Medical Coverage Policy | Eteplirsen for Duchenne Muscular Dystrophy

EFFECTIVE DATE: 03|21|2017
POLICY LAST UPDATED: 03|21|2017

OVERVIEW
Duchenne muscular dystrophy is an inherited disorder that results in progressive muscle weakness and loss of muscle mass. It primarily affects boys. It occurs as a result of mutation(s) in the gene responsible for producing dystrophin, a cohesive protein essential for maintaining muscle support and strength. Eteplirsen is an antisense oligonucleotide that induces skipping of exon 51 and thereby repairing the mutated reading frame. As a result, eteplirsen enables the production of an internally truncated, yet functional, dystrophin protein.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
BlueCHiP for Medicare and Commercial Products
The use of eteplirsen is considered not medically necessary for all indications including treatment of Duchenne muscular dystrophy as the evidence is insufficient to determine the effects of the technology on health outcomes.

COVERAGE
Benefits may vary between groups/contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for applicable infusion coverage/benefits.

BACKGROUND
Duchenne muscular dystrophy (DMD) is an X-linked, recessive disorder that occurs in approximately 1 in every 3,500 to 5,000 boys. It primarily affects boys. However, a small number of girls are also affected, but they are usually asymptomatic, and even when symptomatic, 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, 0.2-1 years), and the mean age at definitive diagnosis is 4.9 years (range, 0.3-8.8 years). DMD occurs as a result of mutation(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 mutations can cause DMD. Most deletion mutations disrupt the translational reading frame in the dystrophin messenger RNA (mRNA) 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 mutation(s) for a definitive diagnosis, even when the absence of dystrophin protein expression has been confirmed by muscle biopsy. There are over 4,700 mutations in the Leiden DMD mutation database and the most common mutations are concentrated between exons 45 and 53.

Eteplirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) class. PMOs are stable oligonucleotide analogues that selectively bind to RNA to alter gene expression. In the case of eteplirsen, the PMO binds to exon 51 of the dystrophin premessenger RNA causing the exon to be skipped and prevents that part of the code from being read during mRNA processing, thereby partially

repairing the mutated reading frame in the mRNA coding sequence. As a result, eteplirsen enables the production of an internally truncated, yet functional, dystrophin protein. The current standard of pharmacotherapy for DMD is corticosteroids for all patients regardless of genetic mutation. Treatment is initiated once patients reach a plateau of motor skill development, generally at ages 4 to 6 years, but prior to onset of motor decline. The goal of corticosteroid therapy is to preserve ambulation and minimize respiratory, cardiac, and orthopedic complications.

Regulatory Status
In September 2016, eteplirsen (Exondys 51™; Sarepta Therapeutics) was approved by the U.S. Food and Drug Administration (FDA) through the orphan drug status process for use in Duchenne muscular dystrophy patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. This indication was approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with eteplirsen.

For individuals with confirmed mutation of the Duchenne muscular dystrophy gene that is amenable to exon 51 skipping who receive eteplirsen, the evidence includes 1 randomized controlled trial (RCT) and its open-labelled follow-up study, and interim data from an ongoing RCT. Relevant outcomes are disease specific survival, change in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related mortality and morbidity. As per FDA analysis, the pivotal RCT and its open-labelled follow-up failed to provide evidence of a clinical benefit in terms of 6-minute walk distance. Evidence regarding the impact of eteplirsen treatment on dystrophin levels was inconclusive. Interim results from an ongoing study provided evidence that eteplirsen increased dystrophin levels in skeletal muscle in some patients by a median of 0.1% after 48 weeks of treatment. In summary, the clinical benefit of treatment for Duchenne muscular dystrophy with eteplirsen, including improved motor function, has not been demonstrated. Establishing a clinical benefit is necessary in ongoing clinical trials. The most frequently reported adverse events across clinical trials were balance disorder, vomiting, and contact dermatitis. The evidence is insufficient to determine the effects of the technology on health outcomes. Therefore, eteplirsen is considered not medically necessary for all indications including treatment of Duchenne muscular dystrophy.

CODING

BlueCHiP for Medicare and Commercial Products
The following HCPCS code is are considered not medically necessary:
C9484 Injection, eteplirsen, 10 mg (New code effective 4/1/2017)

RELATED POLICIES

None

PUBLISHED

Provider Update, June, 2017

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