Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 08/08/2024

Elevidys™ (delandistrogene moxeparvovec-rokl)

HCPCS: J1413

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. Coverage of the requested drug is considered investigational/experimental for all indications due to insufficient evidence of a clinical benefit
      i. BCBSM and BCN are awaiting the results of ongoing clinical trials to provide evidence of a clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Duchenne muscular dystrophy (DMD) is a rare, life-limiting, progressive childhood disease that affects 1 in 3,500 – 5,000 live male births. It is characterized by progressive muscle weakness and wasting due to the absence of dystrophin protein that causes degeneration of skeletal and cardiac muscle. Affected individuals are unable to run and jump properly due to proximal muscle weakness of the leg and pelvic muscles. DMD occurs as a result of mutations in the dystrophin gene, located on the X-chromosome, which normally functions to generate dystrophin, a structural protein of muscle cells. Mutations in the dystrophin gene lead to an absence of or a defect in dystrophin protein resulting in the progressive symptoms seen in DMD patients.

- Glucocorticosteroids are the main pharmacologic treatment option used in DMD. The 2018 treatment guidelines for DMD support the use of glucocorticosteroids as they are the only medication currently available to slow the decline in muscle strength and function which in turn reduces the risk of scoliosis and stabilizes pulmonary function. Trials show muscle strength is improved when treated with prednisone at a dose of 0.75 mg/kg daily for up to 6 months. The goal of glucocorticoids in an ambulatory patient is the preservation of ambulation and the minimization of later cardiac, respiratory, and orthopedic complications. Continued treatment after the patient becomes non-ambulatory has shown reduction in the risk of progressive scoliosis and stabilization of pulmonary function tests. However, it is

important to note that glucocorticosteroids are not able to induce the production of dystrophin-like proteins and therefore do not alter or impact the underlying cause of DMD.

- The exon skipping therapies, including Exondys 51™, Vyondys 53™, Viltepso™, and Amondys 45™, are disease modifying therapies for the treatment of DMD. All were FDA approved under the accelerated approval pathway using a surrogate endpoint of increase in dystrophin in skeletal muscle. There is no evidence the small observed increase in dystrophin from use of these therapies results in a clinically meaningful benefit. Therefore, establishment of a clinical benefit is needed in on-going clinical trials for the exon skipping therapies to not be considered experimental/investigational.

- Elevidys is an adeno-associated virus vector-based gene therapy indicated in ambulatory and non-ambulatory patients at least 4 years of age with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene.

- Similar to the exon skipping therapies, Elevidys for both ambulatory and non-ambulatory patients was originally FDA approved under accelerated approval based on expression of Elevidys micro-dystrophin in skeletal muscle observed in patients treated with Elevidys. The FDA granted full approval for ambulatory patients in June 2024 despite the phase III EMBARK trial not meeting primary endpoints and a lack of evidence supporting the small observed increase in dystrophin results in a clinically meaning benefit.

- EMABRK, the phase III, randomized, double-blind, placebo-controlled confirmatory trial, evaluated the efficacy and safety of Elevidys in 120 patients with DMD. The primary endpoint was change in North Star Ambulatory Assessment (NSAA) total score from baseline to week 52 compared to placebo. The trial included stratification of participants by age and baseline NSAA with a minimum of 50% of enrolled patients being age 4 – 5. Patients were eligible if they were on a stable daily dose of oral corticosteroids and had rAAVrh74 antibody titers less than 1:400. Study results showed Elevidys-treated patients improved 2.6 points on their NSAA total score 52 weeks after treatment compared to 1.9 points for those on placebo which was not statistically significant (p-value = 0.24). Secondary endpoints, including change in time to rise (TTR) and the 10-meter walk test, showed statistically significant improvements and were the basis for the director of the FDA's Center for Biologics Evaluation and Research decision to overrule three FDA review teams and two additional directors who opposed the expanded indication and traditional approval for ambulatory patients.

- Multiple groups and individuals at the FDA advised against traditional approval and an expanded indication. A review by FDA statisticians concluded that the collective clinical trial results do not suggest there is substantial evidence to support the effectiveness of Elevidys for the expanded indication to all DMD patients and do not support the conversion of accelerated to traditional approval. An additional joint review from the agency's Clinical and Clinical Pharmacology teams likewise determined that the totality of the data does not provide substantial evidence of effectiveness of Elevidys for treatment of ambulatory DMD patients of any age and that the results argue against expanding access. In a memo, the director of the Office of Clinical Evaluation in the Office of Therapeutic Products (OTP) and the super office director of the OTP, concluded that the clinical results cast significant uncertainty regarding the benefits of treatment of DMD with Elevidys. Furthermore, the two directors found the primary clinical trial endpoint results were not statistically significant and smaller analyses looking at secondary endpoints of specific patient measures, such as, the time it takes patients to rise from the floor or walk 10 meters, were inconclusive, in some cases conflicting, and overall illustrated the unreliability of exploratory analyses to support regulatory decision-making. The director of the Office of Clinical Evaluation in the OTP wrote that they would have recommended Sarepta conduct an additional adequate and well-controlled study of Elevidys in the subgroup(s) of patients for which Sarepta believes the effects of Elevidys to be most promising.

- Based on the current information available, there is insufficient evidence that Elevidys provides a clinical benefit in patients with DMD. Therefore, demonstration of a clinical benefit is warranted in on-going clinical trials.

References:

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<tr><td>1.3</td><td>Effective Date: 08/10/2023</td><td>New Policy</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*