Medical Coverage Policy | Gene Therapies for Duchenne Muscular Dystrophy

EFFECTIVE DATE: 01|01|2024
POLICY LAST REVIEWED: 12|20|2023

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, a small number of 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).

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 very similar to DMD, except that in Becker, symptoms begin later and progress at a slower rate.

For individuals with a confirmed diagnosis of Duchenne muscular dystrophy (DMD) who are ambulatory and who receive delandistrogene moxeparvovec-rokl, the evidence includes 1 randomized controlled trial (RCT) and 1 prospective cohort study. 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 the single pivotal RCT, 41 study participants were randomized 1:1 to receive either delandistrogene moxeparvovec-rokl (n=20) or placebo (n=21). Overall, there was no statistically significant difference in the primary endpoint of change in the North Star Ambulatory Assessment (NSAA) total score from baseline to week 48 between the treated group and the placebo group (1.7 vs 0.9 points, respectively, p =.37). However, the least squares (LS) mean change in NSAA total score from baseline to week 48 among subgroup of study participants aged 4 to 5 years was numerically greater for the treated (n=8) versus the placebo (n=8) group (4.3 vs 1.9 points, respectively). Study 103 included a cohort of 20 participants aged 4 through 7 years who received delandistrogene moxeparvovec-rokl. Muscle biopsies were obtained at baseline prior to infusion of gene therapy and at week 12 in all study participants. The mean delandistrogene moxeparvovec-rokl micro-dystrophin expression levels (change from baseline) at week 12 following infusion was 95.7% in study 102 and 51.7% in study 103. Multiple limitations were noted. First, the exploratory subgroup analysis on which the approval was based was not prespecified for hypothesis testing, and no prespecified multiplicity adjustment strategy was employed. Such post hoc subgroup analysis following an overall nonsignificant test in the overall population can only be considered as hypothesis-generating. Second, while data from open-label studies are interpretable under certain conditions, such as when the disease being studied is homogeneous, the treatment has a large effect, and the clinical endpoint can be objectively assessed, none of these conditions are applicable for DMD. Lastly, biomarker data reported in studies 102 and 103 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 moxeparvovecrokl 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 (New Code Effective 1/1/2024). Prior to Dates of Service 1/1/2024, Unlisted HCPCS code C9399 or J3590 must be used).

RELATED POLICIES

Not applicable.

PUBLISHED

Provider Update, February 2024

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