Medical Policy

Genetic Testing for Muscular Dystrophies

Table of Contents
- Policy: Commercial
- Coding Information
- Information Pertaining to All Policies
- Policy: Medicare
- Description
- References
- Authorization Information
- Policy History
- Endnotes

Policy Number: 828
BCBSA Reference Number: 2.04.86
NCD/LCD: Local Coverage Determination (LCD): Molecular Pathology Procedures (L35000)

Related Policies
None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Duchenne and Becker Muscular Dystrophy
Genetic testing for DMD gene variants may be considered MEDICALLY NECESSARY under the following conditions:
- In a male with signs and symptoms of a dystrophinopathy in order to confirm the diagnosis and direct treatment.
- For at-risk female relatives:*  
  - To confirm or exclude the need for cardiac surveillance
  - For preconception testing to determine the likelihood of an affected offspring in a woman considering a pregnancy.
- For at-risk male offspring:**
  - To confirm or exclude the need for medical and cardiac surveillance.

*At-risk females are defined as first- and second-degree female relatives and include the proband’s mother, female siblings of the proband, female offspring of the proband, the proband’s maternal grandmother, maternal aunts, and their offspring.

**An at-risk male is defined as an asymptomatic male offspring of a female carrier or an asymptomatic male sibling of a patient with a DMD-associated dystrophinopathy.

Genetic testing for DMD gene variants is considered INVESTIGATIONAL in all other situations.

Emery-Dreifuss Muscular Dystrophy
Genetic testing of LMNA with full sequencing may be considered MEDICALLY NECESSARY in an individual with signs and symptoms suggestive of EDMD.
Genetic testing of EDMD and/or FLHI with full sequencing may be considered **MEDICALLY NECESSARY** in an individual with signs and symptoms suggestive of EDMD when family history is suggestive of X-linked inheritance (i.e. no male-to-male transmission).

Genetic testing for mutations associated with EDMD may be considered **MEDICALLY NECESSARY** in an asymptomatic individual to determine future risk of disease when the individual has:
- A close relative (ie, first- or second-degree relative) with a known mutation consistent with EDMD; AND
- Results of testing will lead to changes in cardiac surveillance, OR
- A close relative (ie, first- or second-degree relative) diagnosed with EDMD whose genetic status is unavailable. AND
- The individual is at-risk for EDMD, based on family history analysis (i.e. related through maternal line if X-linked EDMD), AND
- Results of testing will lead to changes in cardiac surveillance.

Genetic testing for EDMD is considered **INVESTIGATIONAL** in all other circumstances.

**Spinal Muscular Atrophy**
Genetic testing for SMA (gene SMN1) with targeted mutation analysis or gene dosage analysis may be considered **MEDICALLY NECESSARY** in an individual with signs and symptoms suggestive of SMA.

Genetic testing for SMA is considered **INVESTIGATIONAL** in all other circumstances.

**Congenital Muscular Dystrophy**
Genetic testing for congenital MD may be considered **MEDICALLY NECESSARY** for diagnosis confirmation when signs and symptoms of congenital MD are present but a definitive diagnosis cannot be made without genetic testing, and when all of the following criteria are met:
- Results of testing may lead to changes in clinical management (e.g. confirm or exclude need for cardiac and/or ophthalmologic screening); OR Genetic testing will allow the affected patient to avoid invasive testing or screening, including muscle biopsy. AND
- Requested testing is directed toward a specific subtype of CMD based on clinical features and/or family history (i.e., LAMA2, dystroglycanopathy, merosinopathy).

Genetic testing for congenital muscular dystrophy is considered **INVESTIGATIONAL** in all other circumstances.

**Myotonic Dystrophy**
Genetic testing via targeted analysis in DM1 (gene DMPK) may be considered **MEDICALLY NECESSARY** in an individual with signs and symptoms of myotonic dystrophy type 1.

Genetic testing via targeted analysis in DM2 (gene CNBP) may be considered **MEDICALLY NECESSARY** in an individual with signs and symptoms of myotonic dystrophy type 2.

Genetic testing for DM1 or DM2 in an asymptomatic individual ≥ age 18 may be considered **MEDICALLY NECESSARY** when a first or second-degree relative has been diagnosed with DM1 or DM2.

Genetic testing for myotonic dystrophy is considered **INVESTIGATIONAL** in all other circumstances.

**Facioscapulohumeral Muscular Dystrophy**
Genetic testing for facioscapulohumeral muscular dystrophy may be considered **MEDICALLY NECESSARY** to confirm a diagnosis in a patient with clinical signs of the disease.

Genetic testing for facioscapulohumeral muscular dystrophy is **INVESTIGATIONAL** for all other indications.
Collagen VI Disorders
Genetic testing for mutations in COL6A1, COL6A2, COL6A3 associated with collagen VI related disorders may be considered MEDICALLY NECESSARY for diagnosis confirmation when signs and symptoms of a collagen VI related disorder are present but a definitive diagnosis cannot be made without genetic testing, and when at least one of the following criteria are met:

- Results of testing may lead to changes in clinical management; OR
- Genetic testing will allow the individual to avoid invasive testing or screening, including muscle biopsy or sedated muscle MRI.

Genetic testing for collagen VI related disorders is INVESTIGATIONAL for all other indications.

Limb Girdle Muscular Dystrophy
Genetic testing for mutations associated with limb-girdle muscular dystrophy (LGMD) to confirm a diagnosis of LGMD may be considered MEDICALLY NECESSARY when signs and symptoms of LGMD are present and the patient meets at least one criterion in section one AND one criterion in section two:

Section One:
- Results of testing may lead to changes in clinical management that improve outcomes (eg, confirming or excluding the need for cardiac surveillance); OR
- Genetic testing will allow the affected patient to avoid invasive testing, including muscle biopsy.

Section Two:
- The individual has a suspected clinical diagnosis of a specific LGMD subtype and the associated single gene testing is being requested, OR
- Clinical features are not consistent with one LGMD subtype but clinical examination and results of conventional testing are suggestive of LGMD and requested testing is directed toward a specific subset of LGMD based on clinical features and/or family history (e.g., sarcoglycanopathy, autosomal dominant LGMD).

Genetic testing for mutations associated with LGMD may be considered MEDICALLY NECESSARY in an asymptomatic individual to determine future risk of disease when the individual has:

- A close relative (ie, first- or second-degree relative) with a known mutation consistent with LGMD; OR
- A close relative (ie, first- or second-degree relative) diagnosed with LGMD whose genetic status is unavailable. AND
- Results of testing will lead to changes in clinical management (eg, confirming or excluding the need for cardiac surveillance).

Genetic testing for mutations associated with LGMD is considered INVESTIGATIONAL in all other situations.

Panel Testing
Targeted multi-gene panel genetic testing for muscular dystrophies (e.g. Emery-Dreifuss muscular dystrophy, limb girdle muscular dystrophy, and congenital muscular dystrophy) may be considered MEDICALLY NECESSARY when signs and symptoms of a specific muscular dystrophy syndrome are present, and when ALL of the following criteria are met:

- Results of testing will lead to changes in clinical management (e.g. confirm or exclude need for cardiac and/or ophthalmologic screening) OR genetic testing will allow the affected patient to avoid invasive testing or screening, including muscle biopsy, AND
- Requested testing is as targeted as possible based on clinical features and/or family history (e.g., dystroglycanopathy, merosinopathy).

Multi-gene panel genetic testing that includes genes for multiple muscular dystrophy syndromes is considered INVESTIGATIONAL.
Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Medical necessity criteria and coding guidance for Medicare Advantage members living in Massachusetts can be found through the link below.

Local Coverage Determination (LCD): Molecular Pathology Procedures (L35000)

For medical necessity criteria and coding guidance for Medicare Advantage members living outside of Massachusetts, please see the Centers for Medicare and Medicaid Services website for information regarding your specific jurisdiction at https://www.cms.gov.

Prior Authorization Information

Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required. Yes indicates that prior authorization is required. No indicates that prior authorization is not required. N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
</tr>
<tr>
<td>Medicare HMO Blue℠</td>
</tr>
<tr>
<td>Medicare PPO Blue℠</td>
</tr>
</tbody>
</table>

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81161</td>
<td>DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed</td>
</tr>
</tbody>
</table>

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT codes above if medical necessity criteria are met:

<table>
<thead>
<tr>
<th>ICD-10 Diagnosis code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F82</td>
<td>Specific developmental disorder of motor function</td>
</tr>
<tr>
<td>G71.0</td>
<td>Muscular dystrophy</td>
</tr>
<tr>
<td>M62.50</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Site</td>
</tr>
<tr>
<td>M62.511</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Right Shoulder</td>
</tr>
<tr>
<td>M62.512</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Left Shoulder</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>M62.519</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Shoulder</td>
</tr>
<tr>
<td>M62.521</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Right Upper Arm</td>
</tr>
<tr>
<td>M62.522</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Left Upper Arm</td>
</tr>
<tr>
<td>M62.529</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Upper Arm</td>
</tr>
<tr>
<td>M62.531</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Right Forearm</td>
</tr>
<tr>
<td>M62.532</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Left Forearm</td>
</tr>
<tr>
<td>M62.539</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Forearm</td>
</tr>
<tr>
<td>M62.541</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Right Hand</td>
</tr>
<tr>
<td>M62.542</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Left Hand</td>
</tr>
<tr>
<td>M62.549</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Hand</td>
</tr>
<tr>
<td>M62.551</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Right Thigh</td>
</tr>
<tr>
<td>M62.552</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Left Thigh</td>
</tr>
<tr>
<td>M62.559</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Thigh</td>
</tr>
<tr>
<td>M62.561</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Right Lower Leg</td>
</tr>
<tr>
<td>M62.562</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Left Lower Leg</td>
</tr>
<tr>
<td>M62.569</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Lower Leg</td>
</tr>
<tr>
<td>M62.571</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Right Ankle And Foot</td>
</tr>
<tr>
<td>M62.572</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Left Ankle And Foot</td>
</tr>
<tr>
<td>M62.579</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Unspecified Ankle And Foot</td>
</tr>
<tr>
<td>M62.58</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Other Site</td>
</tr>
<tr>
<td>M62.59</td>
<td>Muscle Wasting And Atrophy, Not Elsewhere Classified, Multiple Sites</td>
</tr>
<tr>
<td>M62.81</td>
<td>Muscle weakness (generalized)</td>
</tr>
<tr>
<td>R26.0</td>
<td>Ataxic gait</td>
</tr>
<tr>
<td>R26.1</td>
<td>Paralytic gait</td>
</tr>
<tr>
<td>R26.2</td>
<td>Difficulty in walking, not elsewhere classified</td>
</tr>
<tr>
<td>R26.81</td>
<td>Unsteadiness on feet</td>
</tr>
<tr>
<td>R26.89</td>
<td>Other abnormalities of gait and mobility</td>
</tr>
<tr>
<td>R26.9</td>
<td>Unspecified abnormalities of gait and mobility</td>
</tr>
<tr>
<td>R27.9</td>
<td>Unspecified lack of coordination</td>
</tr>
<tr>
<td>R29.6</td>
<td>Repeated falls</td>
</tr>
<tr>
<td>R53.1</td>
<td>Weakness</td>
</tr>
<tr>
<td>R62.0</td>
<td>Delayed milestone in childhood</td>
</tr>
<tr>
<td>Z31.430</td>
<td>Encounter of female for testing for genetic disease carrier status for procreative management</td>
</tr>
<tr>
<td>Z31.438</td>
<td>Encounter for other genetic testing of female for procreative management</td>
</tr>
<tr>
<td>Z31.440</td>
<td>Encounter of male for testing for genetic disease carrier status for procreative management</td>
</tr>
<tr>
<td>Z31.448</td>
<td>Encounter for other genetic testing of male for procreative management</td>
</tr>
<tr>
<td>Z82.0</td>
<td>Family history of epilepsy and other diseases of the nervous system</td>
</tr>
<tr>
<td>Z84.81</td>
<td>Family history of carrier of genetic disease</td>
</tr>
</tbody>
</table>

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CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81400</td>
<td>Molecular pathology procedure, Level 1 (eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis)</td>
</tr>
<tr>
<td>81401</td>
<td>Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)</td>
</tr>
<tr>
<td>81403</td>
<td>Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of &gt;10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)</td>
</tr>
<tr>
<td>81404</td>
<td>Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)</td>
</tr>
<tr>
<td>81405</td>
<td>Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)</td>
</tr>
<tr>
<td>81406</td>
<td>Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)</td>
</tr>
</tbody>
</table>

Description

Dystrophinopathies
The dystrophinopathies include a spectrum of muscle diseases. The mild end of the spectrum includes asymptomatic increases in serum concentration of creatine phosphokinase and clinical symptoms such as muscle cramps with myoglobinuria and/or isolated quadriceps myopathy. The severe end of the spectrum includes progressive muscle diseases that lead to substantial morbidity and mortality. When skeletal muscle is primarily affected, the disease is classified as Duchenne (DMD) or Becker muscular dystrophy (BMD); when the heart is primarily affected, the disease is classified as DMD-associated dilated cardiomyopathy (left ventricular dilation and heart failure).

Duchenne Muscular Dystrophy
DMD, the most common muscular dystrophy, is a severe childhood X-linked recessive disorder that results in significant disability due to skeletal myopathy and cardiomyopathy. The disease is characterized by progressive, symmetric muscle weakness and gait disturbance resulting from a defective dystrophin gene. According to a 2014 systematic review, the incidence of DMD ranges from 1 in 3600 to 1 in 9300 male births. Approximately one-third of DMD cases arise from de novo variants and have no known family history. Infant males with DMD are often asymptomatic. Manifestations may be present as early as the first year of life in some patients, but clinical manifestations most often appear during preschool, from years 2 to 5. Affected children present with gait problems, calf hypertrophy, positive Gower sign, and difficulty climbing stairs. The affected child’s motor status may plateau between 3 and 6 years of life with deterioration beginning at 6 to 8 years. Most patients will be wheelchair bound by ages 9 to 12 years, but will retain preserved upper-limb function until a later period. Cardiomyopathy occurs after 18 years of age. Late complications are cardiorespiratory (eg, decreased pulmonary function as a result of respiratory muscle weakness and cardiomyopathy). These severe complications commonly appear in the second decade of life and eventually lead to death. Few individuals with DMD survive beyond the third decade.

Becker Muscular Dystrophy
BMD is characterized by later onset skeletal muscle weakness. Individuals remain ambulatory into their 20s. Despite the milder skeletal muscle involvement, heart failure from cardiomyopathy is a common cause of morbidity and the most common cause of death in these patients, with a mean age of death in the mid-40s.
Female Carriers

Females heterozygous for a DMD disease-associated variant can manifest symptoms of the disease. An estimated 2.5% to 7.8% of female carriers are manifesting carriers who develop symptoms ranging from a mild muscle weakness to a rapidly progressive DMD-like muscular dystrophy. Female carriers are at increased risk for dilated cardiomyopathy. Most heterozygous women do not show severe myopathic features of DMD, possibly due to compensation by a normal X chromosome with inactivation of the mutated DMD gene in the affected X chromosome. In some cases, this compensation can be reversed by a nonrandom or skewed inactivation of X chromosome, resulting in greater expression of the affected X chromosome and some degree of myopathic features. Other mechanisms of manifesting female carriers include X chromosome rearrangement involving the DMD gene and complete or partial absence of the X chromosome (Turner syndrome).

Clinical Diagnosis

Duchenne Muscular Dystrophy

Suspicion of DMD should be considered irrespective of family history; it is most commonly triggered by an observation of abnormal muscle function in a male child, the detection of an increase in serum creatine kinase tested for unrelated indications, or detection of increased serum transaminases (aspartate aminotransferase and alanine aminotransferases). Clinical examination by a neuromuscular specialist for DMD includes visual inspection of mechanical function such as running, jumping, climbing stairs, and getting up from the floor. Common presenting symptoms include abnormal gait with frequent falls, difficulties rising from the floor or tip-toe walking, and pseudo hypertrophy of the calves. A clinical examination may reveal decreased or lost muscle reflexes and, commonly, a positive Gower sign. An elevation of serum creatine kinase, at least 10 to 20 times normal levels (between 5000 IU/L and 150,000 IU/L), is nonspecific to DMD but is always present in affected patients. Electromyography and nerve conduction studies were traditional parts of the assessment of neuromuscular disorders, but these tests are may not be necessary for assessment of DMD. An open skeletal muscle biopsy is needed when a test for deletions or duplications of the DMD gene is negative. The biopsy will provide general signs of muscular dystrophy, including muscle fiber degeneration, muscle regeneration, and increased content of connective tissue and fat. Dystrophin analysis on a muscle biopsy will always be abnormal in affected patients but is not specific to DMD.

Becker Muscular Dystrophy

BMD is clinically similar to DMD but is milder and has a later onset. BMD presents with progressive symmetric muscle weakness, often with calf hypertrophy, although weakness of quadriceps femoris may be the only sign. Activity-induced cramping may be present in some individuals, and flexion contractures of the elbows may be present late in the course. Neck flexor muscle strength is preserved, which differentiates BMD from DMD. Serum creatine kinase shows moderate-to-severe elevation (5-100 times the normal level).

Molecular Diagnosis

DMD is the only gene of which variants are known to cause DMD, BMD, and DMD-associated cardiomyopathy. Molecular genetic testing of DMD can establish the diagnosis of a dystrophinopathy without muscle biopsy in most patients with DMD and BMD.

The dystrophinopathies are X-linked recessive and penetrance is complete in males. The gene that codes for dystrophin is the largest known human gene. A molecular confirmation of DMD and BMD is achieved by confirming the presence of a pathogenic variant in this gene by a number of available assays. The large size of the dystrophin gene results in a complex variant spectrum with over 5000 reported disease-associated variants, as well as a high spontaneous de novo variant rate.

Treatment

There is no cure for DMD or BMD. Treatment is aimed at controlling symptoms to improve quality of life. However, the natural history of the disease can be changed by strategies such as corticosteroid therapy, proper nutrition, or rehabilitative interventions. Glucocorticoids were shown in a 1991 randomized controlled trial to prolong the period of independent ambulation by 3 years. The goal of this therapy is to
preserve ambulation and minimize later respiratory, cardiac, and orthopedic complications. Glucocorticoids work by decreasing inflammation, preventing fibrosis, improving muscle regeneration, improving mitochondrial function, decreasing oxidative radicals, and stopping abnormal apoptosis pathways. Bone density measurement and immunization are prerequisites for corticosteroid therapy initiation, which typically begins at 2 to 5 years of age, although there has been no demonstrated benefit of therapy before 5 years of age.

New therapeutic trials require accurate diagnoses of these disorders, especially when the therapy is targeted at specific pathogenic variants. Exon-skipping is a molecular therapy aimed at skipping the transcription of a targeted exon to restore a correct reading frame using antisense oligonucleotides. Exon-skipping may result in a DMD protein without the mutated exon and a normal, nonshifted reading frame. Exon-skipping may also restore DMD protein function so that the treated patient’s phenotypic expression more closely resembles BMD. Several therapies are currently in clinical trials and an exon-skipping therapy using antisense oligonucleotides (eteplirsen [Exondys 51]) has been approved for treatment for patients who have a confirmed variant of the dystrophin gene amenable to exon 51 skipping.

Summary
For individuals who are male and have signs and symptoms of a dystrophinopathy who receive genetic testing for DMD gene variants to confirm diagnosis without biopsy, the evidence includes case series and database entries describing screening and results of types of variants found in patients with clinical signs of DMD or BMD. Relevant outcomes are test accuracy and validity, symptoms, change in disease status, morbidity events, quality of life, medication use, and resource utilization. Virtually all males with DMD or BMD have identifiable DMD disease-associated variants, indicating a high clinical sensitivity for genetic testing. The clinical utility of DMD gene testing can be established for the index case to confirm the diagnosis without a muscle biopsy, to initiate effective treatment, and to distinguish between DMD and the less severe BMD. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are female and are a relative of a patient with a DMD-associated dystrophinopathy who receive targeted DMD testing for a known familial variant to determine carrier status, the evidence includes case series and database entries describing screening and results of types of variants found in patients with clinical signs of DMD or BMD. Relevant outcomes are test accuracy and validity, changes in reproductive decision making, symptoms, change in disease status, morbidity events, quality of life, medication use, and resource utilization. Published data for the clinical validity for testing for a known familial variant are lacking, but is expected to be high. Direct evidence on the clinical utility of DMD gene testing in at-risk female relatives is lacking. However, the chain of evidence is strong, because determination of carrier status in a female for a DMD familial variant necessitates or eliminates the need for routine cardiac surveillance and can indicate the likelihood of an affected offspring in women considering children. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are asymptomatic male offspring of a female DMD familial variant carrier or an asymptomatic male sibling of a patient with a DMD-associated dystrophinopathy who receive targeted DMD testing for a known familial variant to determine DMD status, the evidence includes case series and database entries. Relevant outcomes are test accuracy and validity, symptoms, change in disease status, morbidity events, quality of life, medication use, and resource utilization. Published data for clinical validity of testing for a known familial variant are lacking, but is expected to be high. Direct evidence on the clinical utility of DMD gene testing in asymptomatic male offspring of a female DMD familial variant carrier or male sibling of a patient with a DMD-associated dystrophinopathy is lacking. However, the chain of evidence is strong, because detection of the DMD familial variant necessitates or eliminates the need for increased medical surveillance or cardiac surveillance in an asymptomatic male of a female carrier or the asymptomatic male sibling of a patient with a DMD-associated dystrophinopathy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.
Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/2017</td>
<td>BCBSA National medical policy review. The policy statement was updated to add a third indication for male offspring of female carriers and male sibling of affected male. “Mutations” was changed to “variants.” Effective 8/1/2017.</td>
</tr>
</tbody>
</table>

Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:
- [Medical Policy Terms of Use](#)
- [Managed Care Guidelines](#)
- [Indemnity/PPO Guidelines](#)
- [Clinical Exception Process](#)
- [Medical Technology Assessment Guidelines](#)

References

11. Kang PB1, Morrison L1, Iannaccone ST1, Graham RJ1, Bönnemann CG1, Rutkowski A1, Hornyak J1, Wang CH1, North K1, Oskouei M1, Getchius TS1, Cox JA1, Hagen EE1, Gronseth G1, Griggs RC1; Guideline Development Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine.


Endnotes

1 Based on BCBSA MPRM 2.04.86
2 Based on expert opinion