Genetic Testing for Hereditary Ataxias

Humana

Medical Coverage Policy

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Disclaimer

Description

The hereditary ataxias are a group of genetic disorders characterized by motor incoordination that results from dysfunction of the cerebellum and/or spinal cord that is associated with dysarthria (abnormal speech), poor eye-hand coordination and an unsteady gait. These disorders are categorized by mode of inheritance and causative gene or chromosomal locus. Hereditary ataxias can be inherited in an autosomal dominant, autosomal recessive or X-linked manner.

Friedreich ataxia (FRDA) is an autosomal-recessive, progressive, neurodegenerative disorder and is the most common hereditary ataxia. FRDA is caused by mutations in the *FXN* gene on chromosome 9 which produces a protein called frataxin. It is characterized by progressive ataxia with onset starting between 5 and 15 years of age. Symptoms typically associated with the disorder include: absent lower-limb reflexes, bladder dysfunction, dysarthria, muscle weakness, spasticity particularly in

the lower limbs and scoliosis.[15] Diabetes mellitus and heart-related conditions (eg, atrial fibrillation, cardiomegaly, cardiomyopathy, heart murmurs, tachycardia) are also associated with FRDA.

Spinocerebellar ataxia (SCA) is an autosomal-dominant, progressive, neurodegenerative disease. It is characterized by dysfunction of the cerebellum (the part of the brain that controls walking and balance) and is manifested by progressive uncoordinated movements (ataxia). There are over 40 different types of SCA conditions. They typically present in middle age with progressive ataxia, neuronal dysfunction and eventual neuronal loss during the ensuing 10 to 20 years.

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.[37]

Diagnostic genetic testing may be used for an individual with signs and symptoms of CANVAS, FRDA and SCA. Genetic testing has also been proposed for an at-risk individual with a family history of FRDA and SCA. **(Refer to Coverage Limitations section)**

Multigene panels have been proposed to evaluate genes associated with diseases or syndromes. Panels often include medically actionable genes but may also include those with unclear medical management. **(Refer to Coverage Limitations section)**

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 hereditary ataxias 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.

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

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

- Pre- and post-test genetic counseling; **AND**
- Individual to be tested exhibits at least 2 of the following signs and symptoms of CANVAS (progressive gait and limb incoordination, imbalance, dysarthria and disturbances of eye movements); **AND**
- Nongenetic causes of ataxia have been excluded (eg, alcoholism, multiple sclerosis, primary or metastatic tumors or paraneoplastic diseases associated with occult carcinoma of the ovary, breast or lung, vascular disease, vitamin deficiencies)

Testing strategy: Targeted analysis for repeat AAGGG expansions

Friedreich Ataxia (FRDA) (FXN Gene)

Humana members may be eligible under the Plan for **genetic testing** **of *FXN* gene (eg, Genomic Unity FXN analysis [0233U]) to aid in the diagnosis of FRDA** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
- Individual to be tested exhibits at least 2 of the following signs and symptoms of FRDA (progressive gait and limb incoordination, imbalance, dysarthria and disturbances of eye movements); **AND**
- Nongenetic causes of ataxia have been excluded (eg, alcoholism, multiple sclerosis, primary or metastatic tumors or paraneoplastic diseases associated with occult carcinoma of the ovary, breast or lung, vascular disease, vitamin deficiencies)

  Testing strategy: Testing begins with *FXN* expanded allele analysis (looking for expanded GAA repeat in intron 1 of *FXN).* If only 1 abnormal expanded allele is identified, perform sequence analysis. Perform deletion/duplication analysis if no pathogenic variant is detected on sequence analysis.

For information regarding **Skyclarys,** please refer to Skyclarys (omaveloxolone) Pharmacy Coverage Policy.

Spinocerebellar Ataxia (SCA) *(ATXN1, ATXN2, ATXN3, CACNA1A, ATXN7* and *ATN1* Genes)

Humana members may be eligible under the Plan for a **targeted multigene panel** **that includes the following genes: SCAI *(ATXN1* gene), SCA2 *(ATXN2* gene), SCA3 *(ATXN3* gene), SCA6 *(CACNA1A* gene), SCA7 (ATXN7) and dentatorubral-pallidoluysian atrophy (DRPLA) *(ATN1* gene) to aid in the diagnosis of SCA** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
- Individual to be tested exhibits at least 2 of the following signs and symptoms of SCA (progressive gait and limb incoordination, imbalance, dysarthria and disturbances of eye movements); **AND**

- Nongenetic causes of ataxia have been excluded (eg, alcoholism, multiple sclerosis, primary or metastatic tumors or paraneoplastic diseases associated with occult carcinoma of the ovary, breast or lung, vascular disease, vitamin deficiencies)

Testing strategy:

1. Testing begins with single gene or targeted multigene trinucleotide repeat testing of *ATNI, ATXNI, ATXN2, ATXN3, ATXN7* and *CACNAIA*

2. If results of the above gene(s) analysis are normal and a high index of suspicion remains for SCA based on clinical findings, perform single gene trinucleotide repeat testing of any of the following genes:

    - 11q12
    - *AFG3L2*
    - *ATXN10*
    - *ATXN8*
    - *ATXN8O5*
    - *DABI*
    - *ELOVL5*
    - *FGF14*
    - *ITPRI*
    - *KCNC3*
    - *PPP2R2B*
    - *PRKCG*
    - *SPTBN2*
    - *TBP*
    - *TTBK2*

Coverage Limitations

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

- *CACNAIA* full gene sequence analysis (eg, Genomic Unity CACNA1A analysis [0231U]); **OR**

- Determination of risk in an unaffected individual; **OR**
- Genes other than those listed above

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

Humana members may **NOT** be eligible under the Plan for **multigene panels** unless ALL genes in the panel meet disease- or gene-specific criteria (Refer to Coverage Determination section or Limitations section for single genes in a panel). Examples include, but may not be limited to:

- Ataxia Repeat Expansion and Sequence Analysis (eg, Genomic Unity [0216U])
- Comprehensive Ataxia Repeat Expansion and Sequence Analysis (eg, Genomic Unity [0217U])

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

Background

Additional information about **FRDA and SCA** may be found from the following websites:

- MedlinePlus: Genetics
- 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.

CPT® Code(s)	Description	Comments
81177	ATNl (atrophin 1) (eg, dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81178	ATXNl (ataxin 1) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81179	ATXN2 (ataxin 2) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81180	ATXN3 (ataxin 3) (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81181	ATXN7 (ataxin 7) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81182	ATXN8OS (ATXN8 opposite strand [non-protein coding]) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81183	ATXNl0 (ataxin 10) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81184	CACNAIA (calcium voltage-gated channel subunit alphal A) (eg, spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	
81185	CACNAIA (calcium voltage-gated channel subunit alphal A) (eg, spinocerebellar ataxia) gene analysis; full gene sequence	**Not Covered**

81186	CACNAIA (calcium voltage-gated channel subunit alphal A) (eg, spinocerebellar ataxia) gene analysis; known familial variant	
81284	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; evaluation to detect abnormal (expanded) alleles	
81285	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; characterization of alleles (eg, expanded size)	
81286	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; full gene sequence	
81289	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; known familial variant(s)	
81343	PPP2R2B (protein phosphatase 2 regulatory subunit Bbeta) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81344	TBP (TATA box binding protein) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2	
81406	MOLECULAR PATHOLOGY PROCEDURE LEVEL 7	
81407	MOLECULAR PATHOLOGY PROCEDURE LEVEL 8	
81479	Unlisted molecular pathology procedure	**Not Covered if used to report tests outlined in Coverage Limitations section**
96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family	
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	**Not Covered**

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	**Not Covered**
0231U	CACNA1A (calcium voltage-gated channel subunit alpha 1A) (eg, spinocerebellar ataxia), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat {STR) gene expansions, mobile element insertions, and variants in non-uniquely mappable regions	**Not Covered**
0233U	FXN (frataxin) (eg, Friedreich ataxia), gene 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	
0378U	RFC1 (replication factor C subunit 1), repeat expansion variant analysis by traditional and repeat-primed PCR, blood, saliva, or buccal swab	**New Code Effective 04/01/2023**
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	

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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