Geisinger Health Plan Policies and Procedure Manual

Policy: MP350

Section: Medical Benefit Policy

Subject: Genetic and Biochemical Testing for Alzheimer's Disease and Dementia

Applicable line of business:

Commercial	**x**	**Medicaid**	**x**
Medicare	**x**	**ACA**	**x**
CHIP	**x**		

I. Policy: Genetic and Biochemical Testing for Alzheimer's Disease and Dementia

II. Purpose/Objective:

To provide a policy of coverage regarding Genetic and Biochemical Testing for Alzheimer's Disease and Dementia

III. Responsibility:

A. Medical Directors
B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

Commercial

Geisinger Health Plan may refer collectively to health care coverage sponsors Geisinger Health Plan, Geisinger Quality Options, Inc., and Geisinger Indemnity Insurance Company, unless otherwise noted. Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicare

Geisinger Gold Medicare Advantage HMO, PPO, and HMO D-SNP plans are offered by Geisinger Health Plan/Geisinger Indemnity Insurance Company, health plans with a Medicare contract. Continued enrollment in Geisinger Gold depends on contract renewal. Geisinger Health Plan/Geisinger Indemnity Insurance Company are part of Geisinger, an integrated health care delivery and coverage organization.

CHIP

Geisinger Health Plan Kids (GHP Kids) is a Children's Health Insurance Program (CHIP) offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

Medicaid

Geisinger Health Plan Family (GHP Family) is a Medical Assistance (Medicaid) insurance program offered by Geisinger Health Plan in conjunction with the Pennsylvania Department of Human Services (DHS). Geisinger Health Plan is part of Geisinger, an integrated health care delivery and coverage organization.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

DESCRIPTION:
Alzheimer disease is the most common cause of dementia. Alzheimer disease is a progressive, irreversible neurodegenerative disease. Individuals are typically classified into early-onset and late-onset disease using the age of 65 years as a cutoff. Genetic testing and biomarker testing has been proposed as a means to identifying a definitive diagnosis, improving understanding for the family, and allowing at-risk relatives to have predictive testing.

Genetic testing in the setting of neurological disorders lead to management changes primarily affecting the following areas of management: drug selection, drug repurposing, clinical trial eligibility, screening for non-neurologic comorbidities, and prognosis.

Studies of patients with early-onset Alzheimer's disease, both familial and apparently sporadic, have reported genetic testing yields of 5–13% when analyzing APP, PSEN1, and PSEN2. The clinical utility beyond familial risk remains unclear, and this testing is still not widely utilized. However, APOE genotyping has recently been used for dose stratification in experimental and emerging anti-amyloid therapeutics and may impact prescribing decisions for lecanemab and other emerging amyloid-targeting agents.

Frontotemporal dementia (FTD) is an important cause of young-onset and non-autosomal dominant dementia. Three genes account for the majority of genetic FTD: MAPT, GRN, and C9orf72, though many other genes have been implicated. In those with FTD-ALS and family history of either condition, up to 88% have a C9orf72 pathogenic RE. Variants in GRN account for about 5% of all FTD and 20% of FTD with positive family history.

INDICATIONS:
Germline testing via panel sequencing as a first line test is covered and considered medically necessary in the in members meeting the following clinical criteria:

1.Diagnosis of Amyotrophic Lateral Sclerosis (ALS) at any age, regardless of family history AND is considering therapy with Tofersen
2. Diagnosis of frontotemporal dementia at any age, regardless of family history, when necessary to aid in establishing a diagnosis.

Genoptying of APOE is covered and considered medically necessary ONLY in members meeting the following clinical criteria:

1. Clinical diagnosis of Alzheimer's disease AND
2. Required for eligibility to participate in clinical trial for anti-amyloid therapeutics

Genetic testing for amyloid precursor protein (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2) for members with mild cognitive impairment or mild Alzheimer's D dementia who are less than 50 years of age as a companion diagnostic test and are being considered for aducanumab (Aduhelm) or lecanemab-irmb (Leqembi) therapy. **81406**

Cerebrospinal fluid testing for measurement of phosphorylated tau (P-tau) protein and long form amyloid beta (also referred to as Aβ, Aβ1-42, Beta-amyloid [1-42], and Abeta42) is considered medically necessary in individuals when AD is suspected and for whom treatment with amyloid beta targeting therapy is being considered. **0346U, 0358U, 0445U, 0459U**

EXCLUSIONS:
The Plan considers testing of genetic markers APOE, TREM2, APP, PSEN1, and/or PSEN2 for the diagnosis of Alzheimer's disease not meeting the criteria listed above to be **unproven** and therefore **NOT COVERED** as a diagnostic technique for individuals in:

- symptoms suggestive of Alzheimer's disease/ early-onset Alzheimer's disease(EOAD), or
- asymptomatic individuals with a family history of Alzheimer's disease/ early onset Alzheimer's disease.

There is insufficient evidence in the peer-reviewed medical literature to support APOE genotyping OR panel testing for Alzheimer disease-related gene variants. There is not sufficient data to support that this testing improves health outcomes or providers meaningful therapeutic opportunities for people diagnosed with Alzheimer's disease, dementia, or mild cognitive impairment unless otherwise specified in this policy.

The Plan considers measurements of serum, urinary, CSF or skin fibroblast biochemical markers (including but not limited to tau protein, neural thread protein) to be **unproven** and therefore **NOT COVERED** as a diagnostic technique for individuals with symptoms suggestive of Alzheimer's disease. There is insufficient evidence in the peer-reviewed medical literature to support testing for Alzheimer disease-related biomarkers improves health outcomes for people diagnosed with Alzheimer's disease, dementia, or mild cognitive impairment.
0206U, 0207U

The Plan considers genetic testing or measurements of biochemical markers as a screening technique in asymptomatic individuals with or without a family history of Alzheimer's disease to be **unproven** and therefore **NOT COVERED.** There is insufficient evidence in the peer-reviewed medical literature to support testing for Alzheimer disease-related biomarkers improves health outcomes for people diagnosed with Alzheimer's disease, dementia, or mild cognitive impairment.
0289U, 0412U

Medicaid Business Segment:
Any requests for services, that do not meet criteria set in the PARP, may be evaluated on a case by case basis.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

CODING ASSOCIATED WITH: Genetic and Biochemical Testing for Alzheimer's Disease and Dementia
The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov ***or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements.***

81401 Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) [when specified as the following]:

- APOE (apolipoprotein E) (eg, hyperlipoproteinemia type III, cardiovascular disease, Alzheimer disease), common variants (eg, *2, *3, *4)

81405 Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis) [when specified as the following]:

- PSEN1 (presenilin 1) (eg, Alzheimer disease), full gene sequence

81406 Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) [when specified as the following]:

- APP (amyloid beta [A4] precursor protein) (eg, Alzheimer disease), full gene sequence
- PSEN2 (presenilin 2 [Alzheimer disease 4]) (eg, Alzheimer disease), full gene sequence

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]
82233 Beta-amyloid; 1-40 (Abeta 40)
82234 Beta-amyloid; 1-42 (Abeta 42)
84393 Tau, phosphorylated (eg, pTau 181, pTau 217), each
84394 Tau, total (tTau)

84999 Unlisted chemistry procedure [when specified as tau protein, amyloid beta peptide or neural thread protein biochemical testing]

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}*
0289U Neurology (Alzheimer disease), mRNA, gene expression profiling by RNA sequencing of 24 genes, whole blood, algorithm reported as predictive risk score { *MindX Blood Test™* }
0346U Beta amyloid, Aβ40 and Aβ42 by liquid chromatography with tandem mass spectrometry (LC-hyphenMS/MS), ratio, plasma
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-Amyloid Ratio (1-42/1-40) Test}*
S3852 DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease
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,}*
0412U Beta amyloid, Aβ42/40 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}*
0445U B-amyloid (Abeta42) and phospho tau (181P) (pTau181), electrochemiluminescent immunoassay (ECLIA), cerebral spinal fluid, ratio reported as positive or negative for amyloid pathology
0459U β-amyloid (Abeta42) and total tau (tTau), electrochemiluminescent immunoassay (ECLIA), cerebral spinal fluid, ratio reported as positive or negative for amyloid pathology
0479U Tau, phosphorylated, pTau217
0503U Neurology (Alzheimer disease), beta amyloid (AB40, AB42, AB42/40 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), algorithm score reported as likelihood of positive or negative for amyloid plaques

ICD-10 Diagnosis

- F03.90-F03.91 Unspecified dementia
- 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

LINE OF BUSINESS:
Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

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This policy will be revised as necessary and reviewed no less than annually**.**

Devised: 11/21

Revised: 12/22 (clarified exclusion language); 12/23 (expand description, add indications); 12/24 (Add coverage)

Reviewed:

CMS UM Oversight Committee Approval: 12/23, 02/25

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Coverage for experimental or investigational treatments, services and procedures is specifically excluded under the member's certificate with Geisinger Health Plan. Unproven services outside of an approved clinical trial are also specifically excluded under the member's certificate with Geisinger Health Plan. This policy does not expand coverage to services or items specifically excluded from coverage in the member's certificate with Geisinger Health Plan. Additional information can be found in MP015 Experimental, Investigational or Unproven Services.

Prior authorization and/or pre-certification requirements for services or items may apply. Pre-certification lists may be found in the member's contract specific benefit document. Prior authorization requirements can be found at https://www.geisinger.org/health-plan/providers/ghp-clinical-policies