Genetic Testing for Diagnosis of Inherited Conditions

Humana

Medicaid Medical Coverage Policy

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Description

Genetic testing may be performed to analyze an individual's DNA to detect gene variants to assist in confirming a diagnosis in those who exhibit disease signs and symptoms of inherited conditions and to aid with treatment decisions. Examples of genetic conditions that may be evaluated by genetic testing include, but are not limited to, hematological malignancies, hemophilia, mitochondrial disorders, neutropenia, thrombocytopenia and thrombophilia.

Cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS) is an autosomal recessive, adult-onset, slowly progressive neurologic disorder characterized by imbalance due to cerebellar gait and limb ataxia, impaired vestibular function bilaterally and non-length-dependent sensory neuropathy.

Coagulation (blood clotting) disorders are defects in the liver's ability to make enough proteins (eg, fibrinogen, prothrombin) needed to assist in the formation of blood clots and can result in hemorrhage (too little clotting) or thrombosis (too much clotting). Blood and coagulation disorders may be acquired (caused by disease or side effects of medication) or inherited (caused by genes). Most bleeding and clotting disorders are caused by abnormalities in hemostasis (eg, dysfunction of platelets and/or clotting proteins). Less commonly, excessive bleeding or clotting can be caused by abnormalities in the fibrinolytic system (fibrinolysis). **(Refer to Coverage Limitations section)**

Dentatorubral-pallidoluysian atrophy (DPLA) is a progressive autosomal dominant spinocerebellar ataxia caused by cytosine-adenine-guanine (CAG) repeat expansion in the *ATN1* gene. DRPLA is characterized by ataxia, choreoathetosis/dystonia, cognitive impairment/dementia, myoclonic epilepsy and psychiatric disturbances. Clinical presentation varies with the age of onset and may also include corneal endothelial degeneration, head tremor or optic atrophy.

Glycogen storage disease type I (GSD I), also known as von Gierke disease, is a rare disease of variable clinical severity that primarily affects the liver and kidney. Approximately 80 percent of GSD I cases are caused by deficient activity of the glucose 6-phosphatase enzyme (GSD Ia) in the *G6PC* gene. This results in excessive accumulation of glycogen and fat in the liver, kidney and intestinal mucosa. Individuals with GSD present with manifestations related to hypoglycemia around three to four months of age and have a wide spectrum of clinical manifestations, including hepatomegaly, hypoglycemia, lactic acidemia, hyperlipidemia, hyperuricemia and growth retardation.

Intellectual disability (ID) is a neurodevelopmental disorder with multiple etiologies. It is characterized by deficits in intellectual and adaptive functioning of varying severity, presenting before 18 years of age. ID encompasses a broad spectrum of functioning, disability, and strengths. ID affects approximately 1 to 2 percent of the population. X-linked intellectual disability refers to medical disorders associated with X-linked recessive inheritance that result in intellectual disability (eg, X-linked intellectual disability [XLID] deletion/duplication analysis panel) **(Refer to Coverage Limitations section)**

Muscular dystrophies are a group of diseases that cause progressive weakness and loss of muscle mass. In muscular dystrophy, variants (abnormal genes) interfere with the production of proteins needed to form healthy muscle. There are many types of muscular dystrophy including myotonic dystrophy type 1 (DM1) (*DMPK* gene), myotonic dystrophy type 2 (DM2) (*CNBP* gene) and spinal and bulbar muscular atrophy (SBMA) (also known as Kennedy's disease) (*AR* gene).

Optical genome mapping (OGM) is a technology used to enhance the detection and interpretation of whole-gene sequencing (WGS) by analyzing ultra-high molecular weight DNA molecules that provides a high-resolution genome-wide analysis highlighting copy number and structural anomalies, including balanced translocations. Transcriptome analysis is a method that allows evaluation of the functional consequences of DNA variants discovered by optical genome mapping or DNA sequencing. **(Refer to Coverage Limitations section)**

Preimplantation genetic testing for aneuploidy (PGT-A) (formerly known as preimplantation genetic screening [PGS]) is used to screen for aneuploidy in parents who have no known chromosomal anomaly, variant or other genetic abnormality. PGT-A has been proposed for individuals at risk for having an increased occurrence of aneuploid embryos, such as women of advanced maternal age and those with a history of repeated IVF failure or recurrent early pregnancy loss (a nonviable, intrauterine pregnancy with either an empty gestational sac or a gestational sac containing an embryo or fetus without fetal heart activity within the first 12 6/7 weeks of gestation[7]). **(Refer to Coverage Limitations section)**

Rett syndrome is a severe neurodevelopmental disorder that occurs almost exclusively in females. After a brief period of initially normal development, affected individuals experience loss of speech and purposeful hand use, stereotypic hand movements and gait abnormalities. Additional features include deceleration of head growth, seizures, autistic features and breathing abnormalities. Most cases result from pathogenic variants in the *MECP2* gene.

Twin zygosity DNA testing is a genetic test that determines whether twins are identical (monozygotic) or fraternal (dizygotic) which compares the genetic markers of each twin to see if their genetic profiles are the same. The test can be performed in conjunction with cfDNA tests that are used to detect chromosome abnormalities **(Refer to Coverage Limitations section)**

Multigene (or expanded) panels analyze a broad set of genes simultaneously (as opposed to single gene testing that searches for variants in one specific gene) and have been proposed to evaluate the DNA of an individual with a personal and/or family history of more than one hereditary condition or syndrome. Panels often include medically actionable genes but may also include those with unclear medical management Targeted (or focused) multigene panels analyze a limited number of genes targeted to a specific condition. Panels may also use polygenic risk scoring (PRS) to purportedly assess individual risk for disease in combination with other clinical information such as personal and family history, clinical findings and disease biomarkers. **(Refer to Coverage Limitations section)**

Coverage Determination

Cerebellar Ataxia with Neuropathy and Vestibular Areflexia Syndrome (CANVAS) (*RFC1* Gene)

Humana members may be eligible under the Plan for **genetic testing of *RFC1* gene** (0378U) **to aid in the diagnosis of CANVAS** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
- Individual is 35 years of age or older and exhibits one or more of the following signs and symptoms of CANVAS including[16]:
    - Bilateral vestibular areflexia (eg, oscillopsia, absent/reduced vestibulo-ocular reflex); **OR**
    - Cerebellar dysfunction (eg, dysarthria, dysphagia, abnormal eye movements, dysdiadokokinesia, reduced muscle tone); **OR**
    - Complex impairment of balance and coordination of peripheral, vestibular and cerebellar origin (eg, imbalance, dizziness, progressive ataxia of gait and limb dysmetria); **OR**

  - Sensory neuropathy or neuronopathy (eg, altered sensation in limbs, positive Romberg sign, dysmetria worsened by eye closure); **AND**

- Supportive clinical documentation (eg, autonomic function testing, brain or spine MRI, family history, nerve conduction studies, vestibular testing)[16]

Testing strategy: Targeted analysis for repeat AAGGG expansions[16]

Corneal Dystrophy

***TGFBI* gene sequence analysis** (81333) will be considered medically reasonable and necessary for the diagnosis and management of corneal dystrophy when the following criteria are met[**11**]:

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

- Genetic testing is limited to the *TGFBI* gene; **AND**

- Individual exhibits clinical characteristics of corneal dystrophy on ophthalmology exam (eg, slit-lamp microscope)

Dentatorubral-Pallidoluysian Atrophy

Humana members may be eligible under the Plan for **targeted analysis for CAG expansions in *ATN1* gene for DRPLA** (81177) when the following criteria are met[17,28]:

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

- No known pathogenic or likely pathogenic variant***** in a first-, second- or third-degree relative; **AND**

  - Individual exhibits at least 2 of the following signs and symptoms of DRPLA:

    - Ataxia
    - Choreoathetosis/dystonia
    - Cognitive impairment/dementia
    - Family history consistent with autosomal recessive inheritance
    - Myoclonic epilepsy
    - Psychiatric disturbances; **OR**

  - Preimplantation or prenatal genetic diagnosis, for family in which disease-causing mutation in *ATXN1* gene has been identified

Glycogen Storage Disease Type I (*G6PC* Gene)

Humana members may be eligible under the Plan for ***G6PC* gene testing for glycogen storage disease type I (GSD I)** (81250) when the following criteria are met[6,19,33]:

- Pre- and post-test genetic counseling; **AND**
    - Individual exhibits at least 2 of the following signs and symptoms of GSD I:
        - Growth failure
        - Hepatomegaly
        - Hypertriglyceridemia
        - Hyperuricemia
        - Hypoglycemia
        - Lactic acidosis; **OR**
    - Individual is of Ashkenazi Jewish ancestry and of reproductive age; **OR**
    - Preimplantation or prenatal genetic diagnosis, for family in which disease-causing mutation in *G6PC* gene has been identified

Hemophilia B (*F9* Gene)
Humana members may be eligible under the Plan for ***F9* gene** **testing for hemophilia B** (81238) when the following criteria are met[20,29]:

- Pre- and post-test genetic counseling; **AND**
- No known pathogenic or likely pathogenic variant***** in a first-, second- or third-degree relative; **AND**
    - Carrier screening for couples (or individuals) who are known carriers or who have a first- or second-degree relative with confirmed diagnosis and are planning pregnancy or seeking prenatal care and no prior testing results are available for interpretation; **OR**
    - Individual has equivocal or indeterminate diagnosis based on results of prior testing such as a prolonged activated partial thromboplastin time (aPTT) or low factor IX clotting activity; **OR**
    - Preimplantation or prenatal genetic diagnosis, for family in which disease-causing mutation in *F9* gene has been identified; **OR**
    - To establish disease-causing variant in an individual with a confirmed diagnosis

Testing strategy:
1. Perform *F9* gene sequence analysis

2. Perform targeted deletion/duplication analysis of *F9* gene if only 1 or no pathogenic or likely pathogenic variant is identified with sequence analysis

Myotonic Dystrophy Type 1 and Type 2 (*DMPK* and/or *CNBP Genes*)

Humana members may be eligible under the Plan for **myotonic dystrophy type 1 (DM1) (*DMPK* gene) and/or myotonic dystrophy type 2 (DM2) (*CNBP* gene)** testing when the following criteria are met[1,2,5,23,24]:

- Pre- and post-test genetic counseling; **AND**
- No known pathogenic or likely pathogenic variant***** in a first-, second- or third-degree relative; **AND**
    - Individual (see Testing Strategy) exhibits one or more of the following characteristic features of DM1 or DM2 (eg, cardiac conduction defects, cataracts, intellectual disability, muscle weakness, muscle pain, myotonia, progressive cardiomyopathy, respiratory insufficiency); **OR**
    - Preimplantation or prenatal genetic diagnosis, for family in which disease-causing mutation in *CNBP* or *DMPK* gene has been identified

Testing Strategy: Targeted variant analysis of *DMPK* (81234 and 81239) and/or *CNBP* (81187) genes for repeat expansions. **(Refer to Coverage Limitations section** for sequence analysis of *CNBP* and/or *DMPK* genes**)**

Rett Syndrome (*MECP2* Gene)

Humana members may be eligible under the Plan for ***MECP2*** (eg, Genomic Unity *MECP2*) (0234U) **single gene testing and deletion/duplication analysis to confirm a diagnosis of Rett syndrome (classic or atypical [variant])** when the following criteria are met[22,39]:

- Pre- and post-test genetic counseling; **AND**
- No known pathogenic or likely pathogenic variant***** in a first-, second- or third-degree relative; **AND**
    - Individual exhibits 2 or more of the following characteristics suggestive of Rett syndrome:
        - A period of regression followed by recovery or stabilization
        - Gait abnormalities
        - Partial or complete loss of acquired purposeful hand skills
        - Partial or complete loss of acquired spoken language
        - Stereotypic hand movements including clapping/tapping, hand wringing/squeezing, mouthing and washing/rubbing automatisms; **OR**
    - Individual has postnatal deceleration of head growth; **OR**

  - Individual is a female presenting with developmental problems of unknown etiology and some features suggestive of Rett syndrome; **OR**
  - Individual is a male infant with severe encephalopathy; **OR**
  - Preimplantation or prenatal genetic diagnosis, for family in which disease-causing mutation in *MECP2* gene has been identified

Spinal and Bulbar Muscular Atrophy (also known as Kennedy's Disease) (*AR* Gene)

Humana members may be eligible under the Plan for ***AR* gene testing for SBMA** when the following criteria are met[26,30]:

- Pre- and post-test genetic counseling; **AND**
- No known pathogenic or likely pathogenic variant***** in a first-, second- or third-degree relative; **AND**
  - Individual (see Testing Strategy) is male and exhibits adolescent-onset signs of androgen insensitivity (eg, dysarthria, dysphagia, fasciculation of the tongue, lips or perioral region, gynecomastia, muscle weakness of the limbs); **OR**
  - Preimplantation or prenatal genetic diagnosis, for family in which disease-causing mutation in *AR* gene has been identified**; OR**
- Carrier screening when the individual is female and has a first-, second- or third-degree relative with known pathogenic or likely pathogenic variant of SMBA (**Testing Strategy**: Test for KFV)

Testing Strategy: Targeted *AR* gene analysis for CAG trinucleotide repeats (81204). **(Refer to Coverage Limitations section for KFV and sequence analysis of *AR* gene)**.

KNOWN FAMILIAL VARIANT ANALYSIS

Known familial variant (KFV) analysis for diagnosis of inherited conditions will be considered medically reasonable and necessary for when the following criteria are met:

- Individual has been diagnosed with an inherited condition listed above; **AND**
- Has an affected first-, second- or third-degree relative with a pathogenic or likely pathogenic variant in any of the following:
  - *AR* gene (analysis for CAG trinucleotide repeats) for SBMA[26,30]; **OR**
  - *ATXN1* gene for DRPLA[17,28]; **OR**
  - *DMPK* or *CNBP* gene (targeted analysis for repeat expansions) for DM1 or DM2[1,2,5,23,24]; **OR**
  - *F9* gene for hemophilia B[20,29]; **OR**
  - *MECP2* gene for Rett syndrome[22,39]

- Testing is limited to the KFV

*****If a pathogenic or likely pathogenic variant has been detected in an affected family member, genetic testing should be limited to the known familial variant

Coverage Limitations

Humana members may **NOT** be eligible under the Plan **for genetic testing for DM1, DM2 or SBMA** for any indications or tests other than those listed above including, but may not be limited to:

- *AR* full gene sequence analysis (eg, 81173 and Genomic Unity AR analysis [0230U]) and KFV (81174) for SBMA (also known as Kennedy's disease)[26]; **OR**

- *CNBP* full gene sequence analysis for DM2[24]; **OR**

- *DMPK* full gene sequence analysis for DM1[23]

A review of the current medical literature shows that the **evidence is insufficient** to determine that these services are standard medical treatments. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Humana members may **NOT** be eligible under the Plan for **genetic testing for the diagnosis of any inherited conditions** other than those listed above including, but may not be limited to:

- Deletion/duplication information is obtained as part of the sequencing procedure but submitted as an independent analysis

- Fragile XE syndrome *AFF2* gene testing (81171, 81172)[18]

- Gene expression profiling (GEP) for congenital epigenetic disorders including, but may not be limited to, EpiSign Complete (0318U)[15]

- Nuclear encoded mitochondrial genomic sequencing panel of at least 100 genes for mitochondrial disorders including, but may not be limited to, neurologic or myopathic phenotypes (81440)[40,41]

- Optical genome mapping including, but may not be limited to, Augusta Optical Genome Mapping (0260U), Praxis Optical Genome Mapping (0264U) and Praxis Transcriptome (0266U)

- POC test (Fetal aneuploidy short tandem-repeat [STR] comparative analysis of fetal DNA obtained from products of conception [POC]) (0252U)

- Rapid or ultrarapid whole genome/exome sequencing including, but may not be limited to, RCIGM Rapid Whole Genome Sequencing (0094U)

- Twin zygosity screening (0060U)[43]

- Whole mitochondrial genome sequence with heteroplasmy detection, deletion analysis and/or nuclear-encoded mitochondrial gene analysis including, but may not be limited to, Genomic Unity Comprehensive Mitochondrial Disorders Analysis (0417U)[40,41]

- X-linked intellectual disability (XLID) deletion/duplication analysis panel (81471)[34]

A review of the current medical literature shows that there is **no evidence** to determine these services are standard medical treatments. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Humana members may **NOT** be eligible under the Plan for **PGT-A** (eg, 0254U) for any indication including the following[10,39]:

- Recurrent implantation failures; **OR**
- Recurrent pregnancy loss; **OR**
- Solely because of maternal age; **OR**
- To improve in vitro fertilization success rates

A review of the current medical literature shows that there is **no evidence** to determine these services are standard medical treatments. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Humana members may **NOT** be eligible under the Plan for **multigene panels or targeted multigene panels** to assess coagulation disorders. Examples include, but may not be limited to:

- Versiti aHUS Genetic Evaluation (0268U)
- Versiti Autosomal Dominant Thrombocytopenia Panel (0269U)
- Versiti Coagulation Disorder Panel (0270U)
- Versiti Comprehensive Bleeding Disorder Panel (0272U)
- Versiti Comprehensive Platelet Disorder Panel (0274U)
- Versiti Congenital Neutropenia Panel (0271U)
- Versiti Fibrinolytic Disorder Panel (0273U)
- Versiti Inherited Thrombocytopenia Panel (0276U)
- Versiti Platelet Function Disorder Panel (0277U)
- Versiti Thrombosis Panel (0278U)

A review of the current medical literature shows that the **evidence is insufficient** to determine that these services are standard medical treatments. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Coding Information

Any codes listed on this 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.

CPT® Code(s)	Description	Comments
81171	AFF2 (ALF transcription elongation factor 2 [FMR2]) (eg, fragile X intellectual disability 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	
81172	AFF2 (ALF transcription elongation factor 2 [FMR2]) (eg, fragile X intellectual disability 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)	
81173	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence	
81174	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant	
81177	ATN1 (atrophin 1) (eg, dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81187	CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81204	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)	
81234	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles	
81238	F9 (coagulation factor IX) (e.g., hemophilia B), full gene sequence	
81239	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)	

81250	G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)	
81312	PABPN1 (poly[A] binding protein nuclear 1) (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81333	TGFBI (transforming growth factor beta-induced) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)	
81440	Nuclear encoded mitochondrial genes (eg, neurologic or myopathic phenotypes), genomic sequence panel, must include analysis of at least 100 genes, including BCS1L, C10orf2, COQ2, COX10, DGUOK, MPV17, OPA1, PDSS2, POLG, POLG2, RRM2B, SCO1, SCO2, SLC25A4, SUCLA2, SUCLG1, TAZ, TK2, and TYMP	
81471	X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); duplication/deletion gene analysis, must include analysis of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2	
81479	Unlisted molecular pathology procedure	
81599	Unlisted multianalyte assay with algorithmic analysis	
84999	Unlisted chemistry procedure	
0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood	
0094U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis	
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	
0252U	Fetal aneuploidy short tandem-repeat comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplications, mosaicism, and segmental aneuploidy	

0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy, per embryo tested	
0260U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping	
0264U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping	
0266U	Unexplained constitutional or other heritable disorders or syndromes, tissue-specific gene expression by whole-transcriptome and next-generation sequencing, blood, formalin-fixed paraffin-embedded (FFPE) tissue or fresh frozen tissue, reported as presence or absence of splicing or expression changes	
0268U	Hematology (atypical hemolytic uremic syndrome [aHUS]), genomic sequence analysis of 15 genes, blood, buccal swab, or amniotic fluid	
0269U	Hematology (autosomal dominant congenital thrombocytopenia), genomic sequence analysis of 14 genes, blood, buccal swab, or amniotic fluid	
0270U	Hematology (congenital coagulation disorders), genomic sequence analysis of 20 genes, blood, buccal swab, or amniotic fluid	
0271U	Hematology (congenital neutropenia), genomic sequence analysis of 23 genes, blood, buccal swab, or amniotic fluid	
0272U	Hematology (genetic bleeding disorders), genomic sequence analysis of 51 genes, blood, buccal swab, or amniotic fluid, comprehensive	
0273U	Hematology (genetic hyperfibrinolysis, delayed bleeding), genomic sequence analysis of 8 genes (F13A1, F13B, FGA, FGB, FGG, SERPINA1, SERPINE1, SERPINF2, PLAU), blood, buccal swab, or amniotic fluid	
0274U	Hematology (genetic platelet disorders), genomic sequence analysis of 43 genes, blood, buccal swab, or amniotic fluid	
0276U	Hematology (inherited thrombocytopenia), genomic sequence analysis of 23 genes, blood, buccal swab, or amniotic fluid	

0277U	Hematology (genetic platelet function disorder), genomic sequence analysis of 31 genes, blood, buccal swab, or amniotic fluid	
0278U	Hematology (genetic thrombosis), genomic sequence analysis of 12 genes, blood, buccal swab, or amniotic fluid	
0318U	Pediatrics (congenital epigenetic disorders), whole genome methylation analysis by microarray for 50 or more genes, blood	
0378U	RFC1 (replication factor C subunit 1), repeat expansion variant analysis by traditional and repeat-primed PCR, blood, saliva, or buccal swab	
0417U	Rare diseases (constitutional/heritable disorders), whole mitochondrial genome sequence with heteroplasmy detection and deletion analysis, nuclear-encoded mitochondrial gene analysis of 335 nuclear genes, including sequence changes, deletions, insertions, and copy number variants analysis, blood or saliva, identification and categorization of mitochondrial disorder-associated genetic variants	
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
S3853	Genetic testing for myotonic muscular dystrophy	

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Appendix

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[14]

Degree of Relationship	**Relative of the Individual to be Tested**
First-degree	Parents, siblings, children
Second-degree	Grandparents, grandchildren, uncles, aunts, nephews, nieces, half-siblings
Third-degree	Great-grandparents, great-grandchildren, great uncles, great aunts, first cousins
Fourth-degree	Great-great-grandparents, great-great-grandchildren, first cousins once-removed (children of the individual’s first cousins)

Change Summary

04/01/2025 New Policy.
05/06/2025 Update, Coverage Change. Updated Coding Information