Elevidys™ (Delandistrogene Moxparvovec-Rokl)

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Community Plan Policy

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Coverage Rationale

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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**
- **Both** of the following:
  - Patient does not have preexisting hepatic impairment, acute liver disease (e.g., acute hepatic viral infection), chronic hepatic condition or elevated GGT; **and**
  - Prescriber attests that liver function (clinical exam, GGT, and total bilirubin) will be monitored weekly for the first 3 months following Elevidys administration and thereafter in accordance with the FDA approved labeling

  and
- **Both** of the following:
  - Patient does not have a left ventricle ejection fraction (LVEF) < 40%; **and**
  - Prescriber attests that troponin-I will be monitored weekly for the first month following Elevidys administration and thereafter per recommendations in the prescribing information

  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**
- 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 not previously received gene therapy for the treatment of DMD; **and**
- Elevidys dosing is in accordance with FDA approved labeling; **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

Elevidys is unproven and not medically necessary for the treatment of:
- Becker muscular dystrophy (BMD)
- Duchenne muscular dystrophy (DMD) in ambulatory patients < 4 years of age and ≥ 6 years of age
- Duchenne muscular dystrophy (DMD) in patients at any age who are non-ambulatory

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
G71.01	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.

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.

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 efficacy of Elevidys was evaluated in three studies: the EMBARK Phase III randomized, double-blind, placebo-controlled, confirmatory trial; a Phase II study; and a Phase Ib study.

Clinical Trial SRP-9001-102 (NCT03769116)

Study 102 is a Phase II, randomized, double-blind, placebo- controlled, multicenter, 2-part study in 41 ambulatory individuals with DMD with either a confirmed frameshift mutation, or a premature stop codon mutation between exons 18

to 58 in the DMD gene. All participants were 4 years or older and less than 8 years of age at time of infusion in Part 1. The primary objectives of this 3-part study were to evaluate micro-dystrophin expression at 12 weeks as measured by western blot of biopsied muscle tissue expressed as a percent of control (levels of dystrophin in normal participants without DMD or Becker muscular dystrophy [BMD]) and to evaluate the effect of Elevidys on physical function as assessed by the NSAA over 48 weeks.

In Part 1, participants were randomized 1:1 to receive either a single intravenous infusion of Elevidys (n = 20) or placebo (n = 21). The study met its primary biological endpoint of micro-dystrophin protein expression. At Week 12 of Study 102 Part 1, the mean (SD) change from baseline levels of micro-dystrophin (% of control) were 3.6 (5.7), 28.2 (52.2), and 43.4 (48.6) for participants receiving Elevidys-dose level 1 (DL1), Elevidys-dose level 2 (DL2), and Elevidys-dose level 3 (DL3), respectively. The study did not demonstrate a statistically significant change in NSAA from baseline to Week 48 after treatment. A subgroup analysis to further evaluate the treatment effect of Elevidys on NSAA scores from baseline to Week 48 stratified participants into two age groups: 4-5 years old and 6-7 years old. The exploratory subgroup analyses demonstrated that for individuals in the age 4-5 years cohort, the least square (LS) mean changes (standard error [SE]) in NSAA total score from baseline to Week 48 were 4.3 (0.7) and 1.9 (0.7) points for the ELEVIDYS and placebo group, respectively. For participants 6-7 years of age, the LS mean changes (SE) in NSAA total score from baseline to Week 48 were -0.2 (0.7) and 0.5 (0.7) points for the ELEVIDYS and placebo group, respectively.

In Part 2, which was also blinded, participants who received placebo in Part 1 received Elevidys and those that had previously received Elevidys received a placebo infusion. All participants were followed for another 48 weeks while safety and efficacy were evaluated. Two participants with substantially high micro-dystrophin baseline values were excluded from analysis. At Week 12 of Part 2, the mean (SD) change from baseline levels of the micro-dystrophin (% of control) were 10.6 (17.0), 10.4 (14.7), and 43.5 (55.6) for participants receiving Elevidys-dose level 1, Elevidys-DL2 dose level 2, and Elevidys-dose level 3, respectively. Elevidys-treated participants from the placebo crossover group (n = 20, aged 5-8 at time of dosing Elevidys) scored a statistically significant 2.0 points higher on the mean NSAA at 48 weeks compared to propensity-score weighted external controls (p value = 0.0009). Mean NSAA scores from these Part 2 participants improved 1.3 points from baseline for the Elevidys-treated group, and the NSAA scores in the external control group (n = 103) declined 0.7 points from baseline. The mean age of the participants who received Elevidys was 7.24 years of age.

Clinical Trial SRP-9001-103 (NCT04626674, ENDEAVOR Trial)

Study 103 (ENDEAVOR) is an ongoing, single-arm, open-label, Phase 1b study evaluating over a 5-year (260 weeks) period of time the safety of and expression of micro-dystrophin from Elevidys in males at least 3 years of age with DMD. The study enrolled male patients across cohorts based on ambulatory status (ambulatory or non-ambulatory) and age group. The primary outcome is the change from baseline in the quantity of micro-dystrophin protein expression at week 12 as measured by western blot. Estimated study completion date is January 2028. Currently, only data from cohort 1 is available which included 20 ambulatory males, aged 4 through 7 years. At week 12, mean (SD) change from baseline in micro-dystrophin expression as measured by western blot was 54.2% (42.6); $p < 0.0001$.

Clinical Trial SRP-9001-301 (NCT05096221, EMBARK Trial)

The EMBARK trial is a global Phase 3, randomized, double blinded, placebo-controlled, Part 1 and a 52-week crossover Part 2. Participants randomized to the placebo arm in Part 1 had the opportunity to receive treatment in Part 2. The trial included 125 ambulatory male patients aged 4 through 7 years. The least square mean change in NSAA total score from baseline to Week 52 between the Elevidys (n = 63) and placebo groups (n = 61) was not statistically significant (p = 0.2441). The least square 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).

Unproven

There is insufficient evidence to demonstrate improved clinical outcomes for non-ambulatory individuals or for individuals outside of the 4 to 5 years age group. Neither EMBARK, the Phase III confirmatory trial, nor Study 102, the Phase II trial, were able to demonstrate a significant difference between the Elevidys and placebo groups in the change in NSAA total score at Week 48. In Study 102, only the subgroup of patients 4 through 5 years of age demonstrated an improvement in the NSAA total score at Week 48 compared with placebo. The subgroup of patients aged 6 through 7 years had a decrease in the NSAA total score compared with placebo.

The use of Elevidys for the treatment Becker muscular dystrophy has not yet been studied.

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 in individuals at least 4 years of age for the treatment of Duchenne muscular dystrophy (DMD) in patients who are ambulatory and have a confirmed mutation in the DMD gene and 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 (noted hereafter as “micro-dystrophin”). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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Policy History/Revision Information

Date	Summary of Changes

04/01/2025	**Coverage Rationale**
	• Revised coverage criteria:
	  ○ Added criterion requiring:
	  ▪ The patient does not have preexisting hepatic impairment, acute liver disease (e.g., acute hepatic viral infection), chronic hepatic condition, or elevated GGT

Date	Summary of Changes
	▪ The prescriber attests that liver function (clinical exam, GGT, and total bilirubin) will be monitored weekly for the first 3 months following Elevidys administration and thereafter in accordance with the FDA approved labeling ▪ The patient does not have a left ventricle ejection fraction (LVEF) < 40% ▪ The prescriber attests that troponin-I will be monitored weekly for the first month following Elevidys administration and thereafter per recommendations in the prescribing information ○ Replaced criterion requiring "the patient has *never received Elevidys treatment in their lifetime*" with "the patient has *not previously received gene therapy for the treatment of DMD*" • Added language to indicate Elevidys is unproven and not medically necessary for the treatment of: ○ Becker muscular dystrophy (BMD) ○ Duchenne muscular dystrophy (DMD) in ambulatory patients < 4 years of age and ≥ 6 years of age ○ Duchenne muscular dystrophy (DMD) in patients at any age who are non-ambulatory **Applicable Codes** • Added ICD-10 diagnosis code G71.01 • Removed ICD-10 diagnosis code G71.02 **Supporting Information** • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version 2024D00126D

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.