periods in elderly participants who are normal at baseline are needed to evaluate this promise.

Roe and colleagues (2013) investigated whether A β 42, tau, phosphorylated tau at threonine 181 (ptau181), tau/A β 42, and ptau181/A β 42 predict future decline in non-cognitive outcomes among individuals who were cognitively normal at baseline. Longitudinal data from 430 participants who donated CSF within 1 year of a clinical assessment indicating normal cognition and were 50 years of age or older were analyzed. Mixed linear models were used to assess whether baseline biomarker values predicted future decline in function (instrumental activities of daily living), weight, behavior, and mood. Clinical Dementia Rating Sum of Boxes (CDR-SB) and Mini-Mental State Examination (MMSE) scores were also assessed. Abnormal levels of each biomarker were related to greater impairment with time in behavior ($p < 0.035$) and mood ($p < 0.012$) symptoms, and increased difficulties with independent activities of daily living ($p < 0.012$). However, biomarker levels were not linked to a change in weight

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with time ($p > 0.115$). Abnormal biomarker values also forecasted more rapidly changing MMSE ($p < 0.041$) and CDR-SB ($p < 0.001$) scores compared with normal values. The investigators concluded that CSF biomarkers among cognitively normal individuals correlate with future decline in some, but not all, non-cognitive Alzheimer's disease symptoms studied. The authors acknowledged that additional work is needed to determine the extent to which these findings generalize to other samples. The investigators also noted that future research should explore whether the ratio of tau/A β 42 and ptau181/A β 42 are better predictors of decline in non-cognitive outcomes compared with individual molecular marker alone.

Rivero-Santana and colleagues (2017) conducted a systematic review of studies analyzing the diagnostic performance of CSF A β 42, t-tau, and p-tau in the discrimination between Alzheimer's disease and frontotemporal lobar degeneration (FTLD) dementias. A Hierarchical Summary Receiver Operating Characteristic (HSROC) model was applied, which circumvents methodological problems of meta-analyses based on summary points of sensitivity and specificity values. They also examined relevant confounders of CSF biomarkers' diagnostic performance such as age, disease duration, and global cognitive impairment. The p-tau/A β 42 ratio demonstrated the best diagnostic performance. No statistically significant effects of the confounders were detected. Nonetheless, the investigators found the p-tau/A β 42 ratio may be especially indicated for younger subjects; p-tau may be preferable for less cognitively impaired individuals (high MMSE scores) and the t-tau/A β 42 ratio for more cognitively impaired individuals (low MMSE scores). The researchers concluded that p-tau/A β 42 ratio has potential for being implemented in the clinical routine for the differential diagnosis between Alzheimer's disease and FTLD. The authors also recommended that future studies report information on confounders such as age, disease duration, and cognitive impairment.

In the Decision Summary section of the Centers for Medicare & Medicaid Services (CMS) National Coverage Analysis of Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease (2022), the authors point out the following limitations of A β as a biomarker of Alzheimer's disease:

- (1) Amyloid is associated with normal physiologic processes. Normal functions of A β include disease prevention by protecting against oxidative stress and regulating cholesterol transport and anti-microbial activity. Additionally, A β protects the brain from infections, promotes recovery from injury and repairs leaks in the blood-brain barrier.
- (2) Amyloid plaques are seen in other diseases, such as cerebral amyloid angiopathy, dementia with Lewy bodies, Parkinson's disease, Huntington's disease, and inclusion body myositis.
- (3) Amyloid plaques can be identified in cognitively normal older adults. Autopsy studies demonstrate that approximately 1/3 of cognitively normal older individuals (20-65% depending on age) have amyloid accumulation at levels consistent with AD pathology (CMS, 2022).

In 2023, Nisenbaum published the results of a follow-up study of the EMERGE and ENGAGE clinical trials used in the FDA application for the anti-amyloid drug aducanumab. As noted below, those studies did not use measurement of CSF A β 42, p-tau, or t-tau as clinical trial inclusion criteria or for subject selection purposes. The Nisenbaum study assessed the use of these biomarkers as an alternative to amyloid PET for confirmation of brain pathology using data from 350 subjects (EMERGE $n=208$, ENGAGE $n=142$) who had an evaluable baseline CSF screening value and baseline PET scan. A total of 308 subjects were identified as PET positive and 42 were identified as PET negative. Compared with the PET negative group, the mean CSF A β 42 level was numerically lower in the PET positive group (484.4 pg/mL in the CSF group vs. 933.3 pg/mL in the PET negative group). The p-tau181 level was numerically higher (91.42 pg/mL in the PET positive group vs. 40.09 pg/mL in the PET negative

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group). The t-tau level was numerically higher in the PET positive group (594.8 pg/mL in the PET positive group vs. 374.6 pg/mL in the PET negative group). In contrast, A β 40 levels were similar between groups (10,973.9 pg/mL in the PET positive group vs. 11,251.0 pg/mL in the PET negative group). The A β 42/A β 40 ratio was numerically lower in the PET positive group (0.048 in the PET positive group vs. 0.087 in the PET negative group). The p-tau181/A β 42 and t-tau/A β 42 ratios were numerically higher in the PET positive group (0.203 in the PET positive group vs. 0.050 in the PET negative group for p-tau181/A β 42; and 1.329 in the PET positive group vs. 0.433 in the PET negative group for t-tau/A β 42). The area under the curve (AUC) for A β 42, p-tau and t-tau were calculated by receiver operating characteristic curve (ROC curve), which indicated high accuracy for all three (AUCs $\geq$ 0.90; $p < 0.0001$). In contrast, A β 40 was found to have an unfavorable AUC and deemed not useful for the detection of the visual status of PET scans (AUC, 0.49; $p = 0.782$). Finally, the combination of A β 42 with A β 40 demonstrated high diagnostic accuracy with PET visual assessment (AUCs, 0.90; $p < 0.0001$). The sensitivity, specificity and overall percent agreement (OPA) was calculated using optimal cutoff values that maximize the Youden J index in the ROC analysis. The maximum Youden J index was observed at a cutoff of 664 pg/mL for A β 42. For the A β 42/A β 40 ratio the best cut-off was 0.062. With these cutoffs, A β 42 showed the highest diagnostic accuracy as a single biomarker with an OPA of 89.4%. Additionally, the sensitivity and specificity were improved when A β 42 was combined with a second analyte (94.4% and 88.1% for A β 42/A β 40, 95.4% and 83.3% for p-tau181/A β 42, and 92.3% and 81.6% for t-tau/A β 42). The authors concluded that their data supported the use of CSF biomarkers as reliable alternatives to PET imaging for brain A β pathology confirmation.

Neural Thread Protein (NTP)

Neural thread protein is a protein that is associated with neurofibrillary tangles. Both CSF and urine levels of this protein have been investigated as a potential biochemical marker of Alzheimer's disease.

Zhang et al (2014) conducted a systematic review and meta-analysis of urinary Alzheimer's disease -associated neural thread protein (NTP) for diagnosing Alzheimer's disease in individuals with suspected Alzheimer's disease. Nine studies met the inclusion criteria (n=841 individuals with probable or possible Alzheimer's disease; 37 individuals with MCI, 992 with non-Alzheimer's disease dementia or controls without dementia). The reference standard consisted of a clinical diagnosis in eight studies and not described in another. Varying cutoffs for positive diagnosis were used amongst included studies. Controls were both healthy volunteers and individuals with other dementias. For a probable Alzheimer's disease D, pooled sensitivity and specificity were 89% (95% confidence interval [CI], 86% to 92%) and 90% (95% CI, 88% to 92%), respectively. Pooled positive and negative likelihood ratios were 8.9 (95% CI, 7.1 to 11.1) and 0.12 (95% CI, 0.09 to 0.16), respectively. The authors concluded that urinary AD7c-NTP is both a sensitive and specific test for the diagnosis of probable Alzheimer's disease. However, whether urinary AD7c-NTP can be used as an early marker is still uncertain.

Neurofilament Light (NF-L)

Neurofilaments are intermediate filaments that serve as structural components of neuronal axons, in particular large, myelinated axons. NF-L has been studied in individuals with neuronal injury and neurodegenerative diseases because it is released into CSF and systemic circulation when neurons are damaged. Sjogren and colleagues (2000) reported that CSF NF-L levels are increased in subjects with frontotemporal dementia (FTD) and late onset Alzheimer's disease compared with control subjects, and the increase in FTD subjects is higher than in late onset Alzheimer's disease.

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In a meta-analysis, Olsson and colleagues (2016) found that NF-L has a large effect size for differentiating individuals with Alzheimer's disease from control subjects. Additionally, Zetterberg and colleagues (2016) demonstrated that higher CSF NF-L concentrations are associated with cognitive deterioration and brain atrophy over time in Alzheimer's disease and MCI groups and concluded that CSF NF-L could be used as a marker for Alzheimer's disease progression. However, elevated CSF levels of NF-L are also found in other neurodegenerative diseases, such as normal-pressure hydrocephalus, multiple sclerosis, Parkinson's disease and amyotrophic lateral sclerosis. Therefore, CSF NF-L could be a representative marker of neurodegeneration, but not a precise marker for distinguishing Alzheimer's disease from other neurological disorders.

Skin Fibroblast

Researchers are also exploring the use of skin fibroblast testing as a means to detect and differentiate Alzheimer's disease from other dementias. The Discern™ Alzheimer's disease test (NeuroDiagnostics, Rockville, MD) examines skin fibroblast cells to identify and quantify three biomarkers (the phosphorylated Erk1 and Erk2, quantitatively measure skin fibroblast networks and protein kinase C levels), each of which is reported to independently identify and differentiate Alzheimer's disease. At the time of this review, peer-reviewed studies assessing the analytical validity of this test were limited (Chirila, 2013; Chirila, 2014; Nelson, 2017). Large, randomized, controlled trials demonstrating this test is as accurate as autopsy results (the gold standard in the definitive diagnosis of Alzheimer's disease) are needed in order to assess the clinical utility of the test.

Tau Protein in CSF

CSF t-tau and p-tau are frequently studied in neurodegenerative disorders. CSF t-tau levels can serve as a neuronal injury marker and are elevated in many neurodegenerative diseases, such as Creutzfeldt-Jakob disease, Alzheimer's disease, and FTD, whereas CSF p-tau 181 or p-tau 231 (tau phosphorylated at threonine 181 or threonine 231) levels are elevated more specifically in Alzheimer's disease than in other neurodegenerative diseases. Like CSF Aβ42, t-tau and p-tau tests are difficult to use in healthy people at the preclinical stage because of the limitation of obtaining CSF samples.

Tau Protein in Plasma

Mattsson and colleagues (2016) investigated if plasma tau is altered in Alzheimer's disease and whether it is related to alterations in cognition, CSF biomarkers of Alzheimer's disease pathology (Aβ and tau), brain metabolism and brain atrophy. This was a study of plasma tau in prospectively followed subjects with Alzheimer's disease (n=179), subjects with MCI (n=195), and cognitive healthy controls (n=189) from the Alzheimer's Disease Neuroimaging Initiative (ADNI) and cross-sectionally studied subjects with Alzheimer's disease (n=61), MCI (n=212), and subjective cognitive decline (n=174) and controls (n=274) from the Biomarkers for Identifying Neurodegenerative Disorders Early and Reliably (BioFINDER) study at Lund University, Sweden. A total of 1284 participants were evaluated. Tested associations were between plasma tau and diagnosis, CSF biomarkers, MRI measures, 18fluorodeoxyglucose-PET, and cognition. The researchers reported that higher plasma tau was associated with Alzheimer's disease dementia, higher CSF tau, and lower CSF Aβ42, but the correlations were weak and differed between ADNI and BioFINDER. The longitudinal analysis in ADNI demonstrated significant associations between plasma tau and worse cognition, more atrophy, and more hypo-metabolism during follow-up. The researchers concluded that plasma tau partly reflected Alzheimer's disease pathology, but the overlap between normal aging and Alzheimer's disease was large, especially in subjects without dementia. They also concluded that despite

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group-level differences, these results did not support plasma tau as an Alzheimer's disease biomarker in individual people.

The authors noted that while this was the largest published study on plasma tau, there were some drawbacks. For example: some ADNI participants had plasma tau below the lower limit of quantification of the assay. Although these measurements were uncertain, they were included because excluding them would have biased the data toward higher plasma tau. Also, the researchers utilized only one plasma tau assay, but it is possible that other assays capture tau fragments that are less sensitive to peripheral degradation and more likely to reflect Alzheimer's disease pathology.

Olsson and colleagues (2020) reported the results of a systematic review and meta-analysis for 15 biomarkers in both CSF and blood to assess which of these were most altered in Alzheimer's disease. Of the eligible studies, 151 provided data on T-tau in CSF. These studies consisted of 164 cohorts with Alzheimer's disease and 153 control cohorts representing a total of 11,341 Alzheimer's disease subjects and 7086 controls. The authors found that increased levels of CSF t-tau and p-tau were strongly associated with Alzheimer's disease and MCI subjects that developed Alzheimer's disease.

Building upon the premise that blood total-tau originates primarily from peripheral, non-brain sources, Gonzalez-Ortiz and colleagues (2022) investigated if an anti-tau antibody that selectively binds brain-derived tau (BD-tau) and avoids the peripherally expressed 'big tau' isoform could be used as a biomarker to identify Alzheimer's disease -type neurodegeneration. The researchers validated their assay in five cohorts that included a total of 609 patient samples. The researchers' observations included the following:

- (1) Blood-based BD-tau demonstrated equivalent diagnostic performance to both CSF total-tau and CSF brain-derived tau in distinguishing biomarker-positive Alzheimer's disease participants from biomarker-negative controls.
- (2) Plasma-based BD-tau accurately differentiated autopsy-confirmed Alzheimer's disease from other neurodegenerative diseases with an area under the receiver operating curve (AUC) of 86.4%, while plasma neurofilament light was not significantly increased (AUC 54.3%).
- (3) Serum BD-tau distinguished Alzheimer's from other neurodegenerative disorders -- including frontotemporal lobar degeneration and atypical parkinsonian disorders -- with AUCs up to 99.6%.
- (4) Plasma/serum BD-tau correlated with neurofilament light only in Alzheimer's disease, but not in the other neurodegenerative diseases.

Researchers plan to conduct large-scale clinical validation of blood brain-derived-tau in a wide range of cohorts including individuals with diverse racial and ethnic backgrounds. Studies will incorporate older adults with no biological evidence of Alzheimer's disease as well as those at different stages of the disease. The authors also acknowledge that more research is needed to address the characteristics of this biomarker, longitudinal changes across the Alzheimer's disease continuum in both sporadic and familial Alzheimer's disease. Additionally, research is needed to verify the generalizability of the biomarker in diverse, multi-ethnic cohorts from a variety of populations.

For additional information, please see the discussion regarding the study by Nisenbaum (2023) above.

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Palmqvist and associates (2024) reported on the diagnostic accuracy of blood tests for Alzheimer's disease using plasma phosphorylated tau 217 (p-tau217) ratios and the amyloid-beta 42 to 40 ratio (APS2, the PrecivityAD2 test). A total of 1213 individuals with cognitive symptoms (subjective cognitive decline, mild cognitive impairment or dementia) underwent plasma analysis using mass spectrometry assays. The APS2 test demonstrated superior diagnostic accuracy compared to standard clinical evaluations. Specifically, APS2 achieved accuracies of 89-90% for Alzheimer pathology and 91% for clinical outcomes, with positive predictive values (PPV) of 97-99% in individuals with cognitive impairment. These findings suggest that APS2 and p-tau217 could potentially replace more invasive and expensive diagnostic methods like CSF testing and PET scans in the future. Further research is needed to evaluate the clinical impact and validate the results.

In a subsequent study (Palmqvist, 2025) researchers evaluated the performance of the Lumipulse plasma pTau217 immunoassay test in 1219 participants in secondary care and 548 in primary care setting across several sites in Italy, Spain, and Sweden. The primary outcome was AD pathology defined as abnormal CSF Aβ42:p-tau181. Researchers used the fully automated Lumipulse plasma pTau217 immunoassay test to measure p-tau217 plasma levels, comparing results to CSF markers of AD (abnormal Aβ42:p-tau181 ratio). The diagnostic performance of the Lumipulse immunoassay test across all cohorts demonstrated AUC ranging from 0.93 to 0.96. In the secondary care settings, accuracy ranged from 89% to 91%, with PPV 89–95% and negative predictive values (NPV) from 77–90%. In the primary care setting, accuracy was slightly lower at 85%, with positive and negative predictive values of 82% and 88%, respectively. Accuracy was somewhat reduced in participants 80 years of age or older (83%) but remained stable regardless of sex, APOE genotype, diabetes, kidney disease, or cognitive stage. Implementing a two-cutoff approach (defining clear positive and negative thresholds) improved overall accuracy to 92–94%, while excluding 12–17% of participants with intermediate results. Using the ratio of plasma p-tau217 to Aβ42 did not increase accuracy but reduced indeterminate outcomes to 10% or less. The authors acknowledged that the generalizability of the study results are limited due to the lack of inclusion of non-European individuals. Further validation including populations from other regions of the world are needed. Additionally, the somewhat reduced performance relative to % p-tau217 in primary care populations and older adults emphasizes the need for additional research.

In October 2025 the FDA granted 510(k) premarket notification clearance for another blood-based biomarker test, the Elecsys pTau181 test (Roche Diagnostics), to assist in the diagnosis of Alzheimer's disease (K252163). According to the FDA premarket notification summary:

The Elecsys Phospho-Tau (181P) Plasma assay result is intended to be used as an aid in the initial assessment for Alzheimer's disease and other causes of cognitive decline in adult patients aged 55 years and older, presenting with signs, symptoms, or complaints of cognitive decline. The result should be interpreted in conjunction with other clinical information.

A negative test result is consistent with a negative amyloid positron emission tomography (PET) scan result and reduced likelihood that a patient's cognitive impairment is due to amyloid pathology. These patients should be investigated for other causes of cognitive decline.

A positive test result may not be consistent with a positive amyloid PET scan result. Patients with an initial positive result should be further investigated to determine whether the amyloid pathology can be a cause of cognitive impairment (FDA Premarket Notification, Elecsys, 2025).

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The FDA premarket clearance also indicates that the Elecsys Phospho-Tau (181P) Plasma assay is not recommended for individuals with signs, symptoms, or complaints of cognitive decline, who have already been referred to a specialist. Additionally, the clearance states that Elecsys Phospho-Tau (181P) Plasma assay has not been proven effective for predicting dementia or other neurological conditions, nor for monitoring treatment responses.

The FDA clearance of the Elecsys Phospho-Tau (181P) Plasma assay was based on the results of a multicenter, prospective, non-interventional clinical study (Roche study RD006263) that evaluated 312 participants ranging from 55-80 years of age that presented with cognitive complaints or impairment of unknown cause at 8 geographically diverse enrollment sites in the U.S and Europe. The study population consisted of 40.7% males and 59.3% females, both groups averaging 69.1 years of age. Most participants were White (59%), followed by Black or African American (34%), Asian (1.6%), Middle Eastern (0.3%), and Other (5.1%). Ethnically, 66.3% were non-Hispanic or Latino, 29.5% were Hispanic or Latino, and 4.2% had missing data. Common comorbidities included cardiovascular disease (56.1%), diabetes (25.6%), depression (19.9%), kidney disease (2.2%), prior stroke (3.5%), and cancer (12.5%). Data collected from participants included cognitive assessments (Quick Dementia Rating System [QDRS], Mini-Mental State Examination [MMSE], Clinical Dementia Rating [CDR], imaging results [amyloid PET and MRI]), and questionnaires covering medical history, medications, quality of life, physical activity, and socio-demographic information. Participants were classified into three diagnostic groups: 41.0% with subjective cognitive decline (SCD), 56.1% with mild cognitive impairment (MCI), and 1.0% with mild dementia. Diagnosis was unknown for 1.9% of participants. Overall, 97.1% of the study population fell into the pre-dementia Alzheimer's disease categories (SCD and MCI).

A total of 313 participants received amyloid PET scans using FDA-approved tracers (18F-Florbetapir, 18F-Florbetaben, or 18F-Flutemetamol). Each scan was independently reviewed by three of five trained readers, blinded to all clinical data. Using majority voting, 41 scans (13.1%) were classified as amyloid positive and 271 (86.9%) as negative. Reader agreement was high, with positive concordance in 28 cases (9%) and negative concordance in 260 cases (83%). Discordant readings were rare, occurring in 24 cases total (7.7%). Only one scan had missing ratings, leaving 312 usable PET scans for analysis. On average, reader agreement was high: the Positive Percent Agreement (PPA) was 81.6%, the Negative Percent Agreement (NPA) was 97.1%, and the Total Percent Agreement (TPA) was 94.9%, indicating strong consistency among readers. Among the 41 participants with a positive PET scan, 3 (7.3%) showed false-negative Phospho-Tau (181) Plasma results. Results demonstrated that in early-stage, low-prevalence populations similar to primary care settings, Elecsys pTau181 Plasma assay effectively ruled out Alzheimer's pathology, showing a 97.9% negative predictive value (NPV).

Amyloid Beta Targeted Therapy

On June 7, 2021, the United States Food and Drug Administration (FDA) granted accelerated approval of the anti-amyloid drug aducanumab based on results of EMERGE and ENGAGE clinical trials. The two trials of 18-month duration were conducted in participants with MCI due to AD or mild Alzheimer's disease, mean age of 70 years. The ENGAGE trial demonstrated no benefit while the high-dose EMERGE trial initially also exhibited no benefit but with longer follow-up demonstrated a significant decrease in amyloid plaque on PET scans. The inclusion criteria for both of these trials required participants to have a positive amyloid PET scan and to consent to apolipoprotein E (ApoE) genotyping, as part of trial entry. Researchers conducted biomarker substudies in subgroups of participants in each trial to assess the effects of Aduhelm on brain amyloid pathology as well as CSF

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A β and tau levels; however, biomarker evaluations did not constitute defined endpoints in either of the trials and only included 30% and 35% of the participants in EMERGE and ENGAGE, respectively. Furthermore, use of CSF A β and tau levels were not used as clinical trial inclusion criteria, or for patient selection purposes. Because the cognitive deterioration associated with MCI and mild Alzheimer's disease dementia often occurs over the span of years, the 78-week follow up duration period of EMERGE and ENGAGE complicates the ability to draw conclusions regarding the effectiveness of Aduhelm for treating early Alzheimer's disease.

In April 2022, CMS announced a National Coverage Determination (NCD) that provides coverage for FDA-approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease when furnished in accordance with Section B (Coverage Criteria) (CMS, 2022).

On January 6, 2023, the FDA granted accelerated approval of another anti-amyloid drug, lecanemab-irmb (Leqembi), for the treatment of individuals diagnosed with Alzheimer's disease with mild cognitive impairment or mild dementia stage of disease. Full approval was granted on July 6, 2023 based on results of an 18-month long double-blind, placebo-controlled, parallel-group, dose-finding study of 856 subjects aged 50 to 90 years with Alzheimer's disease-related mild cognitive impairment or mild dementia stage of disease and confirmed presence of amyloid beta pathology (van Dyck, 2022). Inclusion criteria required amyloid positivity determined by either PET imaging or CSF measurement of A β 42 peptide. Subjects receiving the treatment were reported to have a change of 0.45 points on an 18-point scale in the Clinical Dementia Rating–Sum of Boxes (CDR-SB) over 18 months. A sub study of amyloid burden on PET imaging involving 698 subjects found a significant decrease in mean amyloid level from baseline to 18 months (-55.48 centiloids in the lecanemab group vs. 3.64 centiloids in the placebo group, $p < 0.001$).

A third Alzheimer's disease drug therapy, donanemab-azbt (Kisunla) was approved on July 2, 2024, for affected individuals with mild cognitive impairment or mild dementia stage of disease. The approval was based on a double-blind, placebo-controlled, parallel-group study of 1736 participants. The prescribing information includes a boxed warning for amyloid-related imaging abnormalities. The presence of amyloid beta pathology should be confirmed prior to the initiation of therapy. Monitoring within the study was done via amyloid PET imaging and plasma p-tau217 levels.

[\(Return to Position Statement\)](#)

Recommendations from Authoritative Organizations

In a collaborative position statement, the joint committee of the American Academy of Neurology (AAN), American Neurological Association (ANA), and Child Neurology Society (CNS) stated that biomarker testing in asymptomatic individuals is recommended only in a research setting, in part due to the potential harms and the absence of interventions that can favorably alter the natural history of the disease. For symptomatic individuals, the author indicated that "CSF and PET biomarkers of amyloid and tau aggregation are now also being used to diagnose symptomatic patients with atypical presentations of dementia" (Chiong, 2021).

The Alzheimer's Association supports the use of blood-based biomarker (BBM) tests for diagnosing Alzheimer's disease, but only when conducted by qualified specialists as part of a comprehensive clinical assessment of patients with cognitive impairment presenting to specialized care for memory disorders. This panel provides the following guidance for utilizing BBM tests:

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For triage purposes, a BBM test with at least 90% sensitivity and 75% specificity may help rule out Alzheimer's when results are negative, while positive results should be confirmed with additional biomarker testing, such as amyloid PET scans or cerebrospinal fluid (CSF) analysis. However, for blood-based biomarker tests to serve as a direct replacement for PET or CSF tests in confirming amyloid pathology, they must demonstrate $\geq 90\%$ sensitivity and specificity, ensuring diagnostic accuracy equivalent to established methods.

The panel alerts users of this guideline that there is significant variation in diagnostic test accuracy and many commercially available BBM tests do not meet these thresholds, especially using a single cutoff. Additionally, these tests do not serve as a substitute for comprehensive clinical evaluation by a healthcare professional and should be used only as part of a full diagnostic workup of patients with cognitive impairment presenting to specialized care settings, and with careful consideration of pretest probability of AD pathology (Palmqvist 2025).

Background/Overview

Alzheimer's disease is a progressive and ultimately fatal dementia that can be familial or idiopathic (no family history). The majority of Alzheimer's disease is late-onset, but there is also a less common early-onset form of Alzheimer's disease, which appears before the age of 65 and is associated with a rapid decline, cognitive and behavioral changes, and severe neurochemical and neuropathological changes.

Biomarkers are biological changes that can be quantified to indicate the absence or presence a disease or the risk of developing a disease. Biomarkers may be used to help researchers and medical practitioners diagnose diseases and health conditions, identify health risks in an individual, monitor responses to treatment, and see how an individual's disease or health condition changes over time. Researchers continue to explore the use of biomarkers as an accurate and conclusive means to diagnose and screen for Alzheimer's disease.

Definitions

Alzheimer's disease: A progressive neurological condition, including dementia, which primarily affects memory.

A 510(k) clearance: A process by which the FDA allows a medical device manufacturer to market a new device by demonstrating it is substantially equivalent to a legally marketed predicate (already on the market) device.

Amyloid-beta 42 (A β 42): A protein that accumulates abnormally in the brains of individuals with Alzheimer's disease; the major component of amyloid plaques in the brain.

Biomarker: A naturally occurring, measurable substance in an organism whose presence is indicative of a normal physiological state, pathological processes, or pharmacologic responses to therapy; Objective medical signs that are used to measure the presence or progress of disease, or the effects of treatment.

Frontotemporal dementia: A broad term for a group of brain disorders that primarily affect the frontal and temporal lobes of the brain.

Neurofilament light chain (NFL) protein, A biomarker associated with neurodegeneration, neuronal damage.

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Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met for testing in CSF specimen:

CPT

82233	Beta-amyloid; 1-40 (Abeta 40) [when billed as part of a ratio with Abeta 42]
82234	Beta-amyloid; 1-42 (Abeta 42)
84393	Tau, phosphorylated (eg, pTau 181, pTau 217), each [when billed as part of a ratio with Abeta 42]
84394	Tau, total (tTau) [when billed as part of a ratio with Abeta 42]
0358U	Neurology (mild cognitive impairment), analysis of β -amyloid 1-42 and 1-40, chemiluminescence enzyme immunoassay, cerebral spinal fluid, reported as positive, likely positive, or negative Lumipulse® G β Amyloid Ratio (1-42/1-40) Test, Fujirebio Diagnostics, Inc, Fujirebio Diagnostics, Inc
0445U	β -amyloid (Abeta42) and phospho tau (181P) (pTau181), electrochemiluminescent immunoassay (ECLIA), cerebral spinal fluid, ratio reported as positive or negative for amyloid pathology Elecsys® PhosphoTau (181P) CSF (pTau181) and β Amyloid (1-42) CSF II (Abeta 42) Ratio, Roche Diagnostics Operations, Inc (US owner/operator)
0459U	β -amyloid (Abeta42) and total tau (tTau), electrochemiluminescent immunoassay (ECLIA), cerebral spinal fluid, ratio reported as positive or negative for amyloid pathology Elecsys® Total Tau CSF (tTau) and β -Amyloid (1-42) CSF II (Abeta 42) Ratio, Roche Diagnostics Operations, Inc (US owner/operator)

ICD-10 Diagnosis

G30.0-G30.9	Alzheimer's disease
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When services are Investigational and Not Medically Necessary:

For the procedure and diagnosis codes listed above when criteria are not met or for all other diagnoses not listed.

When services are Investigational and Not Medically Necessary:

For the following procedure and diagnosis codes, or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

82233	Beta-amyloid; 1-40 (Abeta 40) [when specified as blood or plasma specimen or not part of a ratio]
82234	Beta-amyloid; 1-42 (Abeta 42) [when specified as blood or plasma specimen]

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83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified [when specified as amyloid beta peptide testing other than long form A β , A β 1-42, Beta-amyloid (1-42), and Abeta42]
83884	Neurofilament light chain (NfL)
84393	Tau, phosphorylated (eg, pTau 181, pTau 217), each [when specified as blood or plasma specimen or not part of a ratio]
84394	Tau, total (tTau) [when specified as blood or plasma specimen or not part of a ratio]
84999	Unlisted chemistry procedure [when specified as amyloid beta peptide testing other than long form A β , A β 1-42, Beta-amyloid (1-42), and Abeta42, or neural thread protein biochemical testing]
0547U	Neurofilament light chain (NfL), chemiluminescent enzyme immunoassay, plasma, quantitative Neurofilament Light Blood Test, Neurocode USA, Inc, Fujirebio Diagnostics, Inc

ICD-10 Diagnosis

F03.90-F03.94	Unspecified dementia, unspecified severity
F03.A0-F03.C4	Unspecified dementia, mild/moderate/severe
G30.0-G30.9	Alzheimer's disease
G31.1	Senile degeneration of brain, not elsewhere classified
R41.0	Disorientation, unspecified
R41.3	Other amnesia (memory loss NOS)
R41.81	Age-related cognitive decline

When services are also Investigational and Not Medically Necessary:

CPT

0206U	Neurology (Alzheimer disease); cell aggregation using morphometric imaging and protein kinase C-epsilon (PKCe) concentration in response to amylospheroid treatment by ELISA, cultured skin fibroblasts, each reported as positive or negative for Alzheimer disease DISCERN™, NeuroDiagnostics, NeuroDiagnostics
0207U	Neurology (Alzheimer disease); quantitative imaging of phosphorylated ERK1 and ERK2 in response to bradykinin treatment by in situ immunofluorescence, using cultured skin fibroblasts, reported as a probability index for Alzheimer disease DISCERN™, NeuroDiagnostics, NeuroDiagnostics
0412U	Beta amyloid, A β 42/40 ratio, immunoprecipitation with quantitation by liquid chromatography with tandem mass spectrometry (LC-MS/MS) and qualitative ApoE isoform-specific proteotyping, plasma combined with age, algorithm reported as presence or absence of brain amyloid pathology PrecivityAD® blood test, C2N Diagnostics LLC, C2N Diagnostics LLC
0479U	Tau, phosphorylated, pTau217 ALZpath pTau217, Neurocode USA, Inc, Quanterix/ALZpath
0503U	Neurology (Alzheimer disease), beta amyloid (A β 40, A β 42, A β 42/40 ratio) and tau-protein (pTau217, np-tau217, pTau217/np-tau217 ratio), blood, immunoprecipitation with quantitation by liquid chromatography with tandem mass spectrometry (LC-MS/MS),

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0568U	algorithm score reported as likelihood of positive or negative for amyloid plaques PrecivityAD2™, C2N Diagnostics, LLC, C2N Diagnostics, LLC Neurology (dementia), beta amyloid (Aβ40, Aβ42, Aβ42/40 ratio), tau-protein phosphorylated at residue (eg, pTau217), neurofilament light chain (NfL), and glial fibrillary acidic protein (GFAP), by ultra-high sensitivity molecule array detection, plasma, algorithm reported as positive, intermediate, or negative for Alzheimer pathology
0596U	LucentAD™ Complete, Quanterix Corporation, Quanterix Corporation Neurology (Alzheimer disease), plasma, 3 distinct isoform-specific peptides (APOE2, APOE3, and APOE4) by liquid chromatography with tandem mass spectrometry (LC-MS/MS), reported as an APOE proteotype Precivity-ApoE™, C2N Diagnostics, LLC

ICD-10 Diagnosis

All diagnoses

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Websites for Additional Information

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 Neural Thread Protein
 PrecivityAD™
 Tau Protein

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	11/06/2025	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised Rationale, Definitions, References, Websites for Additional Information, and Index sections. Updated Coding section with 01/01/2026 CPT changes to remove 0361U, 0551U deleted as of 1/1/2026; also added 0596U and revised descriptor for 0503U.
	07/01/2025	Updated Coding section with 07/01/2025 CPT changes, added 0568U.
	04/01/2025	Updated Coding section with 04/01/2025 CPT changes; added 0547U, 0551U and revised NFL codes to Inv&NMN based on diagnosis.
	11/14/2024	MPTAC review. Revised formatting and content of MN statement. Updated Description, Rationale, References and Websites for Additional Information sections. Updated Coding section with 01/01/2025 CPT changes; added 82233, 82234, 83884, 84393, 84394; removed 0346U deleted as of 01/01/2025.
Revised	10/01/2024	Updated Coding section with 10/01/2024 CPT changes, added 0479U, 0503U; also revised coding for 0445U, 0459U.
	06/28/2024	Updated Coding section with 07/01/2024 CPT changes, added 0459U.
	04/01/2024	Updated Coding section with 04/01/2024 CPT changes, added 0445U.
	11/09/2023	MPTAC review. Added MN criteria for measurement of amyloid beta. Revised INV/NMN statement. Updated Rationale, Coding, References, Websites for Additional Information and Index sections.
Reviewed	09/27/2023	Updated Coding section with 10/01/2023 CPT changes; added 0412U.
	02/16/2023	MPTAC review. Updated Description/Scope, Rationale, References, Websites for Additional Information sections.
	12/28/2022	Updated Coding section with 01/01/2023 CPT changes; add 0358U and 0361U.
	09/28/2022	Updated Coding section with 10/01/2022 CPT changes to add 0346U, and 10/01/2022 ICD-10-CM changes to add F03.94 and F03.A0-F03.C4.
New	02/17/2022	MPTAC review. Moved content related to biomarker testing for AD from GENE.00003 “Biochemical Markers for the Diagnosis and Screening of Alzheimer’s Disease” to this document, including CPT codes 83520, 84999, 0206U and 0207U.

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