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MEDICAL POLICY

Elevidys (delandistrogene moxeparvovec-rokl)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

This Medical Policy document describes the status of medical technology at the time the document was developed. Since that time, new technology may have emerged or new medical literature may have been published. This Medical Policy will be reviewed regularly and be updated as scientific and medical literature becomes available.

DESCRIPTION

Elevidys (delandistrogene moxeparvovec-rokl) is an adeno-associated virus vector-based gene therapy indicated for:

1. The treatment of ambulatory pediatric patients at least 4 years of age with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* gene.

POLICY

Elevidys (delandistrogene moxeparvovec-rokl) is considered **not medically necessary** for all indications, including the treatment for DMD, due to insufficient evidence to demonstrate clinical efficacy.

CLINICAL RATIONALE

Elevidys (delandistrogene moxeparvovec-rokl) is the first gene therapy approved for ambulatory pediatric patients at least 4 of age with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* and is intended to be administered as a one-time intravenous (IV) infusion as a single dose. Elevidys utilizes an adeno-associated virus (AAVrh74) to deliver a shortened version of the *DMD* gene, known as Elevidys micro-dystrophin, into muscle tissue, partially compensating for the lack of functional *DMD* gene and targeting the underlying genetic defect that causes DMD.

Clinical Studies

The accelerated FDA approval of Elevidys (delandistrogene moxeparvovec-rokl) was based on efficacy data from two ongoing clinical studies (Study 102 and Study 103). Study 102 is a three-part Phase 2 study. Part 1 was a 48-week, randomized, double-blind placebo-controlled period where participants were treated with a single IV dose of Elevidys (n=20) or placebo (n=21) and followed for 48 weeks. Of note, it was retrospectively determined that in the Elevidys group, only 8 subjects received the intended dose. Participants were ambulatory, male patients with DMD between 4-7 years of age with either a confirmed mutation or a premature stop codon mutation between exons 18 and 58 in the *DMD* gene. In Part 2 of the study, participants who received placebo during part 1 were treated with Elevidys and those treated with Elevidys during part 1 received placebo. All patients were followed for an additional 48 weeks. Part 3 is ongoing, and all patients will be followed for up to 212 weeks following treatment with Elevidys. Study 103 is a two-part open-label Phase 1 study in five cohorts of boys with DMD defined by age and ambulatory status. Part 1 is a 12-week assessment of the change in quantity of micro-dystrophin expression via western blot and Part 2 is a 5-year follow-up of patients following treatment with Elevidys.

The primary objectives of Study 102 were to evaluate expression of Elevidys micro-dystrophin in skeletal muscle at week 12, and to evaluate the effectiveness of Elevidys on the clinical outcome measure, North Star Ambulatory Assessment (NSAA), a validated, 17-item instrument frequently used in DMD trials. Change in the NSAA Total Score was assessed from baseline to week 48 after infusion of Elevidys or placebo. The difference between the overall Elevidys group and the placebo group was not statistically significant ($p = 0.37$). The least squares (LS) mean change (standard error, SE) in the NSAA Total Score from baseline to Week 48 was 1.7 (0.6) points for the Elevidys group and 0.9 (0.6) points for the placebo group.

Exploratory subgroup analyses of 16 participants 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, versus 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. In addition, subjects aged 6 to 7 years in the Elevidys group showed no improvement from baseline.

Study 103 is an ongoing, open-label, multicenter follow-up trial which includes a cohort of 20 ambulatory male patients with DMD aged 4 through 7 years of age with a confirmed DMD mutation. The primary objective of the study was to evaluate the effect of Elevidys micro-dystrophin expression as measured by western blot. For subjects aged 4 through 5 years who received 1.33×10^{14} vg/kg of Elevidys, the mean (SD) Elevidys micro-dystrophin expression levels (change from baseline) at Week 12 following Elevidys infusion was 51.7% (N=11, SD:41.0%).

The most common adverse reactions (incidence $\geq 5\%$) in clinical studies were vomiting (61%), nausea (40%), liver function test increased (37%), pyrexia (24%), and thrombocytopenia (12%). The serious adverse reactions observed were acute serious liver injury, immune-mediated myositis, and myocarditis. Patients' liver function should be monitored before treatment with Elevidys, and weekly for the first three months after treatment. Troponin-I levels should be monitored before administration of Elevidys and weekly for the first month after treatment. It is contraindicated in patients with any deletion in exon 8 and/or exon 9 in the *DMD* gene.

The FDA first granted accelerated approval based on an increase in the surrogate endpoint of expression of Elevidys micro-dystrophin that is reasonably likely to predict clinical benefit. In June 2024, the FDA granted traditional approval for the treatment of confirmed DMD in ambulatory patients ages 4 and older and accelerated approval for non-ambulatory patients ages 4 and older. The DMD indication in non-ambulatory patients is approved under accelerated approval based on expression of Elevidys micro-

dystrophin and continued approval is contingent upon verification and description of clinical benefit in confirmatory trials. As published in October 2024, Elevidys did not meet its primary endpoint in EMBARK Part 1. Although patients treated with Elevidys improved 2.6 points on their North Star Ambulatory Assessment (NSAA) total score 52 weeks after treatment compared to 1.9 points in placebo-treated patients, the difference of 0.65 points between treated and placebo groups did not reach statistical significance (n=125; p=0.24). Secondary endpoints such as the time to rise (TTR) and the 10-meter walk/run (10MWR) numerically favored Elevidys, but no statistical significance was met compared to placebo at 52 weeks.

Since the last FDA update, various posters were presented at both the 29th Annual Congress of the World Muscle Society and the Muscular Dystrophy Association Clinical & Scientific Conference further adding to the available evidence surrounding Elevidys. Topline results from EMBARK Part 2 were among the presentations. Investigators observed significant functional improvements after two years of treatment for the primary endpoint of improvement in NSAA score and key secondary endpoints for reduction in TTR and 10MWR. The NSAA total score improved 2.88 points (p<0.001) compared to a pre-specified, propensity-weighted external control group at year two. The TTR declined 2.06 seconds (p<0.0033) and the 10MWR declined 1.36 seconds (p<0.0028) both in favor of Elevidys. Additionally, participants randomized to placebo in EMBARK Part 1 crossed over in Part 2 to receive treatment with Elevidys (n=59). At one year, the crossover group demonstrated statistically significant improvement in functional measures with a NSAA total score increase of 2.34 points (p<0.0001) compared to the external control group. Secondary measures of TTR and 10MWR were reported to be statistically significant in favor of Elevidys compared to the external control group as well.

Exploratory analyses of muscle health and cardiac changes were performed on a subset of the EMBARK population which suggest that Elevidys treatment may offer stabilization or less progression of muscle pathology and that no adverse cardiac events were noted. While no new safety signals were noted at the time of this report, the manufacturer since released information in March 2025 that a patient suffered acute liver failure following treatment with Elevidys which led to death. Acute liver injury is a known side effect of Elevidys; however, this was the first reported fatality related to treatment.

On November 14, 2025, Sarepta Therapeutics and the FDA announced updated prescribing information for Elevidys. The revised label adds a boxed warning for the risk of acute serious liver injury (ALI) and acute liver failure (ALF), following fatal cases in non-ambulatory patients. The indication has been narrowed to ambulatory patients aged 4 years and older with confirmed DMD mutations, removing the non-ambulatory indication. The updated label also provides expanded safety guidance, including modified steroid regimens, weekly liver and cardiac monitoring, and new warnings about infection risk from immunosuppression. Further, the updated labeling states that patients should be instructed “to maintain proximity to an appropriate healthcare facility, as determined by the healthcare provider, for at least two months following Elevidys infusion.”

On November 25, 2025, Sarepta Therapeutics announced approval to begin Cohort 8 of the ENDEAVOR study to evaluate an enhanced immunosuppression regimen for non-ambulatory individuals with DMD treated with Elevidys. The cohort will enroll about 25 non-ambulatory patients, who will receive sirolimus for 14 days before Elevidys and for 12 weeks afterward to help reduce the risk of acute liver injury (ALI) and acute liver failure (ALF)—safety concerns that led the FDA to restrict Elevidys use to ambulatory patients earlier in 2025. Primary endpoints include the incidence of ALI and Elevidys micro-dystrophin expression at 12 weeks.

In summary, the clinical benefit of treatment for DMD with Elevidys (delandistrogene moxeparvovec-rokl) has not been sufficiently demonstrated. The establishment of a clinical benefit, including improved motor function and mobility, is warranted in on-going clinical trials.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J1413 – Injection, delandistrogene moxeparvovec-rokl, per therapeutic dose (effective 1/1/2024)

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POLICY HISTORY

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