MASSACHUSETTS

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Medical Policy

Gene Therapies for Duchenne Muscular Dystrophy

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Policy Number: 022

BCBSA Reference Number: N/A
NCD/LCD: N/A

Related Policies

Prior Authorization Request Form for Elevidys ™ (delandistrogene moxeparvovec-rokl), #025

Policy

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

Delandistrogene moxeparvovec-rokl (Elevidys)

Delandistrogene moxeparvovec-rokl (Elevidys) may be considered **MEDICALLY NECESSARY** for the treatment of Duchenne muscular dystrophy (DMD) in patients who meet **ALL** of the following criteria:

1. Diagnosis of DMD by or in consultation with a pediatric neuromuscular specialist in DMD with:
    a. A confirmed mutation in the DMD gene; **AND**
    b. Mutation is not a deletion in exon 8 and/or 9; **AND**
2. Elevidys is prescribed by or in consultation with a pediatric neuromuscular specialist in DMD; **AND**
3. Patient is 4 - 5 years old; **AND**
4. Patient is ambulatory without need of assistive devices (e.g., cane, walker, wheelchair, side-by-side assistance, etc.) as determined by medical records or physician attestation; **AND**
5. Patient does not have an anti-AAVrh74 total binding antibody titer ≥ 1:400; **AND**
6. Patient is on a corticosteroid regimen:
    a. Stable corticosteroid regimen defined as ≥ 12 weeks prior to screening for Elevidys infusion and following infusion; **OR**
    b. Corticosteroid is not medically/clinically appropriate as per managing provider's recommendations; **AND**
7. Patient has not previously received a gene therapy with Elevidys in their lifetime; **AND**
8. Prescriber attestation patient will not receive any exon skipping therapies for DMD [e.g., Amondys (casimersen), Exondys 51 (eteplirsen), Viltepso (viltolarsen), Vyondys 53 (golodirsen)] concomitantly or following treatment with Elevidys; **AND**
9. Prescriber will assess liver function, platelets, and troponin-I levels prior to Elevidys infusion.

Note: Pre-existing active coverage authorizations for EXONDYS 51, VYONDYS 53, and AMONDYS 45, will not be prematurely discontinued at the time of Elevidys approval as long as the exon-skipping drugs continue to be deemed medically necessary by the Healthcare Provider, and until the patient receives treatment with delandistrogene moxeparvovec-rokl. To support the data requirements for an outcomes-based agreement on this drug, the prescriber is encouraged to provide ongoing clinical information upon request by Plan or Plan's authorized representative (Evio Pharmacy Solutions).

Coverage Limitation:
Authorization will be for no more than one lifetime treatment.
Length of authorization of 180 days from date of approval or up to 6 years of age, which ever comes first.

Note: The safety and effectiveness of repeat administration of delandistrogene moxeparvovec-rokl has not been evaluated. Therefore, coverage will be limited to once per lifetime.

The use of delandistrogene moxeparvovec-rokl that does not meet the criteria as indicated in this policy is considered **EXPERIMENTAL/INVESTIGATIONAL** and therefore non-covered because the safety and/or effectiveness of this service cannot be established by the available published peer-reviewed literature.

Delandistrogene moxeparvovec-rokl is considered **INVESTIGATIONAL** when the above criteria are not met.

Repeat treatment of Delandistrogene moxeparvovec-rokl is considered **INVESTIGATIONAL.**

Delandistrogene moxeparvovec-rokl is considered **INVESTIGATIONAL** for all other indications.

Policy Guidelines
Recommended Dose: The minimum recommended dose is 1.33×10^{14} vector genomes (vg) per kg of body weight.
Dosing Limits: 1 injection per lifetime

Other Considerations:
Due to the risk of acute liver injury, liver function should be monitored before Elevidys infusion, with a weekly monitoring for the first 3 months post infusion. Monitoring should continue until results are unremarkable. Consultation with a specialist is recommended if acute liver injury is suspected.

Elevated troponin-I levels and myocarditis has been observed. It is recommended to monitor troponin-I levels before infusion and weekly subsequently for the first month after Elevidys.

Prior Authorization Information

Inpatient
- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient
- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **required**.
Commercial PPO and Indemnity	Prior authorization is **required.**
Medicare HMO Blue℠	Prior authorization is **required.**
Medicare PPO Blue℠	Prior authorization is **required.**

Requesting Prior Authorization Using Authorization Manager
Providers will need to use Authorization Manager to submit initial authorization requests for services. Authorization Manager, available 24/7, is the quickest way to review authorization requirements, request

authorizations, submit clinical documentation, check existing case status, and view/print the decision letter. For commercial members, the requests must meet medical policy guidelines.

To ensure the request is processed accurately and quickly:
- Enter the facility's NPI or provider ID for where services are being performed.
- Enter the appropriate surgeon's NPI or provider ID as the servicing provider, *not* the billing group.

Authorization Manager Resources
- Refer to our Authorization Manager page for tips, guides, and video demonstrations.

Complete Prior Authorization Request Form for Elevidys (delandistrogene moxparvovec-rokl) (025) using Authorization Manager.

For out of network providers: Requests should still be faxed to 888-973-0726.

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, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
J1413	Injection, delandistrogene moxeparvovec-rokl, per therapeutic dose (Elevidys)
J3590	Unclassified biologics
J3490	Unclassified drugs
C9399	Unclassified drugs or biologicals

ICD-10 Diagnosis Code

ICD-10 Diagnosis Code	Code Description
G71.01	Duchenne or Becker muscular dystrophy

SUMMARY

Background

Duchene Muscular Dystrophy (DMD)

Duchenne muscular dystrophy (DMD) is a progressive, X-linked, degenerative neuromuscular disease that results in disabling muscle weakness and eventually leads to early death. DMD is caused by mutations in the dystrophin gene resulting in reduced or near absence of dystrophin, a protein that helps keep muscle cells intact. The estimated incidence of DMD is 1 in 3500–5000 male births (i.e., 400 to 600 boys per year) with prevalence estimates ranging between 10,000 and 15,000 males. Boys are typically diagnosed at 4-5 years of age. As the disease progresses, muscle weakness and atrophy spread to affect additional muscles of the body. By the early teenage years, patients will typically require a wheelchair and serious life-threatening complications may ultimately develop including cardiomyopathy and respiratory difficulties. DMD mainly affects males and in rare cases may affect females. Although disease severity

and life expectancy vary, patients often succumb to the disease in their 20s or 30s because of heart and/or respiratory failure.[1-4]

Currently, there are two main therapeutic approaches in use for the treatment of DMD. Therapies aimed at improving muscle that target the downstream pathological changes of DMD and therapies aimed at restoring dystrophin function. Pharmacological treatment with corticosteroids, such as prednisone and Emflaza, are the mainstay of DMD treatment strategies because of their beneficial effects for improving motor function and pulmonary function, reducing the risk of scoliosis, delaying the loss of ambulation, and possibly for delaying progression of cardiomyopathy and improving survival. Gene-based therapies that involve exon skipping (Exondys 51, Vyondys 53, Viltepso, Amondys 45) are approved for the treatment of DMD. These therapies increase dystrophin expression, but clinical benefit is still to be established.

Gene Therapy for DMD
The dystrophin gene is one of the largest in the human genome (2.3 million base pairs, over 11,000 of which are for coding). Because of the gene's size, it is difficult to insert the complete coding DNA sequence for dystrophin into a viral vector. The carrying capacity of AAVs is approximately 4.7 kilobases. Therefore, rather than use the full dystrophin gene (2200 kb in size), the gene therapy technology uses a smaller, modified gene that produces shortened forms of dystrophin, called micro-dystrophin (3.5-4 kb in size) and mini-dystrophin (6-8 kb in size).

Both micro- and mini-dystrophin have been designed to function like normal dystrophin protein requiring that these smaller treatments are delivered at high doses.

Elevidys is a recombinant gene therapy designed to deliver into the body a gene that leads to production of Elevidys microdystrophin, a shortened protein (138 kDa, compared to the 427 kDa dystrophin protein of normal muscle cells) that contains selected domains of the dystrophin protein present in normal muscle cells.[1-4]

Summary of Evidence

Accelerated approval was primarily based on data from Study 1 and Study 2 described below.
Study 1 is an ongoing multi-center study including:

- Part 1: a 48-week, randomized, double-blind, placebo-controlled period
- Part 2: a 48-week period that began following completion of Part 1. Patients who received placebo during Part 1 were treated with ELEVIDYS, and patients treated with ELEVIDYS during Part 1 received placebo.

The study population consisted of male ambulatory DMD patients (N=41) aged 4 through 7 years with either a confirmed frameshift mutation, or a premature stop codon mutation between exons 18 to 58 in the *DMD* gene.

All subjects were on a stable dose of corticosteroids for DMD for at least 12 weeks prior to ELEVIDYS infusion. All randomized subjects had baseline anti-AAVrh74 antibody titers <1:400 as determined by an investigational total binding antibody ELISA.

One day prior to treatment with ELEVIDYS or placebo, the subject's background dose of corticosteroid for DMD was increased to at least 1 mg/kg of a corticosteroid (prednisone equivalent) daily and was continued at this level for at least 60 days after the infusion, unless earlier tapering was clinically indicated.

The primary objectives of Study 1 were to evaluate expression of ELEVIDYS micro-dystrophin in skeletal muscle, and to evaluate the effect of ELEVIDYS on the North Star Ambulatory Assessment (NSAA) total score.

Patients were randomized 1:1 to receive either ELEVIDYS (N=20) or placebo (N=21), as a single intravenous infusion via a peripheral limb. Randomization was stratified by age (i.e., aged 4 to 5 years vs.

aged 6 to 7 years). In the ELEVIDYS group, eight patients received 1.33 × 1014 vg/kg of ELEVIDYS, and 12 patients received lower doses.

The change in NSAA total score was assessed from baseline to Week 48 after infusion of ELEVIDYS or placebo. The difference between the ELEVIDYS and placebo groups was not statistically significant (p=0.37). The least squares (LS) mean changes in NSAA total score from baseline to Week 48 was 1.7 (standard error [SE]: 0.6) points for the ELEVIDYS group and 0.9 (SE: 0.6) points for the placebo group.

Exploratory subgroup analyses showed that for subjects aged 4 through 5 years, the LS mean changes (SE) in NSAA total score from baseline to Week 48 were 4.3 (0.7) points for the ELEVIDYS group, and 1.9 (0.7) points for the placebo group, a numerical advantage for ELEVIDYS. For subjects aged 6 through 7 years, the LS mean changes (SE) in NSAA total score from baseline to Week 48 were -0.2 (0.7) points for the ELEVIDYS group and 0.5 (0.7) points for the placebo group, a numerical disadvantage for ELEVIDYS.

Study 2 is an ongoing, open-label, multi-center study which includes a cohort of 20 ambulatory male DMD subjects aged 4 through 7 years. All 20 subjects have a confirmed frameshift mutation, canonical splice site mutation, or premature stop codon mutation in the *DMD* gene.

At study entry, 75% of subjects were white with a mean age of 5.81 years (range: 4.38 to 7.94), mean weight of 21.2 kg (range: 15.2 to 33.1), mean NSAA total score of 22.1 points (range: 18 to 26), and mean time to rise from floor of 4.2 seconds (range: 2.4 to 8.2). Subjects received corticosteroids for DMD before infusion. All subjects had baseline anti-AAVrh74 antibodies titers <1:400 as determined by the investigational total binding antibody ELISA and received a single intravenous infusion of 1.33 × 1014 vg/kg ELEVIDYS.

The primary objective of the study was to evaluate the effect of ELEVIDYS micro-dystrophin expression as measured by western blot.

Micro-Dystrophin Expression in Studies 1 and 2 (Western Blot Assay) [abcd]

Western blot (% of ELEVIDYS micro-dystrophin compared to control)	**Study 1 (Week 12) Part 1 (n = 6)**	**Study 1 (Week 12) Part 2 (n=21)**	**Study 2 (Week 12) Cohort 1 (n = 20)**
Mean change from baseline (SD)	43.4 (48.6)	40.7 (32.3)	54.2 (42.6)
Median change from baseline (Min, Max)	24.3 (1.6, 116.3)	40.8 (0.0, 92.0)	50.6 (4.8, 153.9)

a All patients received 1.33 x 1014 vg/kg, as measured by ddPCR
b Muscle biopsies were obtained from the gastrocnemius
c Change from baseline was statistically significant
d Adjusted for muscle content. Control was level of wild-type (normal) dystrophin in normal muscle

Policy History

Date	Action
3/2024	Clarified coding information and updated to add a note for Outcomes-based contracts.
9/2023	Policy clarified to include prior authorization requests using Authorization Manager.
8/2023	New medical policy describing medically necessary and investigational indications. Effective 8/9/2023.

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

1. Elevidys [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; August 2023.
2. Mendell JR, Sahenk Z, Lehman K, Nease C, Lowes LP, Miller NF, Iammarino MA, Alfano LN, Nicholl A, Al-Zaidy S, Lewis S, Church K, Shell R, Cripe LH, Potter RA, Griffin DA, Pozsgai E, Dugar A, Hogan M, Rodino-Klapac LR. Assessment of Systemic Delivery of rAAVrh74.MHCK7. micro-dystrophin in Children With Duchenne Muscular Dystrophy: A Nonrandomized Controlled Trial. JAMA Neurol. 2020 Sep 1;77(9):1122-1131.
3. A Phase 3 Multinational, Randomized, Double-Blind, Placebo-Controlled Systemic Gene Delivery Study to Evaluate the Safety and Efficacy of SRP-9001 in Subjects with Duchenne Muscular Dystrophy (EMBARK). ClinicalTrials.gov identifier: NCT05096221. Updated November 15, 2022.
4. A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial for Duchenne Muscular Dystrophy Using SRP-9001. ClinicalTrials.gov identifier: NCT03769116. Updated July 1, 2022.