Elevidys™ (Delandistrogene Moxparvovec-Rokl)

Policy Number: 2024D00126D
Effective Date: January 1, 2024

➲ Instructions for Use

Table of Contents **Page**

Community Plan Policy

- Elevidys™ (Delandistrogene Moxparvovec-Rokl)

Coverage Rationale

➲ See Benefit Considerations

Elevidys is proven and medically necessary for the treatment of Duchenne muscular dystrophy (DMD) in patients who meet all of the following criteria:

- Diagnosis of Duchenne muscular dystrophy by, or in consultation with, a pediatric neuromuscular specialist with expertise in the diagnosis of DMD; **and**
- Submission of medical records (e.g., chart notes, laboratory values) confirming **both** of the following:
  - A mutation in the DMD gene; **and**
  - The mutation is not a deletion in exon 8 or exon 9; **and**
- Patient is aged 4 or 5 years of age; **and**
- Submission of medical records (e.g., chart notes) confirming that the patient is ambulatory without needing an assistive device (e.g., without side-by-side assist, cane, walker, wheelchair, etc.); **and**
- Patient does not have an elevated anti-AAVrh74 total binding antibody titer ≥ 1:400; **and**
- Patient will receive a corticosteroid regimen prior to and following receipt of Elevidys in accordance with the United States Food and Drug Administration (FDA) approved Elevidys labeling**; and**
- Elevidys is prescribed by, or in consultation with, a pediatric neuromuscular specialist with expertise in the treatment of DMD; **and**
- Elevidys dosing is in accordance with FDA approved labeling; **and**
- Patient will not receive exon-skipping therapies for DMD [e.g., Amondys (casimersen), Exondys 51 (eteplirsen), Viltepso (viltolarsen), Vyondys 53 (golodirsen)] concomitantly or following Elevidys treatment; **and**
- Patient has never received Elevidys treatment in their lifetime; **and**
- Authorization will be issued for no more than one treatment per lifetime and for no longer than 45 days from approval or until 6 years of age, whichever is first.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service.

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1413	Injection, delandistrogene moxeparvovec-rokl, per therapeutic dose

Diagnosis Code	Description
G71.02	Duchenne or Becker muscular dystrophy

Background

Duchenne muscular dystrophy (DMD) is a rare, progressive, neuromuscular disorder caused by mutations of the dystrophin gene on the x chromosome. The gene regulates the production of the dystrophin protein, which plays an important role in the functioning of muscle cells. The age of onset is usually between 3 and 5 years. DMD is characterized by weakness and wasting of the muscles of the pelvic area followed by the involvement of the shoulder muscles. 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. The birth prevalence is estimated to be 1 in every 3,500 live male births. 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]

Elevidys is a recombinant gene therapy designed to deliver into the body a gene that leads to production of Elevidys micro-dystrophin, 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]

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the member specific benefit plan document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Proven

The accelerated approval of Elevidys was primarily based on data from Study 1 and Study 2.[1,3-4]

Study 1 is an ongoing multi-center two-part study including a: (1) 48-week, randomized, double-blind, placebo-controlled period; and (2) 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 41 male ambulatory DMD patients 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 at least 12 weeks prior to SRP-9001 infusion and had a baseline anti-AAVrh74 total binding antibody titers < 1:100 as determined by clinical trial ELISA. The day prior to treatment, the subject's background dose of corticosteroid for DMD was increased to at least 1 mg/kg of a corticosteroid (prednisone equivalent) daily and continued at this level for at least 60 days after the infusion, unless earlier tapering was clinically indicated.
The primary objectives 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. The table below summarizes the Elevidys micro-dystrophin expression results for patients who received 1.33×10^{14} vector genomes/kilogram (vg/kg) Elevidys. 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. The secondary endpoints in Part 1 include change from baseline to Week 48 in 100-meter timed test, time to ascend 4 steps, time to rise from the floor, and 10-meter timed test. Elevidys group did not show improvement in change from baseline to Week 48 for any of the secondary endpoints compared to the placebo. As the primary functional endpoint, NSAA total score change from baseline to Week 48, failed, the secondary endpoints in this study were not formally tested and the analyses of secondary endpoints can only serve as exploratory.

In Part 2, subjects in the Part 1 placebo group received SRP-9001 and had a mean increase from Part 2 baseline to Week 48 in NSAA total score of 1.3 (standard deviation [SD]: 2.7). For subjects who received SRP-9001 in Part 1, the mean NSAA total score change from Part 2 baseline to Week 48 is 0.1 (SD: 6.6). However, exploratory analysis of the group by age range shows that at Part 2 Week 48, the mean NSAA total score change from Part 2 baseline was 0.4 (SD 2.4) for the 4-5 years old subgroup while the mean NSAA total score declined by 4.3 (SD 5.1) from Part 2 baseline for the 6-7 years old subgroup.

Study 2 is an ongoing, open-label study which includes a cohort of 20 ambulatory male DMD patients aged 4 through 7 years. All 20 patients have a confirmed frameshift mutation, canonical splice site mutation, or premature stop codon mutation in the *DMD* gene. All subjects were on a stable dose of corticosteroids for at least 12 weeks prior to Elevidys infusion and throughout the first year of the study and had a baseline anti-AAVrh74 total binding antibody titers < 1:100 as determined by clinical trial ELISA (only patients with baseline anti-AAVrh74 total binding antibody titers < 1:400 are eligible for enrollment). The table below summarizes the Elevidys micro-dystrophin expression results for patients who received 1.33×10^{14} vector genomes/kilogram (vg/kg) Elevidys. At Week 52 post-Elevidys infusion, a mean change from baseline in NSAA total score of 4.0 (SD: 3.5) was observed.

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)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Elevidys (delandistrogene moxeparvovec-rokl) is an adeno-associated virus vector-based gene therapy indicated for the treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene.[1]

References

1. Elevidys [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; June 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. doi: 10.1001/jamaneurol.2020.1484. PMID: 32539076; PMCID: PMC7296461.

   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. Accessed June 23, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05096221.

3. A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial for Duchenne Muscular Dystrophy Using SRP-9001. ClinicalTrials.gov identifier: NCT03769116. Updated July 1, 2022. Accessed June 23, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT03769116.
4. Birnkrant DJ, Bushby K, Bann CM, Apkon SD, Blackwell A, Brumbaugh D, Case LE, Clemens PR, Hadjiyannakis S, Pandya S, Street N, Tomezsko J, Wagner KR, Ward LM, Weber DR; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol. 2018 Mar;17(3):251-267. doi: 10.1016/S1474-4422(18)30024-3. Epub 2018 Feb 3. Erratum in: Lancet Neurol. 2018 Apr 4;: PMID: 29395989; PMCID: PMC5869704.
5. Birnkrant DJ, Bushby K, Bann CM, Alman BA, Apkon SD, Blackwell A, Case LE, Cripe L, Hadjiyannakis S, Olson AK, Sheehan DW, Bolen J, Weber DR, Ward LM; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol. 2018 Apr;17(4):347-361. doi: 10.1016/S1474-4422(18)30025-5. Epub 2018 Feb 3. PMID: 29395990; PMCID: PMC5889091.

Policy History/Revision Information

Date	Summary of Changes
01/01/2024	**Applicable Codes** • Updated list of applicable HCPCS codes to reflect annual edits; replaced C9399, J3490, and J3590 with J1413 **Supporting Information** • Archived previous policy version 2023D00126C

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.