



Louisiana

eteplirsen (Exondys 51™)

Policy # 00542

Original Effective Date: 03/15/2017

Current Effective Date: 03/21/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of eteplirsen (Exondys 51™)‡ for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of eteplirsen (Exondys 51) for NON-FDA approved indications to be **investigational**.*

Background/Overview

Exondys 51 is an antisense oligonucleotide indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. The package insert notes that "This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51. A clinical benefit of Exondys 51 has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials." Exondys is dosed at 30 mg/kg once weekly via an intravenous infusion. It is supplied as 100 mg and 500 mg vials.

Duchenne Muscular Dystrophy

DMD is an X linked recessive disease affecting 1 in 3,600 to 6,000 newborn male infants. Gene deletions amenable to exon 51 skipping exist in 13% of patients with DMD. The disease is attributed to large frame-shift deletions in the DMD gene which lead to loss of dystrophin, a structural protein of muscle cells. Duchenne's is characterized by progressive proximal muscle weakness caused by muscle fiber degeneration. Of course, other comorbidities occur as well including cardiac and orthopedic issues. Without intervention, death occurs at approximately 19 years of age. With respiratory, cardiac, orthopedic, and rehabilitative interventions and use of steroids, children born today can have a life expectancy of up to 40 years.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Exondys 51 was approved for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. It should be noted that various advisory committees at the FDA

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voted against approval of this drug (or that it offered no effect). However, Exondys 51 was ultimately approved but he FDA in September of 2016.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Exondys 51 was evaluated in three clinical studies in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. In the first study, 12 patients were randomized to receive weekly infusion of Exondys 51 at various doses (30 mg/kg, 50 mg/kg) versus placebo for 24 weeks. The primary endpoint was dystrophin production. The 6 minute walk test (6MWT) was also assessed. There was no significant difference in change in 6MWD between patients treated with Exondys 51 and those treated with placebo. All 12 patients who participated in the first study continued treatment with open label Exondly 51 for an additional 4 years in the second study. Patients in the second study were compared to an external control group. The primary clinical efficacy outcome was the 6MWT. Study 2 failed to provide evidence of a clinical benefit of Exondys 51 compared to the external control group. In the third study, 13 patients were treated with open-label Exondys 51 (30 mg/kg) weekly for 48 weeks and had a muscle biopsy at baseline and after 48 weeks of treatment. In the 12 patients with evaluable results, the pretreatment dystrophin level was 0.16% of the dystrophin level in a healthy subject and 0.44% after 48 weeks of treatment.

As noted in the clinical trials, Exondys 51 failed to demonstrate a clear clinical improvement in patients with DMD. This conclusion is mentioned in the FDA package insert as well: "A clinical benefit of Exondys 51 has not been established." The place in therapy and clinical efficacy of Exondys 51 will need to be established with confirmatory clinical trials.

References

1. Exondys 51 [package insert]. Serapta Therapeutics, Inc. Cambridge, Massachusetts. September 2016
2. Exondys 51 Drug Evaluation. Express Scripts. September 2016
3. Exondys 51 Prior Authorization Criteria. Express Scripts. September 2016

Policy History

Original Effective Date: 03/15/2017

Current Effective Date: 03/21/2018

03/02/2017 Medical Policy Committee review

03/15/2017 Medical Policy Implementation Committee approval. New policy.

07/01/2017 Coding update

03/01/2018 Medical Policy Committee review

03/21/2018 Medical Policy Implementation Committee approval. No change to coverage.

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Next Scheduled Review Date: 03/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3490, J3590 Code deleted eff 1/1/18: C9484 Code added eff 1/1/18: J1428
ICD-10 Diagnosis	G71.0

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

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**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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