Medical Policy

Subject:	Testing for Biochemical Markers for Alzheimer's Disease		
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Description/Scope

This document addresses the use of testing for biochemical markers (for example, tau protein, AB-42, neural thread protein) as a diagnostic or screening technique for 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

Investigational and Not Medically Necessary:

Measurements of biochemical markers (including but not limited to tau protein, AB-42, neural thread protein) is considered **investigational and not medically necessary** as a diagnostic technique for individuals with symptoms suggestive of Alzheimer's disease.

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

Diagnosis of Alzheimer's disease (AD)
AD is an age-related disease caused by unrelenting neurodegeneration and brain atrophy. Behaviorally, AD is characterized by progressive memory loss and cognitive decline. Pathologically, AD is characterized by local accumulations of amyloid β (Aβ) peptide and neurofibrillary tangles (NFTs) comprised of tau protein in the brain. At present, a definitive diagnosis of AD requires postmortem verification of Aβ deposits (plaques) and NFTs in the brain. In current clinical practice, a diagnosis of AD 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 AD criteria is not perfect. Diagnosis of AD 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 AD 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 AD 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 National Institute on Aging and Alzheimer's Association (NIA-AA) published an updated biological definition of AD 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 (Aβdeposition, 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) 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).

Biomarkers for AD
Fluid biomarkers (found in the cerebrospinal fluid [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 Aβ42, 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 AD. 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).

Amyloid Beta (Aβ) Peptide
Aβ 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 Aβ are and by what mechanism Aβ causes dementia

Aβ 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 Aß42 peptide, which may be represented by a low ratio of Aß42 to Aß40 levels, or a low ratio of Aß42 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 AD 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 AD. A total of 21 MRI studies and 14 CSF studies were included in the analysis. The effect sizes of Aβ42, 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 AD 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 AD. 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 Aβ42, tau, phosphorylated tau at threonine 181 (ptau181), tau/Aβ42, and ptau181/Aβ42 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 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 AD 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/Aβ42 and ptau181/Aβ42 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 Aβ42, t-tau, and p-tau in the discrimination between AD 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/Aβ42 ratio demonstrated the best diagnostic performance. No statistically significant effects of the confounders were detected. Nonetheless, the investigators found the p-tau/Aβ42 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/Aβ42 ratio for more cognitively impaired individuals (low MMSE scores). The researchers concluded that p-tau/Aβ42 ratio has potential for being implemented in the clinical routine for the differential diagnosis between AD 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 Aβ as a biomarker of Alzheimer’s disease:

(1) Amyloid is associated with normal physiologic processes. Normal functions of Aβ include disease prevention by protecting against oxidative stress and regulating cholesterol transport and anti-microbial activity. Additionally, Aβ 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).

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 AD.

Zhang et al (2014) conducted a systematic review and meta-analysis of urinary AD-associated neural thread protein (NTP) for diagnosing AD in individuals with suspected AD. Nine studies met the inclusion criteria (n=841 individuals with probable or possible AD; 37 individuals with MCI, 992 with non-AD 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 AD, 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 AD. 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 AD compared with control subjects, and the increase in FTD subjects is higher than in late onset AD.

In a meta-analysis, Olsson and colleagues (2016) found that NF-L has a large effect size for differentiating individuals with AD 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 AD and MCI groups and concluded that CSF NF-L could be used as a marker for AD progression. However, elevated CSF levels of NF-L are also found in other neurodegenerative diseases, such 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 AD from other neurological disorders.

Skin Fibroblast
Researchers are also exploring the use of skin fibroblast testing as a means to detect and differentiate AD 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 AD. 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 AD) are needed in order to assess the clinical utility of the test.

Tau Protein
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, AD, 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 AD 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.

Mattsson and colleagues (2016) investigated if plasma tau is altered in AD and whether it is related to alterations in cognition, CSF biomarkers of AD pathology (Aβ and tau), brain metabolism and brain atrophy. This was a study of plasma tau in prospectively followed subjects with AD (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 AD (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 AD 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 AD pathology, but the overlap between normal aging and AD was large, especially in subjects without dementia. They also concluded that despite group-level differences, these results did not support plasma tau as an AD 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 AD 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 AD and 153 control cohorts representing a total of 11,341 AD subjects and 7086 controls. The authors found that increased levels of CSF t-tau and p-tau were strongly associated with AD and MCI subjects that developed AD.

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 AD-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.

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 AD, 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 Aβ 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 Aβ 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 AD 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 AD.

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 AD when furnished in accordance with Section B (Coverage Criteria) (CMS, 2022).

Recommendations from Authoritative Organizations

In a collaborative position statement, the joint committee of the American Academy of Neurology, American Neurological Association, and Child Neurology Society 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).

Summary
There are inadequate data regarding the role of biochemical testing in asymptomatic individuals or whether test results might alter the medical management, treatment, or clinical outcomes in individuals with AD. With regard to symptomatic individuals, there is inadequate data to suggest that the addition of biochemical markers improves the accuracy of a clinical diagnosis of AD. The majority of available studies focus on those with probable AD, for whom the clinical diagnosis has a sensitivity of 85%. Regarding Aβ plaque targeting therapy (eg, aducanumab), there are inadequate data on the serial use of these tests to determine if there are changes in biomarker results that correlate with clinical cognitive and functional status and/or Aβ imaging to inform continuation of Aβ plaque targeting therapy. Additionally, there are inadequate data to suggest that the use of the above tests would change clinical management in terms of either altering the diagnostic work up or therapy, or informing appropriateness for therapy.

Background/Overview

AD is a progressive and ultimately fatal dementia that can be familial or idiopathic (no family history). The majority of AD is late-onset, but there is also a less common early-onset form of AD, 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 AD.

Definitions

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

Amyloid-beta 42 (Aβ42): A protein that accumulates abnormally in the brains of individuals with AD; 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.

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 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

83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified [when specified as tau protein, amyloid beta peptide testing]
84999	Unlisted chemistry procedure [when specified as tau protein, amyloid beta peptide or neural thread protein biochemical testing]

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
0346U	Beta amyloid, Aβ40 and Aβ42 by liquid chromatography with tandem mass spectrometry (LC-MS/MS), ratio, plasma QUEST AD-Detect™, Beta-Amyloid 42/40 Ratio, Plasma, Quest Diagnostics

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 βAmyloid Ratio (1-42/1-40) Test, Fujirebio Diagnostics, Inc, Fujirebio Diagnostics, Inc
0361U	Neurofilament light chain, digital immunoassay, plasma, quantitative Neurofilament Light Chain (NfL), Mayo Clinic, Mayo Clinic
0412U	Beta amyloid, Aβ42/40 ratio, immunoprecipitation with quantitation by liquid chromatography with tandem mass spectrometry (LC-MS/MS) and qualitative ApoE isoformspecific proteotyping, plasma combined with age, algorithm reported as presence or absence of brain amyloid pathology PrecivityAD® blood test, C2N Diagnostics LLC, C2N Diagnostics LLC

ICD-10 Diagnosis

All diagnoses

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ADmark® Alzheimer's Evaluation
Alzheimer's Disease
ApoE
Apolipoprotein E
C_2N Diagnostics
Discern™
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
	09/27/2023	Updated Coding section with 10/01/2023 CPT changes; added 0412U.
Reviewed	02/16/2023	Medical Policy & Technology Assessment Committee (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.