Geisinger

# Geisinger Health Plan Policies and Procedure Manual

**Policy: MP324**

**Section: Medical Benefit Policy**

**Subject: Genetic Testing for Non-Cancer Heritable Disease Carrier Status**

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**I. Policy:** Genetic Testing for Non-Cancer Heritable Disease Carrier Status

**II. Purpose/Objective:**

To provide a policy of coverage regarding Genetic Testing for Non-Cancer Heritable Disease Carrier Status

**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.

**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**

Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

(i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
(ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.
(iii) The service or benefit 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:** Genetic testing for the purposes of carrier status screening is performed to identify genetic risk that may impact reproductive decision-making. Individuals identified as being "carriers" are typically not affected by the condition but have an increased risk of having a child with a genetic condition. Genetic testing for carrier screening may be available for autosomal recessive genetic conditions, X chromosome-linked conditions, and certain other chromosomal abnormalities.

**GENERAL INDICATIONS**:
Genetic testing for inheritable diseases, offered in a setting with appropriately trained health care professionals who can provide pre- and post-test counseling, and performed by a qualified laboratory, is considered to be medically necessary when:

- Based on family history, pedigree analysis, risk factors, and / or signs or symptoms, there is a reasonable expectation that a genetically inherited condition exists; and
- The testing methodology is considered a proven method for the identification of a genetically-linked disease; and
- The test results will guide disease treatment decisions or prevention strategies**.**

**INDICATIONS:**

## Tay-Sachs disease:

Genetic testing of the HEXA gene may be considered medically necessary when one or more of the following criteria are met:

- Symptomatic member with clinical features suggestive of TSD or variants and abnormal HEX A or HEX B enzymatic testing, but after conventional studies a definitive diagnosis remains uncertain.
- To detect a pseudodeficiency allele in an asymptomatic member with abnormal HEX A or HEX B enzymatic testing
- Member with a first or second-degree relative with a confirmed TSD or variant
- Members with reproductive partners with chronic or adult-onset HEXA or HEXB deficiency with the intention to reproduce
- Members who are pregnant or whose reproductive partner is pregnant or planning a pregnancy when one or more of the following criteria apply:
    - At least one of the couple is of Ashkenazi Jewish origin
    - At least one of the couple is of Cajun or Acadian origin
    - At least one of the couple is of French-Canadian origin
    - At least one of the couple is affected with or is a known carrier of Tay-Sachs disease
    - There is a positive family history of Tay-Sachs disease

## Cystic Fibrosis

Genetic testing of the CFTR gene may be considered medically necessary when one or more of the following criteria are met:

- Member with a negative sweat test who exhibit symptoms of CF
- Male members with congenital bilateral absence of the vas deferens
- Infant members with symptoms consistent with CF who are too young to accomplish a sweat chloride test
- Members who are pregnant or whose reproductive partner is pregnant or are planning a pregnancy

## Hemoglobinopathies (Sickle Cell Anemia, Alpha/beta thalassemia)

Genetic testing may be considered medically necessary when one or more of the following criteria are met:

- Family history of hemoglobinopathy with known mutation
- Hemoglobinopathy is suspected after complete blood count and hemoglobin analysis and the member has origins in a high-risk group (eg, African American, African, Asian, Middle eastern, Carribbean, or Mediterranean **decent)**

## Ashkenazi Jewish Carrier Screening Panel

(Canavan Disease, Fabry Disease, Gaucher Disease, Bloom syndrome, Maple Syrup Urine disease, Cystic Fibrosis, Glycogen Storage disease type 1, Familial Dysautonomia, Franconi Anemia, Mucolipidosis IV, Friederich Ataxia, Niemann-Pick Disease, Tay-Sachs Disease, Tuberous Sclerosis)

Panel testing may be considered medically necessary when the following criteria are met:

- The member is planning a pregnancy or currently pregnant; and

- At least one partner of a couple is of Ashkenazi Jewish heritage (NOTE: If only one partner of a couple is Ashkenazi Jewish, testing should start in that person when possible.)

**Single Ashkenazi Jewish Genetic Diseases Carrier Screening Tests**

Single gene carrier screening may be considered medically necessary when:

- The member has a family history of one of the conditions listed in the panel; OR
- The member's partner is a known carrier or affected with any of the conditions listed in the panel

## Duchenne muscular dystrophy/Becker muscular dystrophy

Genetic testing may be considered medically necessary when one or more of the following criteria are met:

- In a male member with signs and symptoms of a dystrophinopathy in order to confirm the diagnosis and direct treatment.
- For at-risk female member relatives defined as first- and second-degree female relatives and include the proband's mother, female siblings of the proband, female offspring of the proband, the proband's maternal grandmother, maternal aunts and their offspring.

## Fragile X syndrome

Genetic testing may be considered medically necessary when one or more of the following criteria are met:

- Members of either sex with intellectual disability, developmental delay or autism spectrum disorder
- Members seeking reproductive counseling who have a family history of fragile X syndrome or a family history of undiagnosed intellectual disability
- Prenatal testing of fetuses in pregnant members who are known carriers
- Affected members who have had a positive cytogenetic fragile X test result who are seeking further counseling related to the risk of carrier status
- Members with unexplained ovarian insufficiency or failure or an elevated follicle-stimulating hormone level before the age of 40

## Neurofibromatosis type 1 and 2

Genetic testing for neurofibromatosis type 1 may be considered medically necessary when the diagnosis is clinically suspected due to signs of disease, but a definitive diagnosis cannot be made without genetic testing.
The member must meet one of the following:

- A first-, second- or third-degree relative has a known NF mutation; or
- A first-, second- or third-degree relative has been diagnosed with neurofibromatosis but whose genetic status is unavailable

Or

The member meets at least two of the following criteria:

- six or more light brown spots on the skin ("cafe-au-lait" spots), measuring more than 5 mm in diameter in children or more than 15 mm across in adolescents and adults;
- two or more neurofibromas, or one plexiform neurofibroma (a neurofibroma that involves many nerves);
- freckling in the area of the armpit or the groin;
- two or more growths on the iris of the eye (Lisch nodules or iris hamartomas);
- a tumor on the optic nerve (optic nerve glioma);
- abnormal development of the spine (scoliosis), the temple (sphenoid) bone of the skull or the tibia;
- a parent, sibling or child with NF1

Genetic testing for neurofibromatosis type 2 is medically necessary when the diagnosis is clinically suspected due to signs of disease, but a definitive diagnosis cannot be made without genetic testing. The member must meet one of the following criteria:

- Members with a first degree relative with NF2 (i.e., affected parent, sibling or offspring)
- Multiple spinal tumors (schwannomas, meningiomas)
- Cutaneous schwannomas
- Sporadic vestibular schwannoma less than 30 years of age, or spinal tumor or meningioma less than 20 years of age
- Unilateral vestibular schwannoma in those less than 20 years of age

## Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL);

Genetic testing to confirm the diagnosis of CADASIL syndrome may be considered medically necessary when:

- Clinical signs, symptoms and imaging results indicate the pre-test probability of CADASIL is moderate to high (total score of 14)*; or
- The diagnosis of CADASIL is inconclusive following alternate methods of testing, including MRI and skin biopsy

| ***Features*** | ***Points*** |
|---|---|
| *Migraine* | *1* |
| *Migraine with aura* | *3* |
| *Psychiatric disturbance* | *1* |
| *Transient ischemic attack/stroke* | *1 (2 if <50yo)* |
| *Subcortical infarcts* | *2* |
| *Cognitive decline* | *3* |
| *LE (leukoencephalopathy)* | *3* |
| *LE extended to temporal pole* | *1* |
| *LE extended to external capsule* | *5* |

Pooled Frequency of Clinical and Radiologic Features (Pescini et al., 2012)

## Charcot-Marie-Tooth:

Genetic Testing for Charcot-Marie-Tooth (CMT) disease is medically necessary when the member has clinical features of CMT and a definitive diagnosis remains uncertain after history, physical examination, genetic counseling and completion of nerve conduction studies and/or electromyography.

- If nerve conduction studies of ulnar/median nerve indicate demyelinating neuropathy (velocity <38 m/s), test for the most commonly identified CMT subtype: CMT1A (PMP22 duplication).
- If the result is negative, multi-gene panel testing of genes GJB1 (CMTX1), MPZ (CMT1B), MFN2 (CMT2A2), LITAF (CMT1C), EGR2 (CMT1D), PMP22 sequencing (CMT1E), GARS (CMT2D), NEFL (CMT2E/1F), GDAP1 (CMT2H/2K) and SH3TC2 (CMT4C).
- If nerve conduction studies of ulnar/median nerve indicate axonal neuropathy (velocity >38 m/s), multi-gene panel testing of genes GJB1 (CMTX1), MPZ (CMT1B), LITAF (CMT1C), EGR2 (CMT1D), PMP22 sequencing (CMT1E), MFN2 (CMT2A2), GARS CMT2D), NEFL (CMT2E/1F), GDAP1 (CMT2H/2K) and SH3TC2 (CMT4C)

## Alpha-1-antitrypsin deficiency:

Genetic testing for alpha-1 antitrypsin deficiency may be considered medically necessary when the member meets either criteria 1 or 2, and 3:

1. alpha-1 antitrypsin deficiency is suspected in member presenting with clinical factors such as:
   - Early-onset emphysema (45 years or younger); or
   - Emphysema without history of risk factors (smoking, occupational exposure, etc.); or
   - Emphysema with prominent basilar hyperlucency; or
   - Bronchiectasis of unknown etiology; or
   - liver disease of unknown etiology; or
   - Anti-proteinase 3-positive vasculitis; or
   - Necrotizing panniculitis

   Or;

2. Member is at risk due to a first-degree relative with alpha-1 antitrypsin deficiency

   AND

3. Member has a serum alpha-1 antitrypsin level in the range of severe deficiency

| **Phenotype** | **AAT Blood Level** |
|---|---|
| MM | 20–53 µM \| 150–350 Mg/dL |
| MZ | 12–28 µM \| 90–210 Mg/dL |
| SS | 13–27 µM \| 100–210 Mg/dL |
| SZ | 10–16 µM \| 75–120 Mg/dL |
| ZZ | 2.5–7 µM \| 20–45 Mg/dL |
| NULLNULL | 0 µM \| 0 Mg/dL |

## Neimann – Pick Disease:

Genetic testing for SMPD1 and NPC1 gene may be considered medically necessary in either of the following populations:

- Symptomatic members with clinical features suggestive of NPD and abnormal biochemical testing, but a definitive diagnosis remains uncertain after completion of conventional studies.
- First- or second-degree relative members with the capacity and desire to reproduce once the mutations have been identified in the proband.

**Primary Dystonia Type 1**:
Genetic testing for DYT1 gene sequence variants may be considered medically necessary in either of the following populations:
- Members with documented onset of primary dystonia at or before age 30 years
- Members with documented onset of primary dystonia at age 30 years or later with a relative who developed dystonia at 30 years or younger

**Prader-Willi Syndrome**
Genetic testing may be considered medically necessary in symptomatic pediatric members for diagnosis of Prader-Willi syndrome or in symptomatic adult members when all of the following criteria are met:
- Documented history of hypotonia and poor suck
- Global developmental delay

**Angelman Syndrome**
Genetic testing to confirm the absence of maternally expressed gene(s) located on chromosome 15 within bands q11.2 to q13 may be considered medically necessary in symptomatic pediatric members for diagnosis of Angelman Syndrome or in symptomatic adult members when all of the following criteria are met:
- Documentation of absence of major birth defects with normal head circumference
- Evidence of developmental delay by age 6 to 12 months
- Delayed progression and attainment of developmental milestones without overall loss of skills
- Normal metabolic, hematologic and chemical laboratory studies
- Normal brain structure as evidenced by CT or MRI
- Absent or severely impaired speech
- Balance disorder with ataxia or tremulous movement of limbs
- Documentation of behavioral characteristics such as inappropriate happy demeanor, frequent and inappropriate laughter or smiling, short attention span, excitability, hand-flapping, or hypermotor activity

**Gaucher disease**
Genetic testing may be considered medically necessary as follows:

Diagnostic Testing for Symptomatic members:
- Glucosylceramidase enzyme activity in peripheral blood leukocytes is 0 - 15% of normal activity, and
    - bone changes including osteopenia, focal lytic or sclerotic bone lesions or osteonecrosis; or
    - Liver/spleen enlargement and anemia or thrombocytopenia; or
    - Primary neurologic disease including one or more of the following:
        - cognitive impairment,
        - pyramidal signs (e.g., spasticity, hyperactive reflexes)
        - bulbar signs (e.g., dysphagia, dysarthria, dysphonia, etc)
        - eye movement disorders,
        - seizures

Diagnostic Testing for members who are Asymptomatic Carriers:
- a mutation is detected by targeted mutation analysis, and
- Glucosylceramidase enzyme activity in peripheral blood leukocytes is 0-15% of normal activity,

Testing for Members with Family History or Partners of Carriers:
- 1st, 2nd, or 3rd degree biologic relative with confirmed Gaucher diagnosis, or
- the member has the intention to reproduce with a partner who is monoallelic or biallelic for GBA mutation

**Huntington's disease**
Genetic testing related to Huntington's disease may be considered medically necessary for:
a) Confirmatory testing in members with clear symptoms and positive family history; or
b) Diagnostic testing in members with no family history of the disease, but who exhibit symptoms consistent with Huntington's disease such as:
    - Involuntary jerking movements

- Impaired gait, posture and balance
- Dystonia
- Cognitive disorders

**Rett syndrome:**

Genetic testing may be considered medically necessary when:

- The member meets the clinical diagnostic criteria for Rett syndrome; and
- Gene testing is necessary to confirm diagnosis due to clinical uncertainty

**Peutz-Jeghers Syndrome:**

Genetic testing may be considered medically necessary when:

There is a known family history of STK11 (LKB1) gene mutation; or
The member has a clinical diagnosis of PJS based on **at least TWO of the following** features:

- At least TWO PJS-type hamartomatous polyps of the gastrointestinal tract; or
- Mucocutaneous hyperpigmentation of the mouth, lips, nose, eyes, genitalia, or fingers; or
- A family history of PJS.

**Noonan Syndrome:**

Genetic testing may be considered medically necessary when:
There is a known family history of TPN11, SOS1, RADF1 and KRAS gene mutation; or
The member is suspected of Noonan syndrome due to a combination of **any** of the following:

- A characteristic facial appearance.
- Short stature.
- Heart defect present at birth (congenital heart defect).
- A broad or webbed neck.
- Minor eye problems such as strabismus in up to 95 percent of individuals.
- Bleeding problems such as a history of abnormal bleeding or bruising.
- An unusual chest shape with widely-spaced and low set nipples.
- Developmental delay of varying degrees, but usually mild.
- Undescended testes

**Spinal Muscular Atrophy:**

Genetic testing may be considered medically necessary for the indications of:

Diagnostic testing in members with:

- hypotonia and weakness (symmetrical but proximal greater than distal); and
- abnormal deep tendon reflexes (severely decreased or absent)

Carrier testing:

- Members with a family history of SMA or disease suspicious for SMA; or
- Member with a blood relative who is a known carrier or diagnosed with SMA and has a known SMA mutation; or
- Member who is pregnant or is planning a pregnancy
- Members whose reproductive partner has a known carrier status

Prenatal testing in members who are pregnant and both partners are known carriers

**Marfan Syndrome Loeys-Dietz Syndrome, Ehlers-Danlos Syndrome**

Genetic testing may be considered medically necessary when:

- There is a known family pathogenic variant; **or**
- The member presents with signs and symptoms consistent with Marfan syndrome Loeys-Dietz Syndrome, or Ehlers-Danlos Syndrome but a definitive diagnosis cannot be established.

  And
- Targeted mutation testing limited to 1 or more of the following is planned: FBN1, MYH11, ACTA2, COL3A1, SLC2A10, SMAD3, MYLK, TGFBR1, and TGFBR2

**EXCLUSIONS:**

Direct-to-consumer genetic testing, or “home testing” kits, are NOT COVERED.

Genetic testing for the diagnosis or risk assessment of Alzheimer's disease is considered experimental, investigational or unproven and therefore NOT COVERED. There is insufficient published peer reviewed medical literature to support the efficacy of genetic testing in Alzheimer's disease.

## Whole Genome Sequencing (WGS) - REQUIRES PRIOR AUTHORIZATION BY A PLAN MEDICAL DIRECTOR OR DESIGNEE

Whole Genome Sequencing (WGS) is an evolving technology, but currently has limited application outside of a research setting and is generally considered to be unproven for the purposes of screening and evaluating genetic disorders. There is currently insufficient evidence to support the efficacy is using WGS for routine evaluations. Consideration of requests for WGS will be done on a "per-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 Testing for Non-Cancer Heritable Disease Carrier Status**
***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.***

81161 DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81200 ASPA (aspartoacylase) (e.g., Canavan disease) gene analysis, common variants (e.g., E285A, Y231X)
81205 BCKDHB (branched-chain keto acid dehydrongenase E1, beta polypeptide) (e.g., Maple syrup urine disease) gene analysis, common variants (E.g., R183P, G278S, E422X)
81209 BLM (Bloom syndrome, recq helicase-like) (e.g., Bloom syndrome) gene analysis, 2281DEL6INS7 Variant
81220 CFTR Targeted Mutation Analysis
81242 FANCC (Fanconi anemia, complementation group
81243 FMR1 (fragile X mental retardation 1 (e.g., fragile X mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
81244 FMR1 (fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; characterization of alleles (e.g., expended size and methylation status)
81250 G6PC (glucose-6-phosphatase, catalytic subunit) (e.g., glycogen storage disease, type 1A, Von Gierke disease) gene analysis, common variants (e.g., R83C, Q347X)
81251 GBA (glucosidase, beta, acid) (e.g., Gaucher disease) gene analysis, common variants (e.g., N370S, 84GG, L444P, IVS2+1G>A)
81255 HEXA (hexosaminidase A [alpha polypeptide]) (e.g., Tay-Sachs disease) gene analysis, common variants (e.g., 1278INSTATC, 1421+1G>C, G269S)
81256 HFE (hemochromatosis) (e.g., hereditary hemochromatosis) gene analysis, common variants (e.g.,C282Y, H63D)
81257 HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (e.g., southeast Asian, Thai, Filipino, Mediterranean, alpha 3.7, alpha 4.2, alpha 20.5, and constant spring)
81260 IKBKAP 9inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (e.g., familial dysautonomia) gene analysis, common variants (e.g., 2507+6T>C, R696P)
81290 MCOLN1 (mucolipin 1) (e.g. mucolipidosis, type IV) gene analysis, common variants (e.g., IVS3 2A>G, del 6.4kb)
81302 MECP2 (methyl CPG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis
81303 MECP2 (methyl CPG binding protein 2) (e.g., Rett syndrome) gene analysis; known familial variant
81304 MECP2 (methyl CPG binding protein 2) (e.g., Rett syndrome) gene analysis; duplication/deletion variants
81324 PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
81325 PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis
81326 PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability

to pressure palsies) gene analysis; known familial variant
81329 Smn1 (Survival Of Motor Neuron 1, Telomeric) (Eg, Spinal Muscular Atrophy)
81330 SMPD1 (sphingomyelin phosphodiesterase 1, acid lysosomal) (e.g., Neimann-Pick disease, type A) gene analysis; common variants (e.g., R496L, L302P, FSP330)
81331 SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome), methylation analysis
81332 SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1) (e.g., alpha-1-antitrypsin deficiency), gene analysis, common variants (e.g., *S and *Z)
81400 Molecular pathology procedure Level 1 (SMN1 exon7 deletion
81401 Molecular pathology procedure Level 2 (HTT Expansion Analysis; SMN1/SMN2)
81402 Chromosome 15 Uniparental Disomy
81403 Molecular pathology procedure Level 4 (BLM Known Familial Mutation Analysis; SMN1 known familial sequence variants)
81405 Molecular pathology procedure Level 6 (SMN1 (full gene sequence)
81406 NOTCH3 (notch 3) (e.g., cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy [CADASIL]), targeted sequence analysis (e.g., exons 1-23)
81408 Molecular pathology procedure Level 9 ( FBN1, eg, Marfan syndrome)
81410 Aortic dysfunction or dilation (e.g., Marfan Syndrome, Loeys-Dietz Syndrome, Ehler-Danlos Syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK
81411 Aortic dysfunction or dilation (e.g., Marfan Syndrome, Loeys-Dietz Syndrome, Ehler-Danlos Syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, AND COL3A1
81412 Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1
81425 genome sequence analysis
81426 each comparator genome
81427 re-evaluation of previously obtained genome sequence
81442 Noonan spectrum disorders, genomic sequence analysis panel, must include sequencing of at least 12 genes including, BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1
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
0207U 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 (List separately in addition to code for primary procedure) (Use 0207U in conjunction with 0206U) (DISCERN™ Test)
0216U Neurology (inherited ataxias), genomic DNA sequence analysis of 12 common genes including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants
0217U Neurology (inherited ataxias), genomic DNA sequence analysis of 51 genes including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants
0218U Neurology (muscular dystrophy), DMD gene sequence analysis, including small sequence changes, deletions, duplications, and variants in non-uniquely mappable regions, blood or saliva, identification and characterization of genetic variants
0230U AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation), full sequence analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions
0234U MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions
0236U SMN1 (survival of motor neuron 1, telomeric) and SMN2 (survival of motor neuron 2, centromeric) (eg, spinal muscular atrophy) full gene analysis, including small sequence changes in exonic and intronic regions, duplications and deletions, and mobile element insertions

**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 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:** 2/19

**Revised:** 1/20 (Added PA for WGS), 8/20(add Alzheimer's exclusion); 3/21 (add Peutz-Jeghers, Noonan syndromes), 6/21 (add Marfan Syndrome Loeys-Dietz Syndrome, Ehlers-Danlos Syndrome)

**Reviewed:**

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.

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