Drug Coverage Policy

Effective Date 8/1/2025
Coverage Policy Number.....IP0571
Policy Title.....Elevidys

Muscular Dystrophy – Gene Therapy – Elevidys

- Elevidys® (delandistrogene moxeparvovec-rokl intravenous infusion – Sarepta)

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Coverage Policy

Policy Statement
Due to serious safety concerns leading to patient deaths, **approval is not supported** for Elevidys.

Conditions Not Covered

Elevidys is considered to be experimental, investigational, or unproven due to insufficient data establishing safety, efficacy, and improved health outcomes for any condition, regardless of U.S. Food and Drug Administration (FDA) approval status. Criteria will be updated as new published data are available.

1. **Duchenne Muscular Dystrophy (DMD).** As of June 15, 2025, Sarepta had suspended Elevidys shipment to non-ambulatory patients due to a second patient death.[9] The two reported patient deaths were due to acute liver failure. On July 18, 2025, the FDA requested a halt on shipment of Elevidys.[10] This is after the death of another patient who was non-ambulatory, in a Phase I study for Limb-Girdle Muscular Dystrophy (LGMD). The patient was given an investigational gene therapy, SRP-9004. Both Elevidys and the investigational agent, SRP-9004 use the same adeno-associated virus vector, which has been linked to liver toxicity. Sarepta, in a community letter (July 18, 2025), noted that they declined FDA's request to voluntarily stop shipping Elevidys to ambulatory patients, since the manufacturer does not think there is any new or changed safety information for Elevidys use in this group.[11] It was mentioned that Sarepta will assemble a panel of experts to evaluate the protocol and the use of additional immunosuppressants to further mitigate the risk of acute liver failure. After reconsideration of the FDA's request, Sarepta agreed to voluntarily and temporarily pause shipment of Elevidys, effective as of July 22, 2025.[13] The FDA will continue to assess whether Elevidys should remain on the market.[12] On July 28, 2025 the FDA notified Sarepta that it may lift its voluntary pause on shipments of Elevidys for ambulatory patients.[14] FDA's review of safety data in ambulatory population included a patient death in an 8-year old boy in Brazil. The Brazilian health authorities deemed the death unlikely to be related to Elevidys treatment; FDA's investigation also concluded the same, leading to the decision to resume shipment. Sarepta noted that will continue to work with the FDA to update its label with the safety update for non-ambulatory patients. Elevidys shipment to the non-ambulatory patient population is still on hold.

Overview

Elevidys, an adeno-associated virus (AAV) vector-based gene therapy, is indicated for the treatment of individuals at least 4 years of age with Duchenne muscular dystrophy (DMD).[1] It is specifically indicated in the following populations:

- For patients who are ambulatory and have a confirmed mutation in the *DMD* gene.
- For patients who are non-ambulatory and have confirmed mutation in the *DMD* gene.

The DMD indication in non-ambulatory patients is approved under accelerated approval based on expression of Elevidys micro-dystrophin in skeletal muscle. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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reconsideration of the FDA's request, Sarepta agreed to voluntarily and temporarily pause shipment of Elevidys, effective as of July 22, 2025.[13] The FDA will continue to assess whether Elevidys should remain on the market.[12] On July 28, 2025 the FDA notified Sarepta that it may lift its voluntary pause on shipments of Elevidys for ambulatory patients.[14] FDA's review of safety data in ambulatory population included a patient death in an 8-year old boy in Brazil. The Brazilian health authorities deemed the death unlikely to be related to Elevidys treatment; FDA's investigation also concluded the same, leading to the decision to resume shipment. Sarepta noted that will continue to work with the FDA to update its label with the safety update for non-ambulatory patients. Elevidys shipment to the non-ambulatory patient population is still on pause.

Disease Overview

DMD is a rare, progressive X-linked disease resulting from mutation(s) of the *DMD* gene, also known as the *Dystrophin* gene.[2-3] The incidence of DMD in the US is approximately 1 in 5,000 live male births. The *DMD* gene is the largest known human gene, totaling 2.3 megabases in size. The gene encodes for a functional dystrophin protein, which is part of a transmembrane protein complex that spans the sarcolemma of skeletal and cardiac muscle cells. This complex links the cytoskeleton to the extracellular matrix providing structural integrity to the sarcolemma and helps to transmit and absorb the shock associated with muscle contraction. Mutations in the *DMD* gene prevent the production of functional dystrophin protein or dystrophin is minimally produced. Without dystrophin, normal activity in patients with DMD causes excessive damage to muscle fiber cells. Over time, the muscle cells are replaced with fat and fibrotic tissue. Progressive muscle weakness is the primary manifestation of DMD. This leads to loss of ambulation, associated motor delays, respiratory impairment, and progressive decline in cardiac function. The first clinical symptoms of DMD are delay in motor development milestones, such as walking, which is observed around 2 years of age. Often there is a delay in diagnosis until the age of 3 to 5 years. Age is an important prognostic factor in the progression of DMD. There is no cure for DMD currently. The goal of treatment is to manage symptoms, slow disease progression, and to delay disability. Boys with DMD typically lose the ability to walk by age 12 or 13 years. In the past, mortality occurred by late adolescence or early twenties, however with advances in respiratory and cardiac management, some patients are living into the fourth decade. The most common cause of death for patients with DMD are respiratory failure, respiratory infection, cardiomyopathy, and cardiac arrhythmias. Corticosteroids are a mainstay of therapy in DMD; however, its mechanism of action in DMD is unknown. Corticosteroids ameliorate the symptoms of the disease and delay time to loss of ambulation and other sequelae. Four anti-sense oligonucleotide therapies (exon-skipping) have been approved by the FDA: Exondys 51® (eteplirsen intravenous infusion), Vyondys 53™ (golodirsen intravenous infusion), Viltepso™ (viltolarsen intravenous infusion), and Amondys 45™ (casimersen intravenous infusion). The clinical benefit of these exon-skipping therapies remains unknown since none of the confirmatory clinical studies have been completed.

Clinical Efficacy

The efficacy of Elevidys was evaluated in three studies:[1,2,6-8] the EMBARK Phase III randomized, double-blind, placebo-controlled, confirmatory trial; a Phase II study; and a Phase Ib study. The clinical studies included mostly ambulatory boys with DMD who were ≥ 4 years to < 8 years of age. Cohorts 3 and 5b of the Phase Ib study included eight non-ambulatory boys who were 10 to 20 years of age. All patients were on a stable dose of corticosteroids for at least 12 weeks and had baseline anti-adeno-associated virus serotype rh 74 (AAVrh74) antibody titers < 1:400.

In the EMBARK Phase III study (n = 125), ambulatory male patients ≥ 4 years of age and < 8 years of age were enrolled.[1,6,7] Some of the key inclusion criteria were patients with North Star Ambulatory Assessment (NSAA) score > 16 and < 29 and the time-to-rise from floor (TTR) < 5 seconds at the screening visit. One of the study exclusion criteria was the use of any investigational medication or any treatment designed to increase dystrophin expression (e.g.,

exon-skipping therapies) within 6 months of Elevidys administration and during the study. The primary endpoint of change from baseline to Week 52 in the North Star Ambulatory Assessment (NSAA) total score was not significantly different for the Elevidys and placebo-treated groups.[6] The between-group difference least squares mean (LSM) was 0.65 points (95% confidence interval [CI]: -0.45, 1.74; P = not significant). The key secondary endpoints of change from baseline to Week 52 in time-to-rise (TTR) and the 10 meter walk/run (10MWR) were statistically significantly different between Elevidys and placebo. However, since the primary endpoint failed to meet statistical significance, these secondary endpoint results are thought to be hypothesis generating. Updated 2-year data from the EMBARK study are available. The data are from a poster presented at the Muscular Dystrophy Association Clinical & Scientific Conference in March 2025.[7] The data are not yet published in a peer-reviewed journal. Due to the crossover study design in EMBARK, patients treated with placebo in Part 1 were treated with Elevidys. For this reason, there is no longer a placebo arm in the EMBARK study. The Elevidys-treated patients in Part 1 were compared with an external control (EC) cohort of patients with DMD using propensity-score weighting. Patients in the EC had received only corticosteroids. In order to be included in the EC, patients were selected from the FOR-DMD, BioMarin PRO-DMD-01, and CINRG DNHS studies. Based on the baseline characteristics, the EC cohort and patients in the EMBARK study were well-matched. In patients treated with Elevidys, the micro-dystrophin expression increased from 34.29% at Week 12 (n = 17) to 45.68% at Week 64 (n = 16). Sacrolemmal localization, as measured by percent dystrophin-positive fibers (PDPF), increased from 28.13% at Week 12 to 38.60% at Week 64. At 2 years, Elevidys-treated patients demonstrated statistically significant differences in functional outcome scores compared with the EC cohort. The LSM change difference for the primary endpoint of NSAA score improved by 2.88 points with Elevidys. For the key secondary endpoints, there was a decrease of -2.06 seconds in the TTR and the 10MWR also decreased by -1.36 seconds.

The Phase II study (n = 41) included two parts: Part I was a 48-week randomized, double-blind, placebo-controlled study in which patients received a single-dose of Elevidys (n = 20) or placebo (n = 21); in Part II, patients treated with placebo in Part I received Elevidys.[1,2] Patients in this study were stratified by age (age 4 to 5 years vs. age 6 to 7 years) at randomization. Retrospective analysis identified that 60% of patients in Part I received a dose lower than Elevidys 1.33×10^{14} vector genomes (vg)/kg, due to variability in quantification methods. In Part I, only 8 patients received the approved dose of Elevidys 1.33×10^{14} vg/kg; 12 patients received one-half to two-thirds of the approved dose. In Part II, all patients from the placebo group received the recommended dose of Elevidys 1.33×10^{14} vg/kg. The primary objectives were to evaluate the expression of micro-dystrophin in skeletal muscle and to evaluate the effect of Elevidys on the NSAA total score. For patients 4 through 5 years of age who received the FDA-approved Elevidys dose, the mean micro-dystrophin expression levels (change from baseline) at Week 12 were 95.7% (n = 3; standard deviation [SD]: 17.9%) for Parts I and II. In exploratory subgroup analyses, patients 4 through 5 years of age had a LSM change (NSAA total score from baseline to Week 48 of 4.3 points for the Elevidys group and 1.9 points for the placebo group [baseline scores were about 20]). This was a numerical advantage for patients treated with Elevidys. The change in NSAA total score was not statistically significant for the ITT population; it was also numerically disadvantageous for the patients in the subgroup who were 6 through 7 years of age.

In the Phase Ib study [n = 48], all patients in Cohort 1 received the FDA-approved Elevidys dose.[1,8] The primary efficacy endpoint of change from baseline in quantity of micro-dystrophin protein expression at Week 12, as quantified by western blot, was 51.0% for ambulatory patients (n = 40) and 40.1% for
non-ambulatory patients (n = 8). The median change from baseline was 46.9% for ambulatory patients and 32.7% for non-ambulatory patients. In cohort 1, for patients 4 through 5 years of age, the mean Elevidys micro-dystrophin change from baseline was 51.7% of normal (n = 11; SD:

41.0%). For the exploratory endpoint, there was a mean increase (improvement) in NSAA total score of 4.0 points from baseline to Week 52 (baseline NSAA score for cohort 1: 22).

Guidelines
Elevidys is not addressed in current guidelines for DMD. The guidelines from the DMD Care Considerations Working Group (2018) notes that genetic testing for confirming DMD diagnosis is always required.[3-5] In patients with no mutations identified, but with signs/symptoms of DMD, muscle biopsy is clinically indicated. Glucocorticoids and physical therapy are the mainstays of treatment and should be continued even after the patient is non-ambulatory. Corticosteroids reduce the risk of scoliosis and stabilize pulmonary function. In patients who are non-ambulatory, continuing corticosteroid treatment provides a reduction in the risk of progressive scoliosis and stabilization of pulmonary function tests. Due to this benefit, glucocorticoids should be considered in all patients with DMD.

Dosing
The recommended dose is 1.33×10^{14} vg/kg of body weight (or 10 mL/kg body weight) for patients weighing < 70 kg or 9.31×10^{15} vg total fixed dose for patients ≥ 70 kg.[1] Re-administration of Elevidys is not recommended. Immune responses to the AAVrh74 vector can occur after Elevidys administration. To reduce this risk, corticosteroids should be administered starting one day prior to Elevidys infusion and continued for a minimum of 60 days after the infusion, unless earlier tapering is clinically indicated.

Safety
Elevidys is contraindicated in patients with any deletion in exon 8 and/or exon 9 in the *DMD* gene.[1] Warnings/Precautions include acute serious liver injury, immune-mediated myositis, myocarditis, and pre-existing immunity against AAVrh74. For the administration of Elevidys, the anti-AAVrh74 total antibody binding titer should be < 1:400.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

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

References

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2. Mendell JR, Shieh PB, McDonald CM, et al. Expression of SRP-9001 dystrophin and stabilization of motor function up to 2 years post-treatment with delandistrogene moxeparvovec gene therapy in individuals with Duchenne muscular dystrophy. *Front Cell Dev Biol.* 2023:11;1167762.
3. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol*. 2018;17(3):251-267.

4. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. *Lancet Neurol*. 2018;17(4):347-361.
5. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency medicine, psychological care, and transitions of care across the lifespan. *Lancet Neurol*. 2018;17(5):445-455.
6. Mendell JR, Muntoni F, McDonald CM, et al. AAV gene therapy for Duchenne muscular dystrophy: the EMBARK phase 3 randomized trial. *Nat Med.* 2025;31(1):332-341.
7. Mendell JR, Muntoni F, McDonald CM, et al. Long-term functional outcomes, safety, and micro-dystrophin expression following delandistrogene moxeparvovec treatment in DMD: EMBARK 2-year results. Presented at: Muscular Dystrophy Association (MDA) Clinical & Scientific Conference, Dallas, TX; March 16-19, 2025.
8. Zaidman CM, Proud CM, McDonald CM, et al. Delandistrogene moxeparvovec gene therapy in ambulatory patients (aged > 4 to < 8 years) with Duchenne muscular dystrophy: 1 year interim results from SRP-9001-103 (ENDEAVOR). *Ann Neurology*. 2023;94(5):955-968.
9. Sarepta Press Release. Sarepta provides safety update for Elevidys and initiates steps to strengthen safety in non-ambulatory individuals with Duchenne. Available at: https://investorrelations.sarepta.com/news-releases/news-release-details/sarepta-provides-safety-update-elevidys-and-initiates-steps Accessed on June 17, 2025.
10. Sarepta Press Release. July 18, 2025. Sarepta Therapeutics Provides Statement on Elevidys. Available at: https://investorrelations.sarepta.com/news-releases/news-release-details/sarepta-therapeutics-provides-statement-elevidys?_ga=2.96014101.820140099.1753120058-103273225.1753120058. Accessed on July 21, 2025.
11. Sarepta Press Release. July 18, 2025. Community Letter: Update regarding Elevidys. Available at: https://www.sarepta.com/community-letter-update-regarding-elevidys. Accessed on July 21, 2025.
12. FDA mulls Elevidys market withdrawal following 3rd death after a Sarepta gene therapy. July 18, 2025. Available at: https://www.fiercepharma.com/pharma/fda-mulls-elevidys-market-withdrawal-following-3rd-death-after-sarepta-gene-therapy. Accessed on July 21, 2025.
13. Sarepta Press Release. July 21, 2025. Sarepta Therapeutics Announces Voluntary Pause of Elevidys Shipments in the U.S. Available at: https://investorrelations.sarepta.com/news-releases/news-release-details/sarepta-therapeutics-announces-voluntary-pause-elevidys. Accessed on July 22, 2025.
14. Sarepta Press Release. July 28, 2025. FDA Informs Sarepta That It Recommends That Sarepta Remove Its Pause and Resume Shipments of Elevidys for Ambulatory Individuals with Duchenne Muscular Dystrophy. Available at: https://investorrelations.sarepta.com/news-releases/news-release-details/fda-informs-sarepta-it-recommends-sarepta-remove-its-pause-and. Accessed on July 29, 2025.

Revision History

Type of Revision	Summary of Changes	Approval Date
New		11/28/2023
Annual Revision	**Policy Name.** **Updated from** "Muscular Dystrophy – Gene Therapy – Elevidys (delandistrogene moxeparvovec-rokl intravenous infusion)" **to** "Muscular Dystrophy – Gene Therapy – Elevidys" **Conditions Not Covered.**	11/1/2024

	Added "The current Elevidys efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits. In the absence of additional clinical trials, there is not enough information to support approval."	
Selected Revision	**Updated** experimental, investigational or unproven statement with the addition of "regardless of U.S. Food and Drug Administration (FDA) approval status. Criteria will be updated as new published data are available." **Conditions Not Covered** **Updated** Duchenne Muscular Dystrophy (DMD)	8/1/2025

The policy effective date is in force until updated or retired.