Genetic Testing for Carrier Screening

Humana

Medical Coverage Policy

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Change Summary: Updated Provider Claims Codes

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Disclaimer

Description

Genetic testing may be performed on prospective parents to identify potential diseases that may be passed to their offspring. This is known as carrier screening. Carriers are usually themselves unaffected by the disease, showing no symptoms, however may be at risk for passing the disease onto their children. Preferably, carrier screening takes place before pregnancy (preconception), but can occur during the early stages of pregnancy.

A consensus from the professional organization guidelines and recommendations is used when considering which genetic conditions may be appropriate for carrier screening and includes the following:

- Ability to be diagnosed prenatally and allow opportunities for antenatal intervention to improve perinatal outcomes, changes in delivery management to

optimize newborn and infant outcomes and education of the parents about special care needs after birth.[11]

- Carrier frequency of 1 in 100 or greater with a well-defined phenotype that would have a detrimental effect on quality of life (eg, cause cognitive or physical impairment, require surgical or medical intervention).
- Should not include conditions primarily associated with adult-onset of disease.
- Should not replace newborn screening or risk-based genetic testing (eg, known family history).
- Targeted testing based on an individual's race, ethnicity or family history for single-gene disorders that have an autosomal or X-linked recessive inheritance pattern. Examples of these diseases include, but may not be limited to: alpha thalassemia, cystic fibrosis (CF) and fragile X syndrome.

Other conditions, such as nonsyndromic hearing loss may have one or more inheritance patterns. **(Refer to Coverage Limitations section)**

Expanded carrier screening refers to the practice of screening for a large number of conditions in a panethnic approach (without regard to race or ethnicity) and can include testing for many genetic disorders depending on specific laboratory offerings. **(Refer to Coverage Limitations section)**

For information regarding **carrier screening for muscular dystrophy or spinal muscular atrophy (SMA)**, please refer to Genetic Testing for Muscular Dystrophy and Spinal Muscular Atrophy Medical Coverage Policy.

For information regarding **carrier screening for inherited thrombophilias**, please refer to Genetic and Coagulation Testing for Noncancer Blood Disorders Medical Coverage Policies.

For information regarding **prenatal genetic testing**, please refer to Prenatal Invasive Diagnostic Genetic Testing and Noninvasive Prenatal Testing Medical Coverage Policies.

For information regarding **genetic testing for the following**, please refer to Genetic Testing Medical Coverage Policy:

- DNA banking or preservation
- General population screening
- Individual 17 years of age or younger for adult-onset conditions
- Interpretation and reporting for molecular pathology procedure
- Polygenic risk score (PRS) and single nucleotide polymorphisms (SNPs)
- Repeat germline or somatic genetic testing
- Retrieved archival tissue

Humana recognizes that the field of genetic testing is rapidly changing and that other tests may become available.

Coverage Determination

Any state mandates for genetic testing for carrier screening take precedence over this medical coverage policy.

Genetic testing may be excluded by certificate. Please consult the member's individual certificate regarding Plan coverage.

Apply General Criteria for Genetic and Pharmacogenomics Tests when disease- or gene-specific criteria are not available on a medical coverage policy. For information regarding **General Criteria for Genetic and Pharmacogenomics Tests**, please refer to Genetic Testing Medical Coverage Policy.

Ashkenazi Jewish Carrier Screening/Panel Testing

Humana members may be eligible under the Plan for **genetic testing for Ashkenazi Jewish carrier screening or panel testing for the genetic conditions listed in Table 1** for reproductive decision making when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
- Individual to be tested is of reproductive age and is of Ashkenazi Jewish ancestry* or is the reproductive partner of an individual of Ashkenazi Jewish ancestry*;

AND ANY of the following:

- Individual to be tested has an affected family member, carrier family member or reproductive partner with a known pathogenic variant in a gene which causes any of the genetic conditions listed in Table 1; **OR**

- Individual to be tested has a family member or reproductive partner with at least one of the genetic conditions listed in Table 1:

Table 1: Ashkenazi Jewish Carrier Screening – Genetic Conditions

Bloom syndrome	Joubert syndrome
Canavan disease	Lipoamide dehydrogenase deficiency (E3)
CF	Maple syrup urine disease
Familial dysautonomia	Mucolipidosis IV
Familial hyperinsulinism	Nemaline myopathy
Fanconi anemia	Niemann-Pick Type A
Gaucher disease	Tay-Sachs disease
Glycogen storage disease Type 1	

*****If only one individual of the couple is of Ashkenazi Jewish ancestry, then testing begins with the individual of Ashkenazi Jewish ancestry. If positive for a disease listed above, proceed to test the non-Ashkenazi Jewish partner for that disease using the most appropriate technology for his/her ethnicity. If the individual to be tested is already pregnant, both partners may be screened simultaneously.

For information regarding **CF carrier screening for individuals of non-Ashkenazi Jewish ancestry or for expanded CF carrier screening for individuals of Ashkenazi Jewish ancestry**, please refer to Genetic Testing for Cystic Fibrosis Medical Coverage Policy.

Fragile X Syndrome (*FMR1* Gene)

Humana members may be eligible under the Plan for **genetic testing of the *FMR1* gene for carrier screening for fragile X syndrome** for reproductive decision making when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**

- Individual to be tested has a family history of fragile X-related disorders or unexplained intellectual disability or developmental delay, autism or primary ovarian insufficiency (POI)** (also known as premature ovarian failure [POF]); **OR**

- Individual to be tested has an affected or carrier family history with a known pathogenic variant

**POI is defined as female 39 years of age or younger with FSH levels in the postmenopausal range and at least three months of amenorrhea, oligomenorrhea or dysfunctional uterine bleeding.[71]

Alpha Thalassemia (*HBA1* and *HBA2* Genes) and Beta Thalassemia (*HBB* Gene)
Humana members may be eligible under the Plan for **genetic testing for carrier screening for alpha and beta thalassemias** for reproductive decision making when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**

- Individual to be tested is of reproductive age or is the reproductive partner **AND ANY** of the following:

  - Individual to be tested has a first-degree relative with confirmed diagnosis of alpha or beta thalassemia; **OR**

  - Individual to be tested is affected or is a known carrier of alpha or beta thalassemia; **OR**

  - Individual to be tested has equivocal or indeterminate diagnosis based on results of prior testing such as complete blood count (CBC) and hemoglobin analysis by qualitative/quantitative electrophoresis, high performance liquid chromatography (HPLC) or isoelectric focusing

Tay-Sachs Disease (*HEXA* Gene)

Humana members may be eligible under the Plan for **genetic testing of the *HEXA* gene^ for carrier screening for Tay-Sachs disease** for reproductive decision making when **ANY** of the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
    - Individual to be tested has an abnormal or inconclusive beta-hexosaminidase A enzyme activity; **OR**
    - Individual to be tested has an affected or carrier family member in whom a variant has been identified; **OR**
    - Individual to be tested is of Ashkenazi Jewish ancestry***** or the reproductive partner of an individual of Ashkenazi Jewish ancestry*****; **OR**
    - Individual to be tested is the reproductive partner of an individual affected with or carrier of Tay-Sachs disease

^Testing begins with a targeted gene panel. If negative, gene sequence analysis may be considered.

Other Inherited Conditions

Humana members may be eligible under the Plan for **genetic testing for carrier screening of other inherited conditions** including, but not limited to: **Canavan disease, Fabry disease, Gaucher disease, mucolipidosis IV** for reproductive decision making when **ANY** of the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
    - Individual to be tested has an affected or carrier family member in whom a variant(s) have been identified; **OR**
    - Individual to be tested is of reproductive age with a family history of a genetic condition that puts that individual at higher risk than the general population to be a carrier; **OR**

- Individual to be tested is the reproductive partner of an individual affected with or carrier of an inherited condition

Note: The criteria for **genetic testing for carrier screening** are not consistent with the Medicare National Coverage Policy and therefore may not be applicable to Medicare members. Refer to the CMS website for additional information.

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **genetic testing for carrier screening** for any indications other than those listed above including, but may not be limited to:

- *AFF2* gene testing for fragile X syndrome (81171 and 81172)
- *CFTR* deletion/duplication analysis for CF (81222)

These are considered experimental/investigational as they are not identified as widely used and generally accepted for any proposed use as reported in nationally recognized peer-reviewed medical literature published in the English language.

Humana members may **NOT** be eligible under the Plan for **genetic testing for carrier screening** for any indications other than those listed above including, but may not be limited to:

- Detection of genetic susceptibility to adult-onset/late-onset disorders including, but not limited to, genetic testing for breast cancer (eg, BRCA gene testing); **OR**
- *GJB2* and *GJB6* gene testing for nonsyndromic hearing loss (81252, 81253, 81254, 81430, 81431 and S3844)**; OR**
- Screening for hemoglobinopathies or thalassemias other than alpha and beta thalassemia including, but not limited to, sickle cell anemia (*HBB* gene) (S3850)

These indications are considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition.

Humana members may **NOT** be eligible under the Plan for **expanded carrier screening panels for multiple heritable conditions (81443)** including, but may not be limited to:

- Carrier Status DNA Insight
- FirstGene
- Foresight Carrier Screen
- GeneAware (Basic, ACMG and ACOG, Ashkenazi Jewish and Complete) Panels
- Genesys Carrier Panel (0400U)
- InheriGen, InheriGen Plus
- Inheritest (Society-Guided, Ashkenazi Jewish and Comprehensive) Panels
- Invitae (Broad and Comprehensive) Carrier Screens
- Natera Horizon Carrier Screen
- NxGen MDx (Essential, Super, Early Advantage) Carrier Panels
- Otogenetics GxVISION (Basic with CF, ACOG/ACMG with CF, Ashkenazi Jewish, Pan-Ethnic) Carrier Screening Tests
- QHerit Expanded Carrier Screen
- Unity Carrier Screen (0449U)

These are considered not medically necessary as defined in the member's individual certificate. Please refer to the member's individual certificate for the specific definition. Please refer to panel testing language above in the Coverage Determination section.

Background

Additional information about **inherited genetic conditions** may be found from the following websites:

- National Library of Medicine

Medical Alternatives

Physician consultation is advised to make an informed decision based on an individual's health needs.

Humana may offer a disease management program for this condition. **The member may call the number on his/her identification card to ask about our programs to help manage his/her care.**

Provider Claims Codes

Any CPT, HCPCS or ICD codes listed on this medical coverage policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and or reimbursement for a service or procedure.

The table below includes general codes for Genetic Testing for Carrier Screening. For codes related to a specific gene and/or genetic condition, please refer to the appropriate genetic testing medical coverage policy.

CPT® Code(s)	Description	Comments
81171	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	**Not Covered**
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)	**Not Covered**
81200	ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)	

81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (eg, maple syrup urine disease) gene analysis, common variants (eg, R183P, G278S, E422X)	
81209	BLM (Bloom syndrome, RecQ helicase-like) (eg, Bloom syndrome) gene analysis, 2281del6ins7 variant	
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)	
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants	
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants	**Not Covered if used to report any test outlined in Coverage Limitations section**
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence	
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)	
81242	FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia, type C) gene analysis, common variant (eg, IVS4+4A>T)	
81243	FMR1 (fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	
81244	FMR1 (fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and promoter methylation status)	
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)	
81251	GBA (glucosidase, beta, acid) (eg, Gaucher disease) gene analysis, common variants (eg, N370S, 84GG, L444P, IVS2+1G>A)	

81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence	**Not Covered**
81253	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants	**Not Covered**
81254	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])	**Not Covered**
81255	HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)	
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; common deletions or variant (eg, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, Constant Spring)	
81258	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant	
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence	
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (eg, familial dysautonomia) gene analysis, common variants (eg, 2507+6T>C, R696P)	
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants	
81290	MCOLN1 (mucolipin 1) (eg, Mucolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)	
81330	SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)	

81361	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)	**Not Covered if used to report any test outlined in Coverage Limitations section**
81362	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)	**Not Covered if used to report any test outlined in Coverage Limitations section**
81363	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)	**Not Covered if used to report any test outlined in Coverage Limitations section**
81364	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence	**Not Covered if used to report any test outlined in Coverage Limitations section**
81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2	**Not Covered if used to report any test outlined in Coverage Limitations section**
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	
81430	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1	**Not Covered**

81431	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes	**Not Covered**
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)	**Not Covered**
81479	Unlisted molecular pathology procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
83080	b-Hexosaminidase, each assay	
96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family	
0400U	Obstetrics (expanded carrier screening), 145 genes by next-generation sequencing, fragment analysis and multiplex ligation- dependent probe amplification, DNA, reported as carrier positive or negative	**Not Covered** **New Code Effective 07/01/2023**
0449U	Carrier screening for severe inherited conditions (eg, cystic fibrosis, spinal muscular atrophy, beta hemoglobinopathies [including sickle cell disease], alpha thalassemia), regardless of race or self-identified ancestry, genomic sequence analysis panel, must include analysis of 5 genes (CFTR, SMN1, HBB,HBA1, HBA2)	**Not Covered** **New Code Effective 04/01/2024**
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		

HCPCS Code(s)	Description	Comments
S0265	Genetic counseling, under physician supervision, each 15 minutes	
S3844	DNA analysis of the connexin 26 gene (GJB2) for susceptibility to congenital, profound deafness	**Not Covered**
S3845	Genetic testing for alpha-thalassemia	
S3846	Genetic testing for hemoglobin E beta-thalassemia	
S3849	Genetic testing for Niemann-Pick disease	
S3850	Genetic testing for sickle cell anemia	

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Appendix A

Pre- and Post-Test Genetic Counseling Criteria

Pre- and post-test genetic counseling performed by any of the following qualified medical professionals
Genetic counselor who is board-certified or board-eligible by the American Board of Medical Genetics and Genomics (ABMGG) or American Board of Genetic Counseling, Inc (ABGC) and is not employed by a commercial genetic testing laboratory; **OR**
Genetic clinical nurse (GCN) or advanced practice nurse in genetics (APNG) who is credentialed by the Genetic Nursing Credentialing Commission (GNCC) or the American of Nurses Credentialing Center (ANCC) and is not employed by a commercial genetic testing laboratory; **OR**
Medical geneticist who is board-certified or board-eligible by ABMGG; **OR**
Treating physician who has evaluated the individual to be tested and has completed a family history of three generations

Appendix B

Family Relationships

Degree of Relationship	Relative of the Individual to be Tested
First-degree	Child, full-sibling, parent
Second-degree	Aunt, uncle, grandchild, grandparent, nephew, niece, half-sibling
Third-degree	First cousin, great aunt, great-uncle, great-grandchild, great-grandparent, half-aunt, half-uncle