Utilization Review Policy 312A

POLICY: Muscular Dystrophy – Gene Therapy – Elevidys Utilization Management Medical Policy

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

EFFECTIVE DATE: 2/1/2024
LAST REVISION DATE: 01/12/2024

COVERAGE CRITERIA FOR: UCare Medicaid Plans Only (PMAP, Connect, MSC+, MnCare)

OVERVIEW

Elevidys, an adeno-associated virus (AAV) vector-based gene therapy, is 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] This indication is approved under accelerated approval based on expression of Elevidys micro-dystrophin observed in patients treated with Elevidys. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Disease Overview

DMD is a rare, progressive X-linked disease resulting from mutation(s) of the *DMD* gene, also known as the *Dystrophin* gene.[2-4] 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 occurs 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 two studies:[1-4] a Phase II study and a Phase Ib study.[1] Both studies are unpublished and long-term follow-up is ongoing. 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. 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 x 10^{14} vector genomes (vg)/kg, due to variability in quantification methods.[1-3] In Part I, only 8 patients received the approved dose of Elevidys 1.33 x 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 x 10^{14} vg/kg.

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.[5-7] In patients with no mutations identified, but with signs/symptoms of DMD, a 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 stabilizes 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 x 10^{14} vg/kg of body weight (or 10 mL/kg body weight).[1] 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 are for acute serious liver injury, immune-mediated myositis, myocarditis, and pre-existing immunity against AAVrh74. For 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. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Elevidys as well as the monitoring required for adverse events and long-term efficacy, approval requires Elevidys to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. **Duchenne Muscular Dystrophy**. Approve a single dose if the patient meets the following criteria (A, B, C, D, E, F, G, H, I, J, K, L, and M)
   - **A)** Patient is aged 4 through 5 years old and will be under 6 years of age at time of Elevidys administration; AND
   - **B)** Patient is not on concomitant therapy with DMD-directed antisense oligonucleotides (e.g., golodirsen, casimersen, viltolarsen, eteplirsen, etc.); AND
   - **C)** Patient has a not received a DMD-directed antisense oligonucleotide within the past 30 days; AND
   - **D)** Patient does not have an active infection, including clinically important localized infections; AND
   - **E)** Patient is on a stable dose equivalent of oral corticosteroids (e.g., prednisone) and will continue prior to and following receipt of Elevidys; AND
   - **F)** Patient troponin-I levels will be monitored at baseline and subsequently as clinically indicated; AND
   - **G)** Patient will have baseline liver function assessed prior to and following therapy for at least 3 months and as indicated; AND
   - **H)** Patient has a confirmed mutation of the DMD gene between exons 18-58; AND
   - **I)** Patient is ambulatory as confirmed by the North Star Ambulatory Assessment (NSAA) scale (i.e., patient score of 1 or greater); AND
   - **J)** Patient is receiving physical and/or occupational therapy; AND
   - **K)** Patient must have a baseline anti-AAVrh74 total binding antibody titer of < 1:400 as measured by ELISA (Note: An FDA authorized test for the detection of AAVrh74 total binding antibodies is not currently available. Currently available tests may vary in accuracy and design.); AND
   - **L)** Patient does NOT have any deletion in exon 8 and/or exon 9 in the DMD gene, AND
   - **M)** The medication is prescribed by or in consultation with a pediatric neuromuscular specialist with expertise in the diagnosis of Duchenne muscular dystrophy.

   Dosing. Approve up to 1.33×10^{14} vector genomes per kilogram (vg/kg) of body weight (or 10 mL/kg body weight).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Elevidys is not recommended in the following situations:

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

REFERENCES

1. Elevidys® intravenous infusion [prescribing information]. Cambridge, MA: Sarepta Therapeutics, Inc.; June 2023.
2. US Food and Drug Administration. Cellular, Tissue, and Gene Therapies Advisory Committee Meeting. May 12, 2023. Available at: https://www.fda.gov/advisory-committees/advisory-committee-calendar/cellular-tissue-and-gene-therapies-advisory-committee-may-12-2023-meeting-announcement-05122023 Accessed on May 10, 2023.
3. Sarepta Therapeutics, Inc. Sponsor Briefing Document. Cellular, Tissue, and Gene Therapies Advisory Committee Meeting. May 12, 2023. Available at: https://www.fda.gov/advisory-committees/advisory-committee-calendar/cellular-tissue-and-gene-therapies-advisory-committee-may-12-2023-meeting-announcement-05122023 Accessed on May 10, 2023.

4. 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.* 11;1167762. DOI: 10.3389/fcell.2023.1167762.
5. 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.
6. 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.
7. 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	07/19/2023
UCare Update	UCare identified Elevidys is participating in the Medicaid Drug Rebate program and therefore is eligible for coverage. This policy is an update from the prior policy which recommends denial due unclear clinical benefit of Elevidys based on clinical trials.	01/12/2024