Medical Coverage Policy | Gene Therapies for Duchenne Muscular Dystrophy

EFFECTIVE DATE: 01|01|2024
POLICY LAST REVIEWED: 01|07|2026

OVERVIEW

Duchenne muscular dystrophy (DMD) is an inherited disorder that results in progressive muscle weakness and loss of muscle mass, primarily affecting males. DMD results from non-sense or frame-shifting variant(s) in the DMD gene which is responsible for producing dystrophin, a cohesive protein essential for maintaining muscle support and strength. Delandistrogene moxeparvovec-rokl is an adeno-associated virus vector-based gene therapy which encodes a novel, engineered protein micro-dystrophin protein. This novel micro-dystrophin protein is a shortened version (138 kDa, compared to 427 kDa size of dystrophin expressed in normal muscle cells) that contains selected domains of dystrophin expressed in normal muscle cells.

MEDICAL CRITERIA

Not applicable.

PRIOR AUTHORIZATION

Not applicable.

POLICY STATEMENT

The use of delandistrogene moxeparvovec-rokl is considered not covered for Medicare Advantage Plans and not medically necessary for Commercial Products for all indications including the treatment of Duchenne muscular dystrophy as the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for not medically necessary/not covered pharmacy benefits/coverage.

BACKGROUND

Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is an X-linked, recessive disorder that occurs in approximately 1 in every 3500 to 5000 males. It primarily affects males. However, females are also affected, but are usually asymptomatic. Even when symptomatic, most females typically only present with a mild form of the disease. According to U.S. epidemiologic data, the first signs or symptoms of DMD are noted at a mean age of 2.5 years (range, 0.2 to 1 years). Although histologic and laboratory evidence of myopathy may be present at birth, the clinical onset of skeletal muscle weakness usually does not become evident until early childhood. The average age at diagnosis is approximately 5 years. Symptoms include motor difficulties such as difficulty running, jumping, and walking up stairs, along with an unusual waddling gait. Some improvement in symptoms may be seen from 3 to 6 years of age, though gradual deterioration resumes and most individuals lose ambulation by age 12 and require noninvasive ventilation by the late teenage years. Individuals progress from needing noninvasive ventilation only during night sleeping, followed by noninvasive ventilation during day and night sleeping, and then noninvasive ventilation during day and night over the course of 5 to 10 years. Median life expectancy more recently has increased into the fourth decade, primarily through improved respiratory management and cardiac care.

DMD occurs as a result of variant(s) in the gene responsible for producing dystrophin, a cohesive protein that is essential for maintaining muscle support and strength. DMD is the longest known human gene, and several variants can cause DMD. Most deletion variants disrupt the translational reading frame in the dystrophin messenger RNA resulting in an unstable, nonfunctional dystrophin molecule. As a result, there is

progressive muscle degeneration leading to loss of independent ambulation, as well as other complications, including respiratory and cardiac complications. Genetic testing is required to determine the specific DMD gene variant(s) for a definitive diagnosis, even when the absence of dystrophin protein expression has been confirmed by muscle biopsy. There are over 4700 variants in the Leiden DMD mutation database, and the most common variants are concentrated between exons 45 and 53.

Regulatory Status
In June 2023, delandistrogene moxeparvovec-rokl (Elevidys; Sarepta Therapeutics) was approved by the U.S. Food and Drug Administration (FDA) for treatment of ambulatory pediatric patients aged 4 through 5 years with DMD with a confirmed mutation in the DMD gene. This indication was approved under accelerated approval based on expression of delandistrogene moxeparvovec-rokl micro-dystrophin in skeletal muscle observed in patients treated with delandistrogene moxeparvovec-rokl. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

In June 2024, the U.S. FDA expanded the approval of delandistrogene moxeparvovec-rokl (Elevidys; Sarepta Therapeutics) for ambulatory and non-ambulatory individuals 4 years of age and older with DMD with a confirmed mutation in the DMD gene. It received a traditional approval in ambulatory individuals 4 years of age and older with DMD with a confirmed mutation in the DMD gene, and accelerated approval in non-ambulatory individuals 4 years of age and older with DMD with a confirmed mutation in the DMD gene.

Treatment with delandistrogene moxeparvovec-rokl is intended to slow or stabilize progression of DMD, to alter the disease trajectory to a milder, Becker muscular dystrophy-like phenotype. Becker muscular dystrophy is similar to DMD, except that in Becker, symptoms begin later and progress at a slower rate.

There is no cure for DMD. The following practice is currently being used to treat individuals with a confirmed variant of the DMD gene: standard multidisciplinary care including pharmacotherapy. Pharmacotherapy primarily involves corticosteroids (prednisone or deflazacort) for all individuals regardless of the genetic variant. Treatment is initiated once individuals reach a plateau of motor skill development, generally at ages 4to 6 years, but before the onset of motor decline. The goal of corticosteroid therapy is to preserve ambulation and minimize respiratory, cardiac, and orthopedic complications. In addition, muscle weakness and pain, cardiac, pulmonary, orthopedic, and endocrine symptoms should be managed.

Four antisense oligonucleotides—eteplirsen, golodirsen, viltolarsen, and casimersen have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of DMD via the Accelerated Approval pathway. Each targets a specific exon. For example, eteplirsen targets skipping of exon 51, golodirsen and viltolarsen target skipping of exon 53, and casimersen targets skipping of exon 45. In each case, approval was based on the surrogate endpoint of expression of internally truncated dystrophin protein. The clinical benefit of all 4 of these drugs remains to be verified.

For individuals with a confirmed diagnosis of Duchenne muscular dystrophy (DMD) who receive delandistrogene moxeparvovec-rokl, the evidence includes 2 randomized controlled trials (studies 102 and 301) and 1 prospective cohort trial (study 103). Relevant outcomes are disease-specific survival, change in disease status, functional outcomes, health status measures, quality of life, and treatment-related mortality and morbidity. In study 102, 41 study participants were randomized 1:1 to receive either delandistrogene moxeparvovec-rokl (n=20) or placebo (n=21). In study 301, 125 study participants were randomized 1:1 to receive either delandistrogene moxeparvovec-rokl (n=63) or placebo (n=62). Both studies failed to show a statistically significant difference in the primary endpoint of change in the North Star Ambulatory Assessment (NSAA) total score between the treated and the placebo group. In study 102, the least squares (LS) mean change in the NSAA total score from baseline to week 48 was 1.7 points for the delandistrogene moxeparvovec-rokl group and 0.9 points for the placebo group (p=.37). In study 301, the LS mean change in the NSAA total score from baseline to week 52 was 2.57 points for the delandistrogene moxeparvovec-rokl group and 1.92 points for the placebo group (p=.24). Thus, clinical benefit was not demonstrated in the primary efficacy endpoint of NSAA total score from baseline in both studies. Multiple limitations were noted. The US FDA approval was based on the post-hoc exploratory analysis of secondary outcome measures such

as 10-meter walk/run (10-MWR) and time to rise from floor. These results cannot be interpreted at face value due to the lack of pre-specification and control of type 1 error. Such post hoc analysis following an overall nonsignificant test in the overall population can only be considered as hypothesis-generating. In addition, the observed treatment effect on secondary outcomes was not substantial and of uncertain clinical significance. Further, the results of 10-MWR timed test were inconsistent with opposing results observed in the 2 RCTs. Because of these limitations, an adequately powered, randomized, double-blind, placebo-controlled trial is necessary to clearly ascertain the net health outcome in DMD. Lastly, biomarker data reported in studies only provides information about expression of the transgene product in cells transduced by delandistrogene moxeparvovec-rokl rather than insight into a pharmacologic effect on a known biomarker in the pathway of the disease. Delandistrogene moxeparvovec-rokl micro-dystrophin is a novel, engineered protein that contains selected domains of the normal, wild-type dystrophin expressed in healthy muscle cells. No epidemiologic or pathophysiologic evidence is available regarding the function of delandistrogene moxeparvovec-rokl micro-dystrophin. The protein differs in important ways from both the endogenous shortened forms of dystrophin in patients with Becker muscular dystrophy, and the internally truncated dystrophins expressed through exon-skipping drugs. Thus, the clinical benefit of treating DMD with delandistrogene moxeparvovec-rokl, including improved motor function and pulmonary function, has not been demonstrated. A confirmatory, prospective, and adequately powered trial is necessary to assess the net health outcome of delandistrogene moxeparvovec-rokl in patients with DMD. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CODING

The following HCPCS code(s) are considered not covered for Medicare Advantage Plans and not medically necessary for Commercial Products:

J1413 Elevidys (Sarepta Therapeutics, Inc.); Injection, delandistrogene moxeparvovec-rokl, per therapeutic dose

RELATED POLICIES

Not applicable.

PUBLISHED

Provider Update, January 2026/March 2026
Provider Update, February/November 2024

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