VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Muscular Dystrophy – Gene Therapy – Elevidys Utilization Management Medical Policy
- Elevidys® (delandistrogene moxeparvovec-rokl intravenous infusion – Sarepta)

REVIEW DATE: 06/25/2025

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).

As of June 15, 2025, Sarepta has suspended Elevidys shipment to non-ambulatory patients due to a second patient death.[9] The two reported patient deaths are due to acute liver failure.

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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Elevidys. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Elevidys as well as the specialized training required for administration of Elevidys, approval requires Elevidys to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one-time (per lifetime) single dose. The approval duration is 1 month to allow for an adequate timeframe to prepare and administer one dose of therapy. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. In the criteria for Elevidys, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: males are defined as individuals with the

biological traits of a man, regardless of the individual's gender identity or gender expression. All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required for use of Elevidys as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Elevidys is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Duchenne Muscular Dystrophy – Treatment.** Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, J, K, L, M, N, and O):
   - **A)** Patient is a male*; AND
   - **B)** Patient age is greater than or equal to 4 years 0 days and less than 8 years 0 days; AND
   - **C)** Patient has had a genetic test confirming the diagnosis of Duchenne muscular dystrophy involving a pathogenic variant in the *DMD* gene **[documentation required]**; AND
     Note: This includes frameshift deletion, frameshift duplication, premature stop, canonical splice site mutation or other pathogenic variant in the *DMD* gene.
   - **D)** Patient does not have any deletions in exon 8 or exon 9 in the *DMD* gene **[documentation required]**; AND
   - **E)** Patient has not received Elevidys in the past **[verification in claims history required]**; AND
     Note: If no claim for Elevidys is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Elevidys.
   - **F)** Patient is ambulatory **[documentation required]**; AND
   - **G)** Anti-adeno-associated virus serotype rh74 (AAVrh74) total binding antibody titers are < 1:400 **[documentation required]**; AND
   - **H)** Patient screening is negative for ALL of the following (i, ii, and iii):
     - **i.** Human immunodeficiency virus-1 and -2 **[documentation required]**; AND
     - **ii.** Hepatitis B virus **[documentation required]**; AND
     - **iii.** Hepatitis C virus **[documentation required]**; AND
   - **I)** Patient has left ventricular ejection fraction ≥ 40% **[documentation required]**; AND
   - **J)** Patient has undergone liver function testing within the past 30 days and meets ALL of the following (i, ii, and iii):
     - **i.** Gamma-glutamyl transferase level is ≤ two times the upper limit of normal **[documentation required]**; AND
     - **ii.** Glutamate dehydrogenase level is ≤ 15 U/L **[documentation required]**; AND
     - **iii.** Total bilirubin is ≤ two times the upper limit of normal **[documentation required]**; AND
       Note: A patient who has Gilbert's syndrome does not have o tmeet this requirement.
   - **K)** A complete blood cell count has been obtained within the past 30 days and the patient meets BOTH of the following (i and ii):
     - **i.** White blood cell count is < 18.5 x 10^9/L **[documentation required]**; AND
     - **ii.** Platelet count is >150 x 10^9/L **[documentation required]**; AND
   - **L)** The medication is prescribed by a neurologist, neuromuscular specialist, or a physician who specializes in the management of Duchenne muscular dystrophy; AND

M) According to the prescribing physician, patient has started or will receive systemic corticosteroids equivalent to oral prednisone at a dose of 1 mg/kg per day or more, commencing 1 day prior to Elevidys infusion and continuing for at least 60 days; AND

N) Current patient body weight has been obtained within the past 30 days **[documentation required]**; AND

O) If criteria A through N are met, approve one dose of Elevidys by intravenous infusion to provide a one-time (per lifetime) single dose, according to ONE of the following (i or ii):

i. For a patient weighing less than 70 kg, the Elevidys dose is 1.33×10^{14} vector genomes per kg (vg/kg) based on the current patient weight in kg (or 10 mL/kg body weight) **[verification required]**; OR

ii. For a patient weighing 70 kg or more, the Elevidys dose is 9.31×10^{15} vg total fixed dose **[verification required]**.

Elevidys is provided as a customized kit to meet dosing requirements for each patient based on their weight (in kilograms). Elevidys kit sizes (per the cited NDC) are in Table 1.

* Refer to the Policy Statement

Dosing. The recommended dose of Elevidys is one dose given by intravenous infusion to provide a one-time (per lifetime) single dose based on ONE of the following (A or B):

A) For a patient weighing less than 70 kg, the Elevidys dose is 1.33×10^{14} vector genomes per kilogram (vg/kg) of body weight (or 10 mL/kg body weight) **[verification required]**; OR

B) For a patient weighing 70 kg or more, the Elevidys dose is 9.31×10^{15} vg total fixed dose **[verification required]**.

Elevidys is provided as a customized kit to meet dosing requirements for each patient per their documented weight (in kilograms). Refer to Table 1 below for the number of vials per kit based on weight and the appropriate NDC number.

Table 1. Elevidys Multi-Vial Kits.[1]

Patient Weight (kg)	Total Vials per Kit	Total Dose Volume Per Kit (mL)	NDC Number
10.0 to 10.4	10	100	60923-501-10
10.5 to 11.4	11	110	60923-502-11
11.5 to 12.4	12	120	60923-503-12
12.5 to 13.4	13	130	60923-504-13
13.5 to 14.4	14	140	60923-505-14
14.5 to 15.4	15	150	60923-506-15
15.5 to 16.4	16	160	60923-507-16
16.5 to 17.4	17	170	60923-508-17
17.5 to 18.4	18	180	60923-509-18
18.5 to 19.4	19	190	60923-510-19
19.5 to 20.4	20	200	60923-511-20
20.5 to 21.4	21	210	60923-512-21

Table 1 (continued). Elevidys Multi-Vial Kits.[1]

Patient Weight (kg)	Total Vials per Kit	Total Dose Volume Per Kit (mL)	NDC Number
21.5 to 22.4	22	220	60923-513-22
22.5 to 23.4	23	230	60923-514-23
23.5 to 24.4	24	240	60923-515-24
24.5 to 25.4	25	250	60923-516-25
25.5 to 26.4	26	260	60923-517-26
26.5 to 27.4	27	270	60923-518-27
27.5 to 28.4	28	280	60923-519-28
28.5 to 29.4	29	290	60923-520-29
29.5 to 30.4	30	300	60923-521-30
30.5 to 31.4	31	310	60923-522-31
31.5 to 32.4	32	320	60923-523-32
32.5 to 33.4	33	330	60923-524-33
33.5 to 34.4	34	340	60923-525-34
34.5 to 35.4	35	350	60923-526-35
35.5 to 36.4	36	360	60923-527-36
36.5 to 37.4	37	370	60923-528-37
37.5 to 38.4	38	380	60923-529-38
38.5 to 39.4	39	390	60923-530-39
39.5 to 40.4	40	400	60923-531-40
40.5 to 41.4	41	410	60923-532-41
41.5 to 42.4	42	420	60923-533-42
42.5 to 43.4	43	430	60923-534-43
43.5 to 44.4	44	440	60923-535-44
44.5 to 45.4	45	450	60923-536-45
45.5 to 46.4	46	460	60923-537-46
46.5 to 47.4	47	470	60923-538-47
47.5 to 48.4	48	480	60923-539-48
48.5 to 49.4	49	490	60923-540-49
49.5 to 50.4	50	500	60923-541-50
50.5 to 51.4	51	510	60923-542-51
51.5 to 52.4	52	520	60923-543-52
52.5 to 53.4	53	530	60923-544-53
53.5 to 54.4	54	540	60923-545-54
54.5 to 55.4	55	550	60923-546-55
55.5 to 56.4	56	560	60923-547-56
56.5 to 57.4	57	570	60923-548-57
57.5 to 58.4	58	580	60923-549-58
58.5 to 59.4	59	590	60923-550-59
59.5 to 60.4	60	600	60923-551-60
60.5 to 61.4	61	610	60923-552-61
61.5 to 62.4	62	620	60923-553-62
62.5 to 63.4	63	630	60923-554-63
63.5 to 64.4	64	640	60923-555-64
64.5 to 65.4	65	650	60923-556-65
65.5 to 66.4	66	660	60923-557-66
66.5 to 67.4	67	670	60923-558-67
67.5 to 68.4	68	680	60923-559-68
68.5 to 69.4	69	690	60923-560-69
69.5 and above	70	700	60923-561-70

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of Elevidys is not recommended in the following situations:

1. **Becker Muscular Dystrophy.** Elevidys is not approved for use in this condition.

2. **Patients with Duchenne Muscular Dystrophy Who are Non-Ambulatory.** There are very limited data with Elevidys use in patients with Duchenne muscular dystrophy who are non-ambulatory. Use of Elevidys in non-ambulatory patients is approved under accelerated approval based on expression of Elevidys micro-dystrophin in skeletal muscle. Further confirmatory trials are needed to establish the efficacy of Elevidys in this population. As of June 15, 2025, Sarepta has suspended Elevidys shipment to non-ambulatory patients due to a second patient death.[9] The two reported patient deaths are due to acute liver failure.

3. **Concurrent Use with Anti-Sense Oligonucleotide (Exon-Skipping) Therapies.** Patients should have discontinued use of exon-skipping therapies prior to the administration of Elevidys. The EMBARK confirmatory trial excluded patients who had used exon-skipping therapies within 6 months of Elevidys administration and at any time during the study. There are no data available with concomitant use of any of the exon-skipping therapies with Elevidys.
   Note: Examples of anti-sense oligonucleotide (exon-skipping) therapies include Exondys 51 (eteplirsen intravenous infusion), Vyondys 53 (golodirsen intravenous infusion), Viltepso (viltolarsen intravenous infusion), and Amondys 45 (casimersen intravenous infusion).

4. **Prior Receipt of Gene Therapy.** Elevidys has not been studied in a patient who has received prior gene therapy. Treatment with Elevidys is not recommended.

5. **Prior Hematopoietic Stem Cell Transplantation.** Elevidys has not been studied in a patient who has received prior stem cell transplant. Treatment with Elevidys is not recommended.

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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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.
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9. Sarepta Press Release. Sarepta provides safety update for Elevidys and initiates steps to strengthen safety in non-ambulatory individuals with Duchenne. Available at: Sarepta Provides Safety Update for ELEVIDYS and Initiates Steps to Strengthen Safety in Non-Ambulatory Individuals with Duchenne | Sarepta Therapeutics, Inc. Accessed on June 17, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	07/19/2023
Annual Revision	No criteria changes.	08/14/2024
Early Annual Revision	The Policy Statement was modified from "Due to the lack of clinical efficacy data, approval is not recommended for Elevidys" to as listed. **Duchenne Muscular Dystrophy – Treatment:** This condition of approval was added. **Conditions Not Recommended for Approval:** Removed Duchenne Muscular Dystrophy. Added Becker Muscular Dystrophy, Patients with Duchenne Muscular Dystrophy Who are Non-Ambulatory, Concurrent Use with Anti-Sense Oligonucleotides (Exon-Skipping) Therapies, Prior Receipt of Gene Therapy, and Prior Hematopoietic Stem Cell Transplantation.	06/25/2025