BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 08/17/23**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE: 08/15/24**
	CURRENT EFFECTIVE DATE: 08/15/24
	LAST CRITERIA REVISION DATE: 08/15/24
NEXT ANNUAL REVIEW DATE: 3RD QTR 2025	**ARCHIVE DATE:**

GENE THERAPY FOR DUCHENNE MUSCULAR DYSTROPHY:

- **ELEVIDYS (delandistrogene moxeparvovec-rokl)**

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for therapy:** Elevidys (delandistrogene moxeparvovec-rokl) injection for the treatment of Duchenne muscular dystrophy (DMD) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in Duchenne muscular dystrophy (DMD) or is in consultation with a specialist in Duchenne muscular dystrophy such as Pediatric Neurologist or Neurologist

  2. Individual is male age 4 or 5 years old at the time of infusion

  3. Individual has a confirmed diagnosis of Duchenne muscular dystrophy (DMD) with **ALL** of the following:

     - Documentation of variant in the *DMD* gene
     - Documentation that there is not a deletion in exons 1 to 17 and/or exons 59 to 71 in the *DMD* gene

  4. Individual meets **ALL** the following baseline tests before initiation of treatment and with continued monitoring of the individual as clinically appropriate:

     - Anti-adeno associated virus serotype rh74 (AAVrh74) antibody titer is < 1:400
     - Liver function tests (GGT, total bilirubin)
     - Platelet count
     - Troponin-I
     - Motor function and milestone assessed including **BOTH** of the following:

       a. North Star Ambulatory Assessment (NSAA)
       b. 10 Meter Walk Test (10MWT)

  5. Individual has not received any prior gene therapy and is not being considered for treatment with any other gene therapy

  6. Individual is ambulatory without need for assistive device (e.g., cane, walker, wheelchair, etc.)

  7. Provider attests that Duvyzat (givinostat) and exon-skipping therapies [e.g., Amondys 45 (casimersen), Exondys 51 (eteplirsen), Viltepso (viltolarsen), Vyondys 53 (golodirsen)] will be discontinued and not restarted following Elevidys treatment

  8. There are **NO** contraindications including individuals with any deletion in exon 8 and/or exon 9 in the *DMD* gene

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Approval duration: **ONE** injection per lifetime.
The safety and effectiveness of repeat administrations of Elevidys (delandistrogene moxeparvovec-rokl) have not been evaluated.

- Elevidys (delandistrogene moxeparvovec-rokl) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any one or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration
- Use of Elevidys in individuals under 4 years of age or older than 5 years of age
- Use of Elevidys in non-ambulatory individuals
- Concurrent use of Elevidys with Duvyzat (givinostat) or exon-skipping therapies [e.g., Amondys 45 (casimersen), Exondys 51 (eteplirsen), Viltepso (viltolarsen), Vyondys 53 (golodirsen)]
- Repeat treatment of Elevidys

Description:

Duchenne muscular dystrophy (DMD) is a rare, genetic, X-linked, recessive neuromuscular disorder that primarily afflicts young boys; however, female-manifesting carriers are reported. The disorder is caused by mutations of the dystrophin gene that leads to a disruption in messenger ribonucleic acid resulting in an absence or near absence of dystrophin within muscle cells. Dystrophin is thought to maintain the structural integrity of muscle cell, cushioning it from the stress and strain of repeated contraction and relaxation. Absence of dystrophin leads to muscle damage, with fibrotic and adipose tissue deposition.

Clinical onset of weakness usually occurs between two to three years of age, although affected individuals are often late walkers. Weakness selectively affects proximal before distal limb muscles, and the lower before upper extremities. Wheelchairs are often required by age 12 to 13 years. DMD also causes a primary dilated cardiomyopathy and conduction abnormalities. Symptomatic cardiomyopathy gradually increases in the teenage years. Mortality is common in late teens or twenties from respiratory failure of cardiomyopathy.

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There is no cure for DMD. Glucocorticoids are the mainstay of pharmacologic treatment. Some DMD individuals are candidates for exon skipping therapy that are designed to restore dystrophin expression, but these therapies are lacking studies to determine clinical benefit.

Elevidys (delandistrogene moxeparvovec-rokl) is an adeno-associated virus vector-based gene therapy indicated for the treatment of individuals at least 4 years of age:

- For the treatment of DMD in patients who are ambulatory and have a confirmed mutation in the *DMD* gene
- For the treatment of DMD in patients who are non-ambulatory and have a confirmed mutation in the *DMD* gene. The DMD indication in non-ambulatory patients is approved under accelerated approval based on expression of Elevidys micro-dystrophin. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Elevidys was studied in 3 controlled trials to determine safety and efficacy. Study 1 and 3 are in ambulatory male individuals ages 4 to 7. Study 2, which is ongoing, has multiple cohorts and is evaluating individuals ages 3 to 20 including some non-ambulatory individuals. However, Study 2 had a primary outcome to evaluate the effect on a surrogate marker, micro-dystrophin expression and not clinical benefit.

Study 1: The study showed there was no clinically significant difference in the North Start Ambulatory Assessment (NSAA) total score between Elevidys (n=20) and placebo (n=21) (p=0.37). A subset of ages 4 to 5 years of age demonstrated numerical benefit in the least squares (LS) mean change in NSAA while ages 6 through 7 showed a disadvantage for Elevidys. This was the basis for the accelerated approval for ages 4 to 5 years of age in 2023.

Study 2: Cohorts 1, 2, and 3 evaluated ambulatory males with any mutation in the DMD gene. Cohort 4 included patients with mutations in the DMD gene starting at 18 or higher. Cohort 5 had mutations that partially or fully overlapped with exons 1-17 in the DMD gene. Cohorts 1, 2, 4, and 5a (n=40) were ambulatory individuals ages 3-12. Cohorts 3 and 5b (n=8) were non-ambulatory individuals 10 to 20 years of age.

Study 3: This study in ambulatory males ages 4 to 7 did not show a clinical benefit in the primary outcome of change in NSAA scores in Elevidys (n=63) compared to placebo (n=61). However, clinical relevance was reported in three secondary efficacy endpoints: times to rise from floor, 10-meter walk/run, and time to ascend 4 steps.

Except for ambulatory individuals ages 4 and 5 years old, there is insufficient scientific evidence to permit conclusions concerning the effect on health outcomes and insufficient evidence to support improvement of the net health outcome.

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Definitions:

North Star Ambulatory Assessment (NSAA): NSAA is a validated rating scale used to measure the impact of DMD on ambulatory performance. A higher total score represents better functional performance. Natural history studies show a precipitous decline in the NSAA score for boys with Duchenne after they peak around the age of six.

Age 3: Assess 1-8 for maximum score 16
Age 3 ½: Assess 1-13 for maximum score 26
Age 4-5: Assess 1-17 for maximum score 34

NSAA Assessed Skill	Score
1. Stand	
2. Walk	
3. Rise from chair	
4. Climb step (right leg)	
5. Climb step (left leg)	
6. Gets to sitting	
7. Jump	
8. Run	
9. Stand on right leg	
10. Stand on left leg	
11. Descend box step (right leg)	
12. Descend box step (left leg)	
13. Stand on heels	
14. Rise from floor	
15. Lift head	
16. Hop on right leg	
17. Hop on left leg	
Total	

0= Unable to perform task
1= Able to perform the task, but needed assistance or completed the task independently but struggled
2= Can perform task independently, without difficulty

10 Meter Walk Test (10MWT): The 10MWT assesses walking speed in meters per second over a short duration. 10 meters is marked out on the floor with markings at 2 meters and 8 meters. The individual walks (or runs) as quickly as and is timed for the middle 6 meters (from the 2 meter to 8 meter mark). This is repeated and an average over 3 trials should be recorded.

History:	**Date:**	**Activity:**
Pharmacy and Therapeutics Committee	08/15/24	Review with revisions: criteria
Pharmacy and Therapeutics Committee	03/01/24	Revisions to guideline
Pharmacy and Therapeutics Committee	02/15/24	Revisions to guideline

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Pharmacy and Therapeutics Committee	08/17/23	Approved guideline
Clinical Pharmacist	08/04/23	Development

Coding:

HCPCS: J1413

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Resources:

Literature reviewed 08/15/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Darras BT, Duchenne and Becker muscular dystrophy: Clinical features and diagnosis. In: UpToDate, Patterson MC, Firth HV, Dashe JF (Eds), UpToDate, Waltham, MA. Available at https://uptodate.com. Topic last updated June 22, 2022. Accessed June 25, 2024.

2. Darras BT, Duchenne and Becker muscular dystrophy: Glucocorticoid and disease-modifying treatment. In: UpToDate, Patterson MC, Dashe JF (Eds), UpToDate, Waltham, MA. Available at https://uptodate.com. Topic last updated April 23, 2024. Accessed June 25, 2024.

3. Elevidys (delandistrogene moxeparvovec-rokl). Prescribing information, Sarepta Therapeutics, Inc.; June 2024, at DailyMed http://dailymed.nlm.nih.gov. Accessed June 20, 2024.

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Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html