

Genetic Testing for Dystrophinopathies (Duchenne and Becker Muscular Dystrophy)

Policy Number: PG0411 Last Review: 07/09/2019 HMO & PPO MARKETPLACE MEDICARE – ELITE, MAP

GUIDELINES

- This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.
- Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.
- This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.

SCOPE

X Professional

X Facility

DESCRIPTION

Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are neuromuscular diseases caused by a pathogenic variant or mutation in the dystrophin (DMD) gene, which is located on the X chromosome at band p21. Duchenne muscular dystrophy typically presents in early childhood with delayed motor skills due to skeletal weakness (i.e., sitting, standing, walking, etc.). Duchenne muscular dystrophy is rapidly progressive and typically causes children to be wheelchair dependent by age 12. Additionally, cardiomyopathy affects almost all individuals as they approach adulthood. Becker muscular dystrophy is associated typically with milder and more varied symptoms in comparison to Duchenne muscular dystrophy. As with Duchenne, many individuals with Becker muscular dystrophy are affected by cardiomyopathy. Since DMD and BMD are inherited in an X-linked manner, the conditions primarily affect males (since they have only 1 X chromosome and therefore just 1 copy of the DMD gene). Most carrier females (who have 2 X chromosomes with 1 normal copy of DMD and 1 with a pathogenic DMD variant) are asymptomatic, however do have an increased risk for cardiomyopathy. The incidence of DMD and BMD in boys is approximately 1 in 3500 and 1 in 18,500, respectively.

Some individuals with a DMD mutation will have DMD-associated dilated cardiomyopathy with congestive heart failure. This typically presents in males between ages 20-40 and and females presenting later in life. Individuals with DMD-associated dilated cardiomyopathy do not typically have evidence of skeletal disease; some call this "subclinical" BMD. Males with DMD-associated dilated cardiomyopathy tend to have rapid progression of their disease course, whereas females have a slower progression.

There is no cure for DMD or BMD with primarily symptomatic treatment to improve quality of life and impact survival. Studies suggest a positive impact of corticosteroids (in slowing the decline in muscle strength and function in DMD); other treatments include pharmacologic interventions, cardiac medical therapy, pulmonary ventilation, nutrition management, orthesis (device used in orthopedics such as a brace), physical therapy, psychosocial support, and surgery for tendon retractions and scoliosis. There are ongoing clinical trials related to gene therapy to decrease disease severity.

DMD gene deletions and duplications are identified by multiplex ligation-dependent probe amplification (MLPA) or

array comparative genomic hybridization (aCGH), while sequence variants are detected by direct sequence analysis and/or next-generation sequencing (NGS). *DMD* gene testing may be considered in males or females with symptoms of DMD or BMD. In addition, it may be performed in female relatives of patients with 1 of these conditions, after a pathogenic variant is identified in a symptomatic individual, for the purpose of carrier identification. Prenatal testing and preimplantation genetic diagnosis (PGD) are also possible for families with a previously identified pathogenic DMD variant.

Finally, studies regarding clinical utility of *DMD* gene testing show that testing allows for carrier identification, prenatal diagnosis, and PGD, and may be of value for family planning and reproductive decision making. Studies demonstrated that genetic testing can identify carrier status in more females than previous methods and is more accurate. Recognition of carrier status allows for cardiac surveillance due to the increased risk for cardiomyopathy.

POLICY

Paramount Commercial Insurance Plans, Medicare Advantage Plans, and Paramount Advantage Medicaid

Paramount Commercial Insurance Plans and Paramount Advantage Medicaid

Genetic testing for *DMD* gene mutations (81161, 81408) requires prior authorization for Paramount Commercial Insurance Plans and Paramount Advantage Medicaid.

<u>Medicare Advantage Plans</u> Genetic testing for DMD gene mutations (81161, 81408) is non-covered for Medicare Advantage Plans.

COVERAGE CRITERIA

Paramount Commercial Insurance Plans and Paramount Advantage Medicaid

Genetic testing for *DMD* gene mutations is considered medically necessary when the following criteria are met:

- 1. Carrier screening when the individual to be tested is an asymptomatic female and has an affected blood relative in whom a DMD mutation has been identified. (Note: Test for known mutation); OR
- 2. Individual to be tested* exhibits characteristic features of DMD or BMD (e.g., progressive symmetric muscular weakness [proximal ≥ distal] often with calf hypertrophy, delay (DMD) or deterioration (BMD) of motor skills); and individual has elevated serum creatine kinase (CK) concentration. (Note: normal value ranges may vary slightly among different labs. Some labs use different measurements or test different samples. Additionally, serum CK levels tend to gradually decrease with increasing age due to progressive elimination of dystrophic muscle fibers. In males with DMD, serum CK levels ≥ than 10 times normal and >5 times normal in BMD. Some female carriers of DMD or BMD have levels 2-10 times normal)

*Testing strategy: testing begins with deletion/duplication analysis of DMD gene. Sequence analysis of DMD gene may be considered for individuals with a negative deletion/duplication result.

CODING/BILLING INFORMATION

The inclusion or exclusion of a code in this section does not necessarily indicate coverage. Codes referenced in this clinical policy are for informational purposes only.

Codes that are covered may have selection criteria that must be met.

Payment for supplies may be included in payment for other services rendered.

CPT CODES	
81161	DMD (dystrophin) (e.g., Duchenne/Becker muscular dystrophy) deletion analysis and duplication
	analysis, if performed
81408	Molecular pathology procedure, Level 9 (e.g., analysis of >50 exons in a single gene by DNA
	sequence analysis) –includes DMD (dystrophin) (e.g., Duchenne/Becker muscular dystrophy), full
	gene sequence

REVISION HISTORY EXPLANATION ORIGINAL EFFECTIVE DATE: 09/22/2017

Date	Explanation & Changes
09/22/2017	 Policy created to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
09/27/2018	 Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
07/09/2019	 Updated title to state Dystrophinopathies to encompass the phenotypes tied to DMD Added information in the description section to further detail the phenotypes associated with DMD mutations Minor changes to the testing criteria verbiage Added references
12/28/2020	 Medical policy placed on the new Paramount Medical policy format
03/02/2023	 Medical Policy updated to reflect Medicaid coverage to Anthem as of 02/01/2023

Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to https://www.paramounthealthcare.com/services/providers/medical-policies/.

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services

Ohio Department of Medicaid

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets

U.S. Preventive Services Task Force, <u>http://www.uspreventiveservicestaskforce.org/</u> Industry Standard Review

Hayes, Inc.

Industry Standard Review

Darras, BT, et al. GeneReviews®, Dystrophinopthies

Genetics Home Reference, National Institute of Health, U.S. National Library of Medicine, Duchenne and Becker muscular dystrophy