Genetic Testing for Muscular Dystrophy and Spinal Muscular Atrophy

Humana

Medical Coverage Policy

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Disclaimer

Description

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 Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD), facioscapulohumeral muscular dystrophy (FSHD), myotonic dystrophy, oculopharyngeal muscular dystrophy (OPMD), spinal and bulbar muscular atrophy (SBMA) (also known as Kennedy's disease) and spinal muscular atrophy (SMA).

Genetic testing may also be used for carrier screening of potential parents to identify genetic variants for which they are at risk of passing along to their children.

Carriers may be unaffected but are at risk for producing children who are affected. Preferably, carrier screening takes place before pregnancy, but can take place during the early stages of pregnancy.

For information regarding **preimplantation diagnosis to identify an embryo affected with a muscular dystrophy or SMA,** please refer to Preimplantation Genetic Testing Medical Coverage Policy.

For information regarding **prenatal diagnosis to identify a fetus affected with a muscular dystrophy or SMA,** please refer to Prenatal Invasive Diagnostic Genetic Testing Medical Coverage Policy.

Many laboratories offer multigene panels, often using next-generation sequencing (NGS) technology. With the introduction of NGS, labs can simultaneously analyze numerous genes reportedly associated with muscular dystrophy or SMA. **(Refer to Coverage Limitations Section)**

For information regarding **array comparative genomic hybridization (aCGH) to detect deletions/duplications and/or for full gene sequence analysis for single gene disorders,** please refer to Comparative Genomic Hybridization/Chromosomal Microarray Analysis Medical Coverage Policy.

For information regarding proposed **pharmacological treatments** for Duchenne Muscular Dystrophy (DMD) and Becker Muscular Dystrophy (BMD), please see the following Pharmacy Coverage Policies:

Treatment	**Corresponding Pharmacy Coverage Policy**
casimersen (Amondys 45)	Amondys 45 (casimersen)
deflazacort (Emflaza)	Emflaza (deflazacort)
eteplirsen (Exondys 51)	Exondys 51 (eteplirsen)
golodirsen (Vyondys 53)	Vyondys 53 (golodirsen)

viltolarsen (Viltepso)	Viltepso (viltolarsen)

For information regarding proposed **pharmacological treatments** for Spinal Muscular Atrophy, please see the following Pharmacy Coverage Policies:

Treatment	**Corresponding Pharmacy Coverage Policy**
nusinersen (Spinraza)	Spinraza (nusinersen)
onasemnogene abeparvovec-xioi (Zolgensma)	Zolgensma (onasemnogene abeparvovec-xioi)
risdiplam (Evrysdi)	Evrysdi (risdiplam)

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 muscular dystrophy or SMA 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.

Duchenne Muscular Dystrophy (DMD) or Becker Muscular Dystrophy (BMD) *(DMD* Gene)

Humana members may be eligible under the Plan for ***DMD*** **gene testing** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
  - Carrier screening when the individual to be tested is female; **AND**
    - Has an affected or carrier first-, second- or third-degree relative in whom a disease-causing *DMD* or *BMD* variant has been identified; **OR**

      Testing Strategy: Test for known familial variant (KFV)

    - Has an affected first-degree male relative who is unavailable for testing (eg, deceased, declines genetic testing or unable to contact); **OR**
  - Individual to be tested (see Testing Strategy) exhibits one or more of the following characteristic features of DMD or BMD (eg, cardiomyopathy, progressive symmetric muscular weakness [proximal greater than distal] often with enlargement of calf muscles, delay [DMD] or deterioration [BMD] of motor skills); **AND**
    - Elevated serum creatine kinase (CK) concentration (Normal value ranges may vary slightly among different labs. Some labs use different measurements or test different samples. In males with DMD, serum CK levels are greater than 10 times normal and in BMD 5 times normal. Some female carriers of DMD or BMD have levels 2 to 10 times normal)

Testing Strategy: Testing begins with deletion/duplication analysis of *DMD* gene via serum or saliva. Sequence analysis of *DMD* gene may be considered for an individual with a negative deletion/duplication result (eg, Genomic Unity *DMD* analysis [0218U]).

Facioscapulohumeral Muscular Dystrophy, type 1 (FSHDI) *(D4Z4* Repeat Array)
Humana members may be eligible under the Plan for **FSHDI testing** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
  - Individual to be tested (see Testing Strategy) is affected and has no first-degree relative with a known pathogenic variant; **AND**
    - Exhibits atypical features of FSHDI (eg, scapulohumeral dystrophy with facial sparing, slowly progressive FSHD with progressive external ophthalmoplegia, infantile onset with severe rapidly progressive disease); **OR**
    - Exhibits typical features of FSHDI (eg, scapular winging, facial weakness, protuberant abdomen, exaggerated lumbar lordosis, positive Beevor sign, onset of symptoms by age 20 years of age); **OR**

    Testing Strategy: Test for *D4Z4* repeat. If result is less than or equal to 10 repeats, proceed to A/B allele testing.
  - Individual to be tested is unaffected and has a first-degree relative with a known pathogenic variant **(Testing Strategy:** Test for KFV)

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 (DMI) *(DMPK* gene) and/or myotonic dystrophy type 2 (DM2) *(CNBP* gene) testing** when the following criteria are met:

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

- Individual to be tested (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**

- Individual to be tested is asymptomatic; **AND**

  - At least 18 years of age; **AND**

  - Has an affected first-degree relative with a pathogenic variant **(Testing Strategy:** Test for KFV)

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

Oculopharyngeal Muscular Dystrophy (OPMD) *(PABPN1* Gene)
Humana members may be eligible under the Plan for ***PABPN1* gene testing** when the following criteria are met:

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

  - Carrier screening for couples planning pregnancy or seeking prenatal care who have an affected or carrier first-, second- or third-degree relative with a pathogenic variant **{Testing Strategy:** Test for KFV); **OR**

  - Individual to be tested (see Testing Strategy) has dysphagia (defined as a swallowing time greater than 7 seconds when drinking 80ml of ice-cold water as documented by a swallow study); **AND**

    - Previous corrective surgery for ptosis; **OR**

    - Vertical separation of at least one palpebral fissure that measures less than 8mm at rest

Testing Strategy: *PABPN1* gene sequence analysis or targeted analysis for GCN repeat number in exon 1

Spinal and Bulbar Muscular Atrophy (SBMA) (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:

- Pre- and post-test genetic counseling; **AND**
  - Carrier screening when the individual to be tested is female and has a first-, second- or third-degree relative member with known pathogenic variant of SMBA **(Testing Strategy:** Test for KFV); **OR**
  - Individual to be tested (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)

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

Spinal Muscular Atrophy (SMA) (*SMN1* and *SMN2* Genes)

Humana members may be eligible under the Plan for ***SMN1* and *SMN2* gene testing** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
  - Carrier screening for couples planning pregnancy or seeking prenatal care; **OR**
  - Carrier screening when the individual to be tested is asymptomatic; **AND**
    - Has a family history of SMA or SMA-like disease*; **OR**

- Has an affected or carrier first-, second- or third-degree relative in whom a pathogenic variant has been identified; **OR**

- Is the reproductive partner of an individual affected with or carrier of SMA or SMA-like disease; **OR**

Testing Strategy: Test for KFV

- Confirm diagnosis of newborn screening test that detects an *SMN1* gene pathogenic variant (eg, exon 7 deletion); **OR**

- Individual to be tested (see Testing Strategy) exhibits symptoms of SMA (eg, muscle weakness and atrophy, difficulty swallowing and breathing, developmental delay, absent or markedly decreased deep tendon reflexes)

Testing Strategy: Deletion/duplication analysis of *SMN1/SMN2* genes, full sequence analysis may be considered for an individual with a negative deletion/duplication result (eg, Genomic Unity *SMNl/2* analysis [0236U]).

*SMA includes arthrogryposis multiplex congenital-SMA (AMC-SMA), congenital axonal neuropathy (CAN), SMA0, SMA I (Werdnig-Hoffmann disease), SMA II, SMA III (Kugelberg-Welander disease) and SMA IV.

Coverage Limitations

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

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

- *CNBP* full gene sequence analysis for DM2; **OR**

- OMPKfull gene sequence analysis for DM1

These are considered experimental/investigational as they are not identified as widely used and generally accepted for any other 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 muscular dystrophy or SMA** for any genes, indications or tests other than those listed above including:

- Individual to be tested has an affected first-, second- or third-degree relative with a negative genetic testing result for the associated condition
- Individual to be tested is unaffected and an affected first-, second- or third-degree relative who is available for genetic testing
- KFV detection analysis using either of the following methods:
  - Multigene panel that includes the KFV
  - Sequencing, deletion/duplication analysis or large genomic rearrangement analysis (conducted individually, as comprehensive testing or sequentially) without KFV results of a first, second- or third-degree relative
- Deletion/duplication analysis is performed concurrently with sequencing but is submitted as an independent analysis

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.

Humana members may **NOT** be eligible under the Plan for **genetic testing for facioscapulohumeral muscular dystrophy type 2 (FSHD2)** including, but may not be limited to *SMCHD1* gene. This is 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 **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).** 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 **BMD, DMD, FSHD, myotonic dystrophy OPMD, SBMA and SMA** may be found from the following websites:

- MedlinePlus: Genetics
- National Library of Medicine

Medical Alternatives

Alternatives to **genetic testing for DMD or BMD** include, but may not be limited to, the following:

- Skeletal muscle biopsy for immunocytochemistry and immunoblotting studies of dystrophin

Alternatives to **genetic testing for FSHD and OPMD** include, but may not be limited to, the following:

- Muscle biopsy
- Serum CK

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

Humana may offer a disease management program for these conditions. **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
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed	
81173	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence	**Not Covered**
81174	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant	**Not Covered**
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 (DMI protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles	
81239	DMPK (DMI protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)	
81312	PABPNI (poly[A] binding protein nuclear 1) (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81329	SMNI (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed	
81336	SMNI (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence	
81337	SMNI (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)	

81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2	**Not Covered if used to report any test outlined in Coverage Limitations section**
81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5	
81408	MOLECULAR PATHOLOGY PROCEDURE LEVEL 9	
81479	Unlisted molecular pathology procedure	**Not Covered if used to report any test outlined in Coverage Limitations section**
96040	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family	
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	**Not Covered**
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	
CPT® Category Ill Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
S0265	Genetic counseling, under physician supervision, each 15 minutes	

S3853	Genetic testing for myotonic muscular dystrophy	**Not Covered if used to report any test outlined in Coverage Limitations section**

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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 3 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