Geisinger

Geisinger Health Plan Policies and Procedure Manual

Policy: MP324

Section: Medical Benefit Policy

Subject: Genetic Testing for Disease Carrier Status

Applicable Lines of Business

Commercial	**X**	**CHIP**	**X**
Medicare	**X**	**ACA**	**X**
Medicaid	**X**		

I. Policy: Genetic Testing for Disease Carrier Status

II. Purpose/Objective:

To provide a policy of coverage regarding Genetic Testing for 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

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:
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 status may be available for autosomal recessive genetic conditions, X chromosome-linked conditions, and certain other chromosomal abnormalities.

The cost of carrier screening for an individual condition may be higher than the cost of testing for multiple conditions through expanded carrier screening panels. When selecting a carrier screening approach, the cost of each option to the patient and the health care system should be considered.

Universal carrier screening, regardless of ethnic background, is considered medically necessary for members and their current reproductive partner. Many genetic syndromes are a public health issue in today's pan-ethnic population, and ethnicity-based testing is no longer the recommended approach.

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**.**
- The test result(s) will guide reproductive risks, fetal outcomes, treatment for the fetus, parent, or parent(s) of the pregnant couple, or birth plan

SPECIFIC INDICATIONS:

Carrier Screening During or Before Pregnancy:

Genetic Screening:

Universal carrier screening via genetic sequencing is considered medically necessary in the following scenarios:

1. The member is currently pregnant, OR
2. The member's current reproductive partner is pregnant (see below), OR
3. Preconception planning for a member AND their current reproductive partner, OR
4. Family member with known recessive genetic syndrome or known carrier of recessive disease; OR
5. Ethnicity-based screening has been completed previously but was limited to specific or targeted variants and the results were uninformative**.**

AND

The genetic test includes at least:

I. cystic fibrosis (CF) AND spinal muscular atrophy (SMA); OR
II. The single gene concern based on family history of a specific syndrome for which an association with a disorder has medical management impacts (example: Tay-Sach's disease, rare recessive disorders),

Hemoglobinopathies (alpha thalassemia, beta thalassemia, sickle cell disease or trait)

Universal screening for hemoglobinopathies via complete blood count is considered medically necessary if the member is pregnant, has a reproductive partner who is pregnant, or the member is planning pregnancy.

1. A Complete Blood Count (CBC) with red blood cell indices should be performed in all people who are members who are currently pregnant OR considering future pregnancy.
2. Hemoglobin electrophoresis is medically necessary when CBC results demonstrate a low mean corpuscular volume (MCV) CBC and/or are suggestive of any hemoglobinopathy.

3. Genetic sequencing is not recommended as a first-line approach after abnormal CBC but may be considered when universal genetic carrier screening is performed as a cost-saving approach.

Fragile X syndrome:

1. Diagnostic testing of the FMR1 gene related to for Fragile X syndrome is considered medically necessary for the member, in the following scenarios:
    a. personal or family history of unexplained ovarian insufficiency or elevated FSH <40y; OR
    b. family history of intellectual disability; OR
    c. known family history of Fragile X syndrome or carrier status in any 1st, 2nd, or 3rd degree relative; OR
    d. the member has no clinical signs or symptoms related to Fragile X syndrome in their personal or family history, but universal carrier screening is already being performed.
2. Carrier screening for specific syndromes, called ("single gene testing" or "targeted testing)" can be considered medically necessary if there is a reported family history in the member's 1st, 2nd, or 3rd degree biological relative.
3. Ashkenazi Jewish Carrier Screening Panel may be offered in individuals who report any percentage Ashkenazi Jewish heritage.
    a. (Examples include: 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)
    b. At least one partner of a couple is of Ashkenazi Jewish heritage
    c. (NOTE: If only one partner of a couple is Ashkenazi Jewish, testing should start in that person when possible.)

Reproductive Partner of the Pregnant Person:

1. Universal carrier screening for spinal muscular atrophy (SMA) and/or cystic fibrosis (CF) in a pregnant person's reproductive partner is considered medically necessary in today's pan-ethnic population.
2. Targeted carrier screening through single gene testing, or testing for specific syndromes, is considered medically necessary when:
    a. The member has a known mutation (P/LP variant) in a gene associated with a recessive genetic syndrome.
        i. Common Examples: Tay-Sachs disease, Cystic Fibrosis, Spinal Muscular Atrophy, Noonan syndrome, other genetic syndromes with known recessive inheritance..

OR

    b. The member has a known mutation in a gene associated with risk for a dominant hereditary cancer syndrome where biallelic variants cause risk for a recessive, pediatric-onset, hereditary cancer syndrome.

Condition	Gene	Risk to Pregnancy
Ataxia Telangiectasia	ATM	AT is characterized by progressive cerebellar ataxia with onset in early childhood, telangiectasias, immune defects, and a predisposition to malignancy.
Fanconi Anemia	BRCA1, BRCA2, PALB2, BRIP1, RAD51C	Fanconi anemia is characterized by developmental abnormalities in major organ systems, early-onset bone marrow failure, and a high predisposition to cancer. Bone marrow failure with pancytopenia often presents in the first decade of life.
Constitutional Mismatch Repair Deficiency	MLH1, MSH2, MSH6, PMS2, EPCAM	CMMRD is a childhood cancer predisposition syndrome characterized by hematologic malignancies, brain/central nervous system tumors, colorectal tumors and multiple intestinal polyps, and other malignancies including embryonic tumors and rhabdomyosarcoma.
Fumarate Hydratase deficiency	FH	Inborn error of metabolism characterized by rapid neurologic impairment, hypotonia, seizures, and cerebral atrophy.
Mitochondrial Complex II Deficiency Syndrome	SDHA, SDHB, SDHD	Characterized by neurodegeneration and encephalomyopathy.

Noonan Syndrome:

Genetic testing via panel 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
- There is a known family history of TPN11, SOS1, RADF1 and KRAS gene mutation

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) - Please reference MP280: Whole Exome Sequencing

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.

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.

CODING ASSOCIATED WITH: Genetic Testing for 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
81171 AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81172 AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)
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)
81258 known familial variant
81259 full gene sequence
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) **(Non-covered for Medicare - LCD A53624)**
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)
81361 HBB (hemoglobin subunit bets), sickle cell anemia, beta thallasemia, hemoglobinopathy, common variants
81362 known familial variants
81363 duplication/deletion variants
81364 full gene sequence
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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Aronson M, Colas C, Shuen A, et al. Diagnostic criteria for constitutional mismatch repair deficiency (CMMRD): recommendations from the international consensus working group. J Med Genet. 2022 Apr;59(4):318-327. PMID: 33622763.

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); 6/23 (extensive review and revision)

Reviewed: 6/22