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Delandistrogene moxeparvovec-rokl

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Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current peer-reviewed scientific literature. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and acceptable standards of medical practice. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For Illinois only: Illinois Public Act 103-0458 [Insurance Code 215 ILCS 5/356z.61] (HB3809 Impaired Children) states all group or individual fully insured PPO, HMO, POS plans amended, delivered, issued, or renewed on or after January 1, 2025 shall provide coverage for therapy, diagnostic testing, and equipment necessary to increase quality of life for children who have been clinically or genetically diagnosed with any disease, syndrome, or disorder that includes low tone neuromuscular impairment, neurological impairment, or cognitive impairment.

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug

approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Delandistrogene moxeparvovec-rokl (Elevidys) **may be considered medically necessary** when **ALL** the following criteria are met:

1. Individuals ≥ 4 years of age; AND
2. Individual has a diagnosis of Duchenne muscular dystrophy (DMD) confirmed by a mutation in the DMD gene; AND
3. Submitted genetic testing for DMD confirms the individual does not have a deletion in exon 8 and/or 9; AND
4. Individual is ambulatory.

Delandistrogene moxeparvovec-rokl (Elevidys) for the treatment of Duchenne muscular dystrophy (DMD) in non-ambulatory individuals **is considered not medically necessary** as a clinical benefit has not been established.

Delandistrogene moxeparvovec-rokl (Elevidys) for the treatment of all other indications **is considered experimental, investigational and/or unproven**.

Policy Guidelines

None.

Description

Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is an X-linked, recessive disorder that occurs in approximately 1 in every 3500 to 5000 males. (1) It primarily affects males. However, a small number of females are also affected, but are usually asymptomatic. Even when symptomatic, most females typically only present with a mild form of the disease. According to U.S. epidemiologic data, the first signs or symptoms of DMD are noted at a mean age of 2.5 years (range, 0.2 to 1 years), and the mean age at definitive diagnosis is 4.9 years (range, 0.3 to 8.8

years). (2) Symptoms include motor difficulties such as difficulty running, jumping, and walking upstairs, along with an unusual waddling gait. Some improvement in symptoms may be seen from 3 to 6 years of age, though gradual deterioration resumes, and most patients lose ambulation by age 12 and require noninvasive ventilation by the late teenage years. Patients progress from needing noninvasive ventilation only during night sleeping, followed by noninvasive ventilation during day and night sleeping, and then noninvasive ventilation during day and night over the course of 5 to 10 years.

DMD occurs as a result of variant(s) in the gene responsible for producing dystrophin, a cohesive protein that is essential for maintaining muscle support and strength. *Duchenne muscular dystrophy* is the longest known human gene, and several variants can cause DMD. Most deletion variants disrupt the translational reading frame in the dystrophin messenger RNA resulting in an unstable, nonfunctional dystrophin molecule. As a result, there is progressive muscle degeneration leading to loss of independent ambulation, as well as other complications, including respiratory and cardiac complications. (3) Genetic testing is required to determine the specific *Duchenne muscular dystrophy* gene variant(s) for a definitive diagnosis, even when the absence of dystrophin protein expression has been confirmed by muscle biopsy. There are over 4700 variants in the Leiden Duchenne muscular dystrophy mutation database, and the most common variants are concentrated between exons 45 and 53.

Delandistrogene moxeparvovec-rokl (Elevidys)
Elevidys is an adeno-associated virus vector-based gene transfer therapy designed to treat the underlying cause of DMD by delivering a functional shortened dystrophin into the muscle tissue.

Regulatory Status
On June 22, 2023, the U.S. Food and Drug Administration (FDA) approved delandistrogene moxeparvovec-rokl (Elevidys) (Sarepta Therapeutics, Inc.) for the treatment of ambulatory pediatric patients aged 4 through 5 years with DMD with a confirmed mutation in the *Duchenne muscular dystrophy* gene. This indication was approved under accelerated approval based on expression of Elevidys microdystrophin in skeletal muscle observed in patients treated with Elevidys. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (4)

In June 2024, the FDA revised the approved indications for delandistrogene moxeparvovec-rokl (Elevidys). It is now indicated for individuals at least 4 years of age for the treatment of Duchenne muscular dystrophy (DMD) 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 microdystrophin. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. (4)

Rationale

Delandistrogene moxeparvovec-rokl (Elevidys) (4)

The efficacy of Elevidys was evaluated in two double-blind, placebo-controlled studies (Study 1 [NCT03769116] and Study 3 [NCT05096221]) and one open-label study (Study 2 [NCT04626674]) which a total of 214 male patients with a confirmed disease-causing mutation in the Duchenne muscular dystrophy (DMD) gene were dosed.

Study 1

Study 1 is a completed 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 Duchenne muscular dystrophy (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 *Duchenne muscular dystrophy* gene. 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 4 through 5-year-old subgroup, the mean age, mean weight and mean North Star Ambulatory Assessment (NSAA) total score (range) for the Elevidys-treated patients (n=8) were 4.98 years, 20.1 kg and 20.1 (17-23), and for the placebo patients (n=8) were 5.15 years, 19.8 kg and 20.4 (15-24). In the Elevidys group, eight patients received 1.33×10^{14} vg/kg of Elevidys, and 12 patients received lower doses. Key demographic and baseline characteristics are presented in Table 1 below.

Table 1. Key Demographic and Baseline Characteristics (Study 1 Part 1)

Characteristic	All (n=41)	Elevidys (n=20)	Placebo (n=21)
Race (%) Asian/Black or African American/White/Other	12/0/73/15	20/0/65/15	5/0/81/14
Ethnicity (%) Hispanic or Latino/Other	12/88	5/95	19/81
Mean age [range] (years)	6.3 [4.3-7.9]	6.3 [4.5-7.9]	6.2 [4.3-7.9]
Mean weight [range] (kg)	22.4 [15.0-34.5]	23.3 [18.0-34.5]	21.6 [15.0-30.0]
Mean NSAA total score [range]	21.2 [13-29]	19.8 [13-26]	22.6 [15-29]

Mean time to rise from floor [range] (seconds)	4.3 [2.7-10.4]	5.1 [3.2-10.4]	3.6 [2.7-4.8]

kg: kilogram; NSAA: North Star Ambulatory Assessment.

All patients were on a stable dose of corticosteroids for DMD for at least 12 weeks prior to the Elevidys infusion. All randomized patients 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 patient'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 efficacy outcomes of Study 1 were to evaluate expression of micro-dystrophin in skeletal muscle, and to evaluate the effect of Elevidys on the North Star Ambulatory Assessment (NSAA) total score.

Results of micro-dystrophin measured by western blot are presented in Table 2.

Table 2. Micro-Dystrophin Expression in Study 1 and Study 2 at Week 12 from Baseline (Western Blot Assay)[abc]

Western blot (% of micro-dystrophin compared to control)	**Study 1 Part 1 (n=6)**	**Study 1 Part 2 (n=21)**	**Study 2 Ambulatory (n=40)**	**Study 2 Non-ambulatory (n=8)**
Mean change from baseline (SD)	43.4 (48.6)	40.7 (32.3)	51.0 (47)	40.1 (35.9)
Median change from baseline (Min, Max)	24.3 (1.6, 116.3)	40.8 (0.0, 92.0)	46.9 (1.9, 197.3)	32.7 (1.4, 116.3)

Max: maximum; Min: minimum; SD: standard deviation.

[a] All patients received 1.33 X 10^{14} vg/kg, as measured by ddPCR.

[b] Change from baseline was statistically significant.

[c] Adjusted for muscle content. Control was level of wild-type (normal) dystrophin in normal muscle.

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 patients 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 patients 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

Study 2 is an ongoing, open-label, multi-center study which includes 5 cohorts of 48 male DMD patients.

Patients in cohorts 1, 2 and 3 have a confirmed frameshift, splice site or premature stop codon mutation anywhere in the *DMD* gene, while patients in cohort 4 included patients with mutations on the *DMD* gene at or after exon 18. All patients in cohort 5 had mutations that partially or fully overlap with exons 1-17 in the DMD gene. Patients received corticosteroids for DMD before infusion. All patients had baseline anti-AAVrh74 antibodies titers ≤1:400 as determined by the investigational total binding antibody ELISA. Patients received a single intravenous infusion of 1.33×10^{14} vg/kg ELEVIDYS if they weighed less than 70 kg or 9.31×10^{15} vg/kg total fixed dose if they weighed 70 kg or greater.

Cohorts 1, 2, 4 and 5a enroll 40 ambulatory patients 3 to 12 years of age, with weights ranging from 12.5 to 50.5 kg, baseline mean NSAA total score of 20.3 (11 to 30), and mean time to rise from floor of 4.7 seconds (2.4 to 9.7). Cohorts 3 and 5b include 8 non-ambulatory patients 10 to 20 years of age, with weights ranging from 36.1 to 80.1 kg. Overall key demographics and key baseline characteristics by Cohort are presented in Table 3.

Table 3. Key Demographic and Baseline Characteristics for Study 2

Characteristics	**All (n=48)**	**Cohort 1 (n=20)**	**Cohort 2 (n=7)**	**Cohort 3[a] (n=6)**	**Cohort 4 (n=7)**	**Cohort 5a (n=6)**	**Cohort 5b[a] (n=2)**
Race (%) Asian/Black or African American/White/Other	8/6/77/8	5/5/75/15	14/0/71/14	0/0/100/0	14/0/86/0	0/33/67/0	50/0/50/0
Ethnicity (%) Hispanic or Latino/Not Hispanic or Latino	15/85	24/75	14/86	0/100	14/86	0/100	0/100
Mean age [range] (years)	7.7 [3.2 to 20.2]	5.8 [4.4 to 7.9]	10.1 [8.0 to 12.1]	15.3 [9.9 to 20.2]	3.5 [3.2 to 3.9]	6.7 [4.7 to 8.6]	13.4 [12.3 to 14.6]
Mean weight [range] (kg)	30.1 [12.5 to 80.1]	21.2 [15.2 to 33.1]	37.1 [28.0 to 50.5]	59.9 [36.1 to 80.1]	15.2 [12.5, 16.5]	32.1 [19.1, 47.4]	51.2 [43.4, 59.0]
Mean NSAA total score [range]	20.3 (11 to 30)	22.1 [18 to 26]	20.7 [17 to 26]	N/A	12.9 [11 to 17]	22.5 [18 to 30]	N/A

Mean time to rise from floor [range] (seconds)	4.7 (2.4 to 9.7)	4.2 [2.4 to 8.2]	5.9 [3.8 to 9.7]	N/A	5.2 [3.8 to 6.7]	4.6 [2.5 to 7.7]	N/A
Mean Performance of Upper Limb v 2.0 score [range]	30.7 [18 to 42]	N/A	38.9 [33 to 42]	22.2 [18 to 31]	N/A	N/A	27.5 [21 to 34]

Kg; kilograms; N/A: not applicable; NSAA: North Star Ambulatory Assessment.

[a] NSAA and time to rise from floor were not evaluated in non-ambulatory patients.

The efficacy outcome measure of the study was to evaluate the effect of micro-dystrophin expression as measured by western blot. Results are presented in Table 2 above.

Study 3

Study 3 is a multi-center, randomized, double-blind, placebo-controlled study in which 125 ambulatory male patients aged 4 through 7 years, with a confirmed frameshift, splice site, premature stop codon, or other disease-causing mutation in the DMD gene starting at or after exon 18, were dosed. Patients with exon 45 (inclusive), or in-frame deletions, in-frame duplications, and variants of uncertain significance ("VUS"), were excluded. Patients received corticosteroids for DMD before infusion. All patients had baseline anti-AAVrh74 antibodies titers <1:400 as determined by the investigational total binding antibody ELISA and received a single intravenous infusion of 1.33×10^{14} vg/kg Elevidys. Key demographic and baseline characteristics are presented in Table 4.

The efficacy outcome measure of the study was to evaluate the effect of ELEVIDYS on physical function as assessed by the NSAA total score. Key secondary outcome measures were to evaluate expression of microdystrophin in skeletal muscle, time to rise from floor, and time of 10-meter walk/run. Additional efficacy outcome measures included time of 100-meter walk/run, and time to ascend 4 steps. Results of microdystrophin measured by western blot are presented in Table 2 above.

Table 4. Key Demographic and Baseline Characteristics for Study 3

Characteristic	**Elevidys (n=63)**	**Placebo (n=62)**
Race (%) Asian/Black or African American/ White/Multiple/Other/Not Reported	13/0/78/2/3/5	18/3/74/0/2/3
Ethnicity (%) Hispanic or Latino/Not Hispanic or Latino/ Not Reported/Unknown	24/75/0/2	13/86/2/0
Mean age [range] (years)	6.0 [4.1, 7.9]	6.1 [4.0, 7.9]
Mean weight [range] (kg)	21.3 [13.5, 38.5]	22.4 [14.4, 41.6]
Mean NSAA total score [range]	23.10 (14 to 32)	22.82 (15.5 to 30)

Mean time to rise from floor [range] (seconds)	3.52 (1.9 to 5.8)	3.60 (2.3 to 5)
Mean time of 10-meter walk/run [range] (seconds)	4.82 (3.2 to 6.9)	4.92 (3.7 to 7)
Mean time of 100-meter walk/run [range] (seconds)	60.67 (38.0 to 129.2)	63.01 (38.7 to 118.1)
Mean time to ascend 4 steps [range] (seconds)	3.17 (1.6 to 7.1)	3.37 (1.5 to 7.1)

Kg: kilograms; NSAA: North Star Ambulatory Assessment.

The change in NSAA total score was assessed from baseline to Week 52 after infusion of Elevidys or placebo. The difference between the Elevidys (n=63) and placebo groups (n=61) was not statistically significant (p=0.24). The least squares (LS) mean changes in NSAA total score from baseline to Week 52 was 2.57 (95% confidence interval [CI]: 1.80, 3.34) points for the Elevidys group and 1.92 (95% CI: 1.14, 2.70) points for the placebo group, with a LS mean difference from placebo of 0.65 (95% CI: -0.45, 1.74). Changes of clinical relevance were noted in three secondary efficacy endpoints, including time to rise from the floor, 10-meter walk/run and time to ascend 4 steps.

Table 5. Change from Baseline to Week 52 of Timed Function Tests in Study 3 Part 1

	Elevidys	**Placebo**	**LS Mean Difference from Placebo (95% CI)**
Time to rise from the floor (seconds)	N=63	N=61	-
LS mean change (95% CI)	-0.27 (-0.56, 0.02)	0.37 (0.08, 0.67)	-0.64 (-1.06, -0.23)
Time of 10-meter walk/run (seconds)	N=63	N=61	-
LS mean change (95% CI)	-0.34 (-0.55, -0.14)	0.08 (-0.13, 0.29)	-0.42 (-0.71, -0.13)
Time of 100-meter walk/run (seconds)	N=59	N=57	-
LS mean change (95% CI)	-6.57 (-10.05, -3.09)	-3.28 (-6.86, 0.29)	-3.29 (-8.28, 1.70)
Time to ascend 4 steps (seconds)	N=62	N=60	-
LS mean change (95% CI)	-0.44 (-0.69, -0.20)	-0.08 (-0.33, 0.17)	-0.36 (-0.71, -0.01)

CI: confidence interval; LS: least squares

Summary of Evidence

For individuals who have been diagnosed with Duchenne muscular dystrophy (DMD) who received delandistrogene moxeparvovec-rokl (Elevidys), the evidence includes two double-

blind, placebo-controlled studies and one open-label study in which a total of 214 male individuals with a confirmed disease-causing mutation in the *DMD* gene were dosed. Relevant outcomes are disease-specific survival, change in disease status, functional outcomes, health status measures, quality of life, and treatment-related mortality and morbidity. The studies provided to the U.S. Food and Drug Administration (FDA) for approval concluded Elevidys is reasonably likely to predict clinical benefit in ambulatory individuals 4 years of age or older with DMD. However, the clinical benefit of Elevidys, including improved motor function, has not been firmly established at this time for non-ambulatory individuals.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J1413

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

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2. Center for Disease Control and Prevention. Muscular Dystrophy: MD STARnet Data and Statistics (2024). Available at: <https://www.cdc.gov> (accessed July 7, 2023).
3. Falzarano MS, Scotton C, Passarelli C, et al. Duchenne Muscular Dystrophy: From Diagnosis to Therapy. Molecules. Oct 07 2015; 20(10):18168-18184. PMID 26457695
4. FDA. Highlights of Prescribing Information - Elevidys (Delandistrogene moxeparvovec-rokl). Revised 6/2024. Available at: <https://www.fda.gov> (accessed July 1, 2024).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
07/01/2025	Document updated. The following change was made to Coverage: Added "Submitted genetic testing for DMD confirms the individual does not have a deletion in exon 8 and/or 9; AND" to conditional criteria. No new references added.
02/15/2025	Reviewed. No changes.
09/01/2024	Document updated with literature review. Coverage was revised to state Delandistrogene moxeparvovec-rokl (Elevidys) may be considered medically necessary when ALL the following criteria are met: Individuals ≥ 4 years of age; AND Individual has a diagnosis of Duchenne muscular dystrophy (DMD) confirmed by a mutation in the DMD gene; AND Individual is ambulatory. Delandistrogene moxeparvovec-rokl (Elevidys) for the treatment of Duchenne muscular dystrophy (DMD) in non-ambulatory individuals is considered not medically necessary as a clinical benefit has not been established. References revised; none added.
01/15/2024	New medical document. Delandistrogene moxeparvovec-rokl (Elevidys) for the treatment of Duchenne muscular dystrophy (DMD) is considered not medically necessary as a clinical benefit has not been established. Delandistrogene moxeparvovec-rokl (Elevidys) for the treatment of all other indications is considered experimental, investigational and/or unproven.