delandistrogene moxeparvovec-rokl (Elevidys®)

Policy # 00859
Original Effective Date: 03/11/2024
Current Effective Date: 03/11/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of delandistrogene moxeparvovec-rokl (Elevidys®)‡ 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 to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of delandistrogene moxeparvovec-rokl (Elevidys) for non-FDA approved indications to be **investigational.***

Background/Overview

Elevidys is a gene therapy indicated for one-time infusion in ambulatory patients 4 through 5 years of age with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* gene. It uses an AAV viral vector to deliver a truncated form of the dystrophin gene known as micro-dystrophin to muscle cells. The gene then drives the production of micro-dystrophin in these cells which is theorized to work in place of the missing dystrophin protein. It is contraindicated in patients with any deletion in exon 8 and/or exon 9 in the *DMD* gene due to the increased risk of immune-mediated myositis in these patients. Risk of immune-mediated myositis may also be elevated in patients with mutations in exons 1-17 and 59-71 of the *DMD* gene, but these are not listed as contraindications in the product label.

DMD is a progressive, X-linked, degenerative neuromuscular disease that results in disabling muscle weakness and eventually leads to early death. It is caused by mutations in the *DMD* gene resulting in reduced or near absence of dystrophin, a protein that helps keep muscle cells intact. Boys with

DMD are typically diagnosed at 3-5 years of age, and the estimated U.S. prevalence of DMD ranges from 10,000 to 15,000 males. There is no curative treatment for DMD. Current pharmacological approaches include corticosteroids and exon-skipping therapies. Corticosteroids, such as Emflaza (deflazacort) are the standard of care for treatment of DMD due to their beneficial effects for improving motor function and pulmonary function, reducing the risk of scoliosis, delaying the loss of ambulation, and possibly delaying progression of cardiomyopathy and improving survival. Exon-skipping therapies work to increase dystrophin protein expression in patients that have skippable deletions in exons 51, 53, or 45, representing about 30% of the DMD population. Exon-skipping therapies increase dystrophin protein expression and may at best slow disease progression, but have not been proven to improve survival or functional outcomes.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Elevidys was approved in June 2023 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.

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).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Accelerated approval for Elevidys was granted based on data from Study 1 and Study 2 described below.

Study 1 is an ongoing multi-center study including:

- Part 1: a 48-week, randomized, double-blind, placebo-controlled period.
- Part 2: a 48-week period that began following completion of Part 1. Patients who received placebo during Part 1 were treated with Elevidys, and patients treated with Elevidys during Part 1 received placebo.

The study population consisted of male ambulatory DMD patients (n=41) aged 4 through 7 years with either a confirmed frameshift mutation, or a premature stop codon mutation between exons 18 to 58 in the DMD gene.

Patients were randomized 1:1 to receive either Elevidys (n=20) or placebo (n=21) as a single intravenous infusion via a peripheral limb. Randomization was stratified by age (i.e., aged 4 to 5 years vs ages 6 to 7 years). In the Elevidys group, eight patients received 1.33 x 10^{14} vg/kg of Elevidys, and 12 patients received lower doses.

All subjects were on a stable dose of corticosteroids for DMD for at least 12 weeks prior to Elevidys infusion. All randomized subjects had baseline anti-AAVrh74 antibody titers <1:400 as determined by an investigational total binding antibody ELISA. One day prior to treatment with Elevidys or placebo, the subject's background dose of corticosteroid for DMD was increased to at least 1 mg/kg of a corticosteroid (prednisone equivalent) daily and was continued at this level for at least 60 days after the infusion, unless earlier tapering was clinically indicated.

The primary objectives of Study 1 were to evaluate expression of Elevidys micro-dystrophin in skeletal muscle, and to evaluate the effect of Elevidys on the North Star Ambulatory Assessment (NSAA) total score. The mean change from baseline in the percentage of Elevidys micro-dystrophin compared to control was 43.4 in part 1 and 40.7 in part 2. The change in NSAA total score was assessed from baseline to Week 48 after infusion of Elevidys or placebo. The difference between the Elevidys and placebo groups was not statistically significant (p=0.37). The least squares (LS) mean changes in NSAA total score from baseline to Week 48 was 1.7 (standard error [SE]: 0.6) points for the Elevidys group and 0.9 (SE:0.6) points for the placebo group. Exploratory subgroup analyses 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, and 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.

Study 2 is an ongoing, open-label, multi-center study which includes a cohort of 20 ambulatory male DMD subjects aged 4 through 7 years. All 20 subjects have a confirmed frameshift mutation, canonical splice site mutation, or premature stop codon mutation in the DMD gene. All subjects had baseline anti-AAVrh74 antibodies titers <1:400 as determined by the investigational total binding antibody ELISA and received a single intravenous infusion of 1.33×10^{14} vg/kg Elevidys.

The primary objective of the study was to evaluate the effect of Elevidys micro-dystrophin expression as measured by western blot. The mean change from baseline at Week 12 was found to be 54.2% (standard deviation 42.6).

References

1. Elevidys [package insert]. Sarepta Therapeutics, Inc. Cambridge, MA. Updated June 2023.

Policy History

Original Effective Date: 03/11/2024
Current Effective Date: 03/11/2024
02/01/2024 Medical Policy Committee review
02/14/2024 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 02/2025

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J1413
ICD-10 Diagnosis	G71.01

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.