Molina Clinical Policy
Elevidys (delandistrogene moxeparvovec): Policy No. 436

Last Approval: 12/11/2024
Next Review Due By: August 2025

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy addresses the use of Elevidys for the treatment of individuals with Duchenne Muscular Dystrophy.

Duchene Muscular Dystrophy (DMD) is a progressive, fatal, genetic myopathy resulting from genetic lesions in the DMD gene. The DMD gene codes for the dystrophin protein critical to normal muscle function. When the DMD gene is mutated an important protein link between the inside of a muscle cell and the surrounding tissue breaks. This disruption leads to mechanical stress, inflammation, and muscle degeneration. Cardiac and diaphragmatic muscle are affected as well as skeletal muscle. The DMD gene is located on the X chromosome, hence DMD inheritance is X-linked and boys who inherit a pathogenic mutation in the DMD gene are affected whereas girls are typically carriers. Symptom onset is first seen when children begin to walk around 2-3 years of age. People with DMD experience pain, progressive symmetric weakness, frequent falls, difficulty climbing stairs and a waddling gait. Loss of ambulation occurs around 10-12 years of age and assistance with ventilation is required at approximately 20 years of age. Death is secondary to cardiac muscle failure and / or respiratory failure. Median life expectancy with optimal care is 20 - 40 years of age. Extra-muscular manifestations include cognitive deficits (~30%) and behavioral issues. The incidence of individuals affected by DMD is approximately 1 in 3,500 boys worldwide (NORD 2023). The prevalence of DMD is less than 10 cases per 100,000 males (Duan et al. 2021).

Diagnosis of DMD is suggested by the combination of typical symptoms and signs (Gower's maneuver) along with creatine kinase (ck) elevations. Genetic testing to confirm the diagnosis is required. Knowledge of the specific mutation is needed for therapeutic decisions including whether contraindications exist to Elevidys and whether other mutation specific therapies might apply. There are no curative therapies for DMD although management by multidisciplinary teams improve quality and length of life. Corticosteroids are the primary pharmacologic treatment. Four exon skipping drugs are FDA approved via the accelerated approval pathway however clinical benefit of these drugs are uncertain and confirmatory trials are incomplete.

Becker Muscular Dystrophy (BMD) is a milder form of DMD with later onset and slower progression. It is also caused by mutations in the DMD gene, but those mutations result in retention of some function of the dystrophin protein. Becker muscular dystrophy patients would likely not benefit from Elevidys gene therapy.

Elevidys (Delandistrogene moxeparvovec-rokl; formerly SRP-9001) is the first approved gene therapy for Duchenne Muscular dystrophy. It is an engineered form of microdystrophin delivered via adeno-associated virus (AAV), serotype rh74 with the MHCK7 (Myosin heavy-chain creatine kinase 7) promoter that promotes expression in muscle. It is a one-time infusion of a synthetic microdystrophin gene based on a patient with mild Becker muscular dystrophy. Dystrophin is the largest gene in the human genome and its size prevents delivery via viral vectors. Microdystrophins are "micro" because they encode only the most important parts of the dystrophin protein, and their smaller size allows for vector delivery. Because the genetic construct of this therapy is based on a partially functional microdystrophin protein from a BMD patient, it is not intended to be fully curative. This therapy is intended to lessen the severity of the most severe forms of DMD. It is indicated for the treatment of ambulatory and non-ambulatory patients aged 4 years and older with genetically confirmed Duchenne muscular dystrophy. Patients undergoing gene therapy will still require a multidisciplinary team to address on-going symptoms not ameliorated by this therapy.

In June of 2024 the FDA granted traditional approval to Elevidys for the treatment of ambulatory patients older than 4 years of age and accelerated approval for non-ambulatory patients aged 4 years and older.

The long-term safety, efficacy, and durability of Elevidys remains unknown. The size and design of the studies leads to uncertainty regarding the long-term net benefits of Elevidys. Risks of this therapy include development of antibodies to the viral vector which could diminish the ability to use future gene therapies delivered by similar vectors. Besides the typical side effect profiles for gene therapies, Elevidys has also been observed to cause an immune response leading to myositis and myocarditis (Bonnemann et al. 2023) in certain individuals.

RELATED POLICIES

MHI Policy & Procedure: Specialty Medication Administration Site of Care Policy: MHI Pharm 11

COVERAGE POLICY

All Gene Therapy requests require Molina Medical Director review.

Elevidys (delandistrogene moxeparvovec-rokl) for the treatment of Duchenne Muscular Dystrophy may be **considered medically necessary** when all the following criteria are met (with documentation):

1. A diagnosis of Duchenne muscular dystrophy defined by:
    a. A confirmed mutation in the DMD gene (documentation required)
    b. Clinical findings and mutation analysis consistent with Duchenne muscular dystrophy and not Becker muscular dystrophy
    c. Member does not have any deletion in exon 8 and/ or exon 9 in the DMD gene
2. The member is male
3. The Member is 4 - 20 years of age
4. The member is ambulatory; OR The member is non-ambulatory and has a performance upper limb (PUL) entry item score of ≥ 3 AND total PUL score ≥ 20 (PUL version 2.0)
5. The member has a left ventricular ejection fraction ≥ 40% by echocardiogram or cardiac MRI
6. Liver function tests are obtained within 30 days of request and do not indicate dysfunction per parameters below:
    a. Liver function:
        i. GGT < 3 times the upper limit of normal
        ii. Total bilirubin < 3 times the upper limit of normal
7. Baseline platelet count and Troponin I are obtained within 30 days of request
8. Baseline anti-AAVrh74 antibody titers are <1: 400
9. Member does not currently have an active infection
10. Member will receive systemic corticosteroids (equivalent to oral prednisolone at 1 mg/kg) prior to and following administration of Elevidys in accordance with FDA approved Elevidys labeling
11. Member is not currently enrolled in DMD clinical trials and is ineligible for clinical trial enrollment
    NOTE: Members eligible for, or currently enrolled in, DMD clinical trial enrollment will not be authorized. Individual should receive treatment and monitoring per clinical trial protocols in place by the applicable Institutional Review Board.
12. Member will stop exon skipping therapies (such as Exondys 51, Vyondys 53 or Amondys 45) just prior to

Elevidys administration

LIMITATIONS AND EXCLUSIONS

One contraindication is listed in the manufacturer's labeling. Elevidys is contraindicated in individuals with a deletion in exon 8 or exon 9 of the DMD gene (FDA approved labeling 2024).

The following are considered **experimental, investigational, and unproven** based on insufficient evidence:

1. Any indication other than those listed above
    a. *Based on the peer-reviewed medical literature the safety and effectiveness for indications other than the medically necessary indication listed above has not been established.*
2. Use in Becker muscular dystrophy
3. Prior treatment, or being considered for treatment, with other gene therapy
4. The use of Elevidys in those less than 4 years of age has not been evaluated
5. The safety and efficacy of Elevidys in patients with anti-AAVrh74 antibody titers ≥1:400 has not been studied
6. The use of Elevidys in patients with acute liver disease. Postpone Elevidys until resolved or controlled

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified pediatric neurologist, neuromuscular specialist or neurologist with experience in the diagnosis and management of DMD.

DURATION OF APPROVAL: Infusion may be performed up to 90 days from time of authorization.

QUANTITY LIMITATIONS: FDA approved dosing with one-time dose per lifetime. Additional infusions of Elevidys will not be authorized.

Dosing and Administration Considerations:

1. The intravenous dosage is determined by patient body weight (in kilograms), with a recommended dose of 1.33 × 10^{14} vector genomes (vg) per kg of body weight for pediatric patients and administered as an IV infusion over 1 to 2 hours. Infuse at a rate of 10 ml/kg/hour or less.
2. Calculate the dose as follows:
   ELEVIDYS dose (in mL) = patient body weight (in kilogram) x 10
   Number of ELEVIDYS vials needed = ELEVIDYS dose (in mL) divided by 10 (round to the nearest number of vials).

MONITORING PARAMETERS: Member should be monitored according to FDA-approved labeling and best practice.

CONTINUATION OF THERAPY

Elevidys is indicated as a one-time infusion only. Repeat treatment or re-administration of a dose is not supported by labeling or compendia and is not considered medically necessary.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Elevidys was approved in June 2023 under the accelerated approval pathway and in June 2024, the FDA expanded Elevidys indication to include ambulatory and non-ambulatory patients with Duchenne muscular dystrophy aged 4 years and older. The initial approval was based on a phase 2 study, SRP-9001-102 and phase 1,2 study, SRP-9001-103. The expanded approval was based on the "totality of evidence" from prior clinical trials of Elevidys and new data from trial 301 (NCT05096221, Embark) (CBER Memo 2024). In the final decision memo from the Center for Biologics Evaluation and Research, the FDA acknowledged the phase 3 trial failed to meet its primary endpoints, but the secondary endpoints and exploratory endpoints provided substantial evidence of effectiveness. Additional factors considered were the high unmet need for therapies in Duchenne muscular dystrophy and that changes in secondary

endpoints in the Elevidys treated group were above the thresholds established for minimal clinical important differences (Duong 2021).

SRP-9001-102 (NCT03769116) was a double-blind, placebo-controlled phase 2 trial with crossover blinding maintained for 48 weeks, followed by a 5-year open label follow-up. 41 study participants with DMD aged 4 - 7 years were included. All patients were ambulatory, without anti-AAVrh74 antibody titers >1:400 and other baseline lab values were within normal limits.

The primary endpoints were microdystrophin expression at 12 weeks and evaluation of the effect of Elevidys on the NSAA score throughout 48 weeks relative baseline. Microdystrophin was expressed in all patients.

A statistically significant correlation between the treated group and NSAA change was not seen in the 4 - 7 year age group. Because statistical significance was not obtained for the primary endpoint in the 4 - 7 year-old age group, secondary endpoints were not initially tested. However, a subgroup analysis found treated subjects aged 4 - 5 years, did have a significant positive improvement in NSAA (North Star Ambulatory Assessment) total score (+2.5 points; p = 0.0172). Motor function was stabilized for up to 2 years in the ambulatory patient population (Mendell 2023).

SRP-9001-103 (NCT04626674 – "Endeavor") is a phase 1 open label, single arm study of 4 - 7-year-old ambulatory males with DMD. Total study population was 48 participants. This study used external controls and combined participants from 101, 102 and a new cohort, cohort 1, comprised of 20 males. This trial also included a non-ambulatory cohort of patients up to 20 years of age. The primary endpoint was safety and microdystrophin expression via western blot at 12 weeks. An exploratory objective was to evaluate the effect of SRP-9001 on NSAA total score. There was a positive association between SRP-9001 expression and year 1 NSAA total score changes in the 4 - 5 year aged group but not the 6 or higher year age group. The NSAA change from baseline for cohort 1, as compared to external controls was 3.2 (p=0.0001) (Zaidman 2023). Additional data from study 103 submitted after the initial FDA review included Upper Limb assessments from 6 non-ambulatory patients. Performance on upper limb (PUL) assessments indicated a 2.5 point difference between treated and non-treated individuals. Statistical significance was not stated but the treatment group demonstrated better performance on PUL as compared to placebo (CBER memo 2024).

SRP-9001- 101 (NCT03375164) is an open label, single arm study of 4–7-year-old ambulatory males with DMD. The study began in 2018 and included a total of 4 participants. The primary endpoint for this small study was safety and secondary endpoints were microdystrophin expression and 100 meter timed test as well as NSAA change from baseline. Four years after infusion all patients have shown improvement in NSAA scores from baseline (mean increase of 7 pts) and the median time to walk 100 meters was 7 seconds less than baseline (Mendell et al. 2020; Mendell et al. 2022; Mendell et al. 2024).

Study 301 (NCT05096221, Embark) is an ongoing phase 3, double-blind, randomized placebo-controlled trial of Elevidys in male subjects aged 4 – 7 years old. The primary endpoint was change in the North Star Ambulatory Assessment (NSAA) from baseline to 52 weeks post treatment, as compared to placebo. Total study population was 125 participants. Statistical significance was not reached for the NSAA metric. However, differences in secondary endpoints including, Time-To-Rise from floor (TTR) and the 10 meter walk/run test (10MWR test) were statistically significantly better in the Elevidys treatment group as compared to the placebo group (p=0.0025 & p=0.0048 respectively). Time to climb four stairs (Ascend4) was also faster by 0.36 seconds in the treatment group (p=.0412). In addition, the exploratory end point, creatine kinase (CK), a marker of muscle damage, decreased from baseline to post treatment by - 5138,52 U/L. The Ck in the placebo group also decreased but by much less than the treatment group, -794.9 U/L by least square analysis. This suggests muscle damage decreased over time after Elevidys was administered, as compared to the placebo group.

A confirmatory trial looking into the benefit of Elevidys for non-ambulatory patients is underway.

Safety summary of the SRP-9001 studies revealed rare myocarditis, immune mediated myositis and acute liver injury in addition to minor adverse events associated with the AAV class of gene therapies. One patient developed immune mediated myositis and one patient developed myocarditis. There were no deaths and no adverse events that led to study discontinuation. The most frequent adverse reactions included vomiting (61%), nausea (40%), acute liver injury (37%), pyrexia (24%) and thrombocytopenia (12%). Theoretical risk of oncogenesis with rare integration events is noted.

SUPPLEMENTAL INFORMATION

The NSAA (North Star Ambulatory Assessment) is a motor function evaluation composed of 17 items of increasing difficulty. It is used to measure functional motor abilities in ambulant children with Duchenne Muscular Dystrophy. Performance of various functional skills are graded on a scale from 0 (unable), 1 (completes independently but with modifications), and 2 (completed without compensation). The maximum score is 34 indicating normal muscle function (Zambon et al. 2022).

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)

HCPCS (Healthcare Common Procedure Coding System)

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

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

12/11/2024	Added requirement of Molina Medical Director review.
08/14/2024	Updated with expanded indication from ambulatory 4-5 year olds with DMD to 4 to 20 years of age, either ambulatory or non-ambulatory with appropriate PUL scores. Added LVEF criteria.
02/27/2024	Updated approval period from 30 days to 90 days.
12/13/2023	Coding and Billing section updated. Annual review scheduled for August 2024.
08/09/2023	New policy. IRO Peer Review on July 14, 2023, by a practicing, board-certified physician with a specialty in Neurology.

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