Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Delandistrogene moxeparvovec-rokl (Elevidys)	MP-RX-FP-163-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Elevidys, a vector-based gene therapy, approved by the Food and Drug Administration (FDA) for the treatment of Duchenne muscular dystrophy (DMD) in ambulatory or non-ambulatory patients with a confirmed mutation in the DMD gene.

ELEVIDYS (Delandistrogene moxeparvovec-rokl) is a suspension approved for intravenous administration only, with a dosing regimen based on the patient's body weight.

Background Information

Duchenne muscular dystrophy (DMD) is an X-linked disease caused by mutations in the dystrophin gene. This genetic disorder, results in progressive and irreversible muscle weakness and damage. The disease typically manifests in early childhood, with initial symptoms including difficulty walking, enlarged calves, difficulty standing from a supine position, frequent falls, fatigue, and loss of muscle strength. In the initial stages of Duchenne muscular dystrophy, the disease primarily affects the muscles of the hips and thighs, leading to difficulties with standing, climbing stairs, and maintaining balance. As the disease progresses, these difficulties often result in complete loss of ambulation. In later years of age, the disease affects cardiac and respiratory function, with the potential for life-threatening complications.

Although Duchenne muscular dystrophy (DMD) is considered an irreversible condition, several clinical management strategies have been developed with the objective of slowing the progression of the disease. The following table illustrates the typical clinical signs and symptoms progression of Duchenne muscular dystrophy (DMD) at different age ranges. It should be considered that DMD is a heterogeneous disease, meaning that the progression of Duchenne varies significantly between patients.

Table 1. Disease Progression in Duchenne Muscular Dystrophy (DMD)

Age	Symptoms Description
Commonly observed in 0 to 4 years	• Soon after birth inflammation • Muscle fibrosis seen as early as 1 year of age • Motor delays • Other delays, such as a speech delay
Commonly observed in 5 to 7 years	• Progressive muscular weakness • Enlarged calves

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	• Toe walking • Difficulty standing from a supine position • Muscle fat accumulation
Commonly observed in 8 to 11 years	• Delays in the motor milestones • Decreased ability to walk • Part-time wheelchair use
Commonly observed in 12 to 19 years	• Decreased upper limb, respiratory, and cardiac function • Loss of ambulation • Frequent need for ventilatory support • Inability to perform activities of daily living
Commonly observed in teens and beyond	• Increase in cardiac dysfunction • Heart failure • Life expectancy significantly reduced

An early diagnosis of Duchenne muscular dystrophy (DMD) involves a combination of genetic testing to confirm a mutation in the DMD gene and a physical assessment, as well as laboratory tests such as elevated serum creatine kinase, which indicates muscle damage. In patients aged between 0 and 3 years, creatine kinase (CK) levels are greater than 305 U/L (with a normal range of 60-305 U/L). In patients aged between 4 and 6 years, CK levels above 230 U/L are indicative of an abnormally high level.

For patients who are ambulatory, a rating scale called the North Star Ambulatory Assessment (NSAA) is used to quantify the effect of Duchenne muscular dystrophy on a patient's ability to perform activities of daily living requiring ambulatory capabilities. The NSAA is a validated rating scale that comprises 17 assessments, including: stand, walk, rise from a chair, climb, and descend a box step, gets to sitting, jump, run, rise from floor, lift head, and hop on the legs. These assessments evaluate ability and assistance requirement to perform the task. Each of the 17 assessments is scored on a scale of 0, 1, or 2, depending on the patient's performance of the designated activity. A score of 0 indicates that the subject is unable to perform the task. A score of 1 indicates that the subject is able to perform the task but required assistance or completed the task independently but with evident difficulty. A score of 2 indicates that the subject is able to perform the task independently and without difficulty. A higher total score is indicative of better functional performance. For patients younger than five years old, the NSAA reorders the tasks to align better with age-appropriate abilities and scoring as described in the table below. This approach considers the typical progression of motor skill development in children.

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Table 2. NSAA highest score according to patient age

Age (years)	Highest score and assessment items
3	Highest score: 16 Assessment: 8 items
3 ½	Highest score: 26 Assessment: 13 items
4 and older	Highest score: 34 Assessment: 17 items

The Duchenne muscular dystrophy treatment involves a combination of pharmacologic and non-pharmacologic therapies aimed at managing symptoms, preserving muscle function, and treating complications. Corticosteroids, such as Prednisone and Deflazacort (Emflaza), are commonly used to reduce muscle degeneration. In addition, exon-skipping therapies such as Casimersen (Amondys 45), Eteplirsen (Exondys 51), Golodirsen (Vyondys 53), and Vitolarsen (Viltepso) are designed to bypass specific mutated exons in the DMD gene transcript to mitigate the effects of mutations in patients with specific genotypes. Physical therapy is essential to maintain mobility and quality of life for people with DMD. Emerging gene therapies such as Elevidys represent a new approach to DMD treatment by targeting the DMD gene.

Elevidys (delandistrogene moxeparvovec-rokl) is the first gene therapy approved by the FDA for the treatment of Duchenne muscular dystrophy. This vector-based gene therapy is a single intravenous treatment indicated for ambulatory or non-ambulatory patients 4 years of age and older with a confirmed mutation in the DMD gene. Elevidys is designed to address the absent functional dystrophin in DMD, a protein that stabilizes muscle fibers. Elevidys is contraindicated in patients with deletions in exon 8 and/or exon 9, which may increase the risk of an immune-mediated myositis reaction. Anti-AAV antibody titers must be measured as patients eligible for Elevidys must have anti-AAVrh74 total binding antibody titers <1:400. The recommended dosage of Elevidys is based on the patient's weight, depending on whether it is less or more than 70 kg. It is supplied as a 10 mL single-use vial in a customized kit based on the patient's dosing requirements. Elevidys may cause infusion-related reactions, acute severe liver injury, immune-mediated myositis, and myocarditis. As part of the administration process, it is recommended that patients receive systemic corticosteroid treatment before and after Elevidys to reduce the risk of an immune response.

To date, benefits of Elevidys have been demonstrated in two double-blind, placebo-controlled studies (Study 1 [NCT 03769116] and Study 3 [NCT 05096221]) and one open-label study (Study 2 [NCT 04626674]). Relevant inclusion criteria are shown in the table below.

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Table 3. Clinical Trials Evaluating Elevidys in Duchenne Muscular Dystrophy (DMD).

Trial	Diagnosis	Study population	Age
Study 1 [NCT03769116]	Confirmed frameshift mutation, or a premature stop codon mutation between exons 18 to 58 in the DMD gene.	41 male ambulatory patients	4 through 7 years
Study 2 [NCT 04626674]	Cohorts 1, 2 and 3: Confirmed frameshift, splice site or premature stop codon mutation anywhere in the DMD gene. Cohort 4: Patients with mutations in the DMD gene starting at or after exon 18. Cohort 5: Mutations that partially or fully overlap with exons 1-17 in the DMD gene.	48 male patients (5 cohorts)	Cohorts 1, 2, 4 and 5a: 40 ambulatory patients 3 to 12 years of age. Cohorts 3 and 5b: 8 non-ambulatory patients 10 to 20 years of age.
Study 3 [NCT 05096221]	Confirmed frameshift, splice site, premature stop codon, or other disease-causing mutation in the DMD gene starting at or after exon 18	125 ambulatory male patients	4 through 7 years

Approved Indications

ELEVIDYS is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who are ambulatory or non-ambulatory with at least 4 years with a confirmed mutation in the DMD gene.

Other Uses

None.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

ICD-10	Description
G71.01	Duchenne or Becker muscular dystrophy

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Delandistrogene moxeparvovec-rokl (ELEVIDYS)

A. Criteria For Initial Approval

Initial request of Elevidys may be approved if the following criteria are met:

i. Elevidys is prescribed by a neurologist or neuromuscular specialist.

ii. Documentation provided that evidence a confirmatory diagnosis by:

A. Patient is four (4) years of age or more; **AND**

B. Genetic test that confirms the mutation in the Duchenne muscular dystrophy (DMD) gene; **AND**

C. Genetic test confirms that the mutation is not a deletion in exon 8 and/or exon 9 in the DMD gene.
AND

iii. Documentation evidencing:

A. Anti-AAVrh74 total binding antibody titers <1:400; **AND**

B. Baseline liver function test, platelet counts and troponin levels within normal range; **AND**

C. Current weight of the patient at the time of submitting the request for evaluation; **AND**

iv. Patient meets all the following criteria:

A. The prescribed dose is appropriate to the patient's weight.

- Less than 70 kg: Weight based; **OR**
- 70 kg or greater: Fixed total fixed dose; **AND**

Refer to the section: "Indicated dose based on the patient's weight for more details.

B. Patient has not previously received Elevidys therapy; **AND**

C. Exon-skipping therapies (antisense oligonucleotides) will not be used concurrently or following Elevidys administration (including, but not limited to, Casimersen, Eteplirsen, Golodirsen, Vitolarsen); **AND**

D. Patient will receive a corticosteroid regimen before and after infusion; **AND**

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E. The patient is not currently experiencing an active infection,
AND

v. ELEVIDYS will be administered as an intravenous infusion.

vi. For ambulatory patients only:

A. Documentation evidencing the ambulatory performance evaluation by the North Star Ambulatory Assessment (NSAA).

- NSAA performed for the past six months at the time of submitting the request for evaluation. NSAA performed within the past six (6) months.

Indicated dose based on the patient's weight

- Less than 70 kg: 1.33×10^{14} vector genomes per kilogram (vg/kg) **OR** 10 mL/kg
  - The patient's body weight should be rounded to the nearest kilogram.
    - Example: Elevidys for a 20.5 kg patient
      Round to the nearest kilogram = 21 kg
  - Elevidys dose (mL) = Patient body weight (rounded to the nearest kilogram) x 10mL/kg
    - The multiplication factor 10 represents the per kilogram dose (1.33×10^{14} vg/kg) divided by the amount of vector genome copies per mL of the ELEVIDYS suspension (1.33×10^{13} vg/mL).
  - Number of Elevidys vials needed = ELEVIDYS dose (in mL) divided by 10.
    - Each Elevidys vial has a volume of 10mL (10mL/vial)
    - Round to the nearest number of vials

Calculation Example: Elevidys dose for a 20.5 kg patient.

20.5 kg rounded to the nearest kilogram = 21 kg

Elevidys Volume: $21\ kg \times \left(\frac{10mL}{kg}\right)$= 210 mL

Elevidys vials: $210mL\ \left(\frac{vial}{10\ mL}\right) = 21\ vials$

- 70 kg or greater: 9.31×10^{15} vector genomes (vg) total fixed dose

B. Criteria For Continuation of Therapy

i. MMM does not consider the continuation of Elevidys to be medically necessary. According to the product's updated clinical approved data, Elevidys is approved for single-dose administration only, and there is no recommendation for further doses.

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C. Authorization Duration

i. Initial Approval Duration: 3 months. According to the product's package label, Elevidys is administered as a single-dose intravenous infusion, and readministration is not recommended.

ii. Reauthorization Approval Duration: N/A. MMM does not consider the readministration of Elevidys to be medically necessary, as it is intended for single-dose administration only, and administration is not advised.

Note: The dosage is based on the patient's weight. If weight changes, the dosage should be adjusted accordingly.

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Patients with any deletion in exon 8 and/or exon 9 in the DMD gene; **OR**
ii. When the above criteria are not met and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Patient weight	Recommended Dose
Less than 70 kg	1.33×10^{14} vector genomes per kilogram (vg/kg) **OR** 10 mL/kg
70 kg or greater	9.31×10^{15} vector genomes (vg) total fixed dose
Exceptions	
N/A	

ELEVIDYS is supplied as a patient-specific kit (ten to seventy 10mL single-dose vials) to meet dosing requirements. The total number of vials in each kit is based on the patient's body weight and corresponds to the dosing

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requirement for that individual. Administration is by intravenous infusion over 1-2 hours at a rate of less than 10 mL/kg/hour. For further information regarding the dose and vial quantities calculations, please refer to the section: "Indicated dose based on the patient's weight" in this medical policy. Refer to the full Elevidys FDA Prescribing Information for dosage modifications, vials per kit based on patient weight, Elevidys preparation, and administration instructions.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	New Policy Creation	12/9/2024	12/17/2024

Revised: 12/03/2024