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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Neuromuscular Agents	**Original Policy Date:**	October 7, 2016
Subject:	Exondys 51	**Page:**	1 of 5

Last Review Date: March 12, 2021

Exondys 51

Description

Exondys 51 (eteplirsen)

Background
Exondys 51 is indicated for patients with a diagnosis of Duchenne muscular dystrophy (DMD) who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. DMD is a genetic disorder characterized by progressive muscle degeneration and weakness. DMD is caused by an exon mutation in a gene that codes for dystrophin, a protein that helps keep muscle intact. Exons are the sections of DNA that contain instructions for creating proteins; if an exon is mutated, a functional protein cannot be produced. Exondys 51 is designed to “skip over” a mutated exon and enable the synthesis of a shortened, functional form of dystrophin protein. Patients with DMD experience progressive loss of ambulation, followed by a need for assisted ventilation, and eventual death in mid-20s. (1-2).

Regulatory Status
FDA-approved indication: Exondys 51 is an antisense oligonucleotide indicated 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 (1).

Exondys clinical trials used a double-blind, placebo-controlled protocol to examine eteplirsen's ability to induce dystrophin production and improve distance walked on the 6-minute walk test (6MWT). Boys with DMD aged 7 to 13 years, with confirmed deletions correctable by skipping exon 51 and ability to walk 200 to 400 m on 6 MWT (2).

Dystrophin levels should be measured at baseline to evaluate pretreatment dystrophin-positive fibers and sometime during therapy to evaluate the effect of Exondys dose (2).

Related policies
Emflaza, Viltepso, Vyondys 53

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Exondys 51 may be considered **medically necessary** for patients 20 years of age or younger with Duchenne muscular dystrophy (DMD) and if the conditions indicated below are met.

Exondys 51 may be considered **investigational** in patients older than 20 years of age and for all other indications.

Prior-Approval Requirements

Age 20 years of age or younger

Diagnosis

Patient must have the following:

1. Duchenne muscular dystrophy
    a. Confirmed mutation of the DMD gene that is amenable to exon 51 skipping
    b. Prescribed by or in consultation with a neurologist specializing in DMD
    c. Obtain a baseline muscle strength score from **ONE** of the following:
        i. 6-minute walk test (6MWT)
        ii. North Star ambulatory assessment (NSAA)
        iii. Motor Function Measure (MFM)
    d. **NO** concurrent therapy with another exon skipping therapy for DMD (see Appendix 1)

Prior – Approval *Renewal* Requirements

Age 20 years of age or younger

Diagnosis

Patient must have the following:

1. Duchenne muscular dystrophy
    a. Patient has had an improvement from baseline in **ONE** of the following:
        i. 6-minute walk test (6MWT)
        ii. North Star ambulatory assessment (NSAA)
        iii. Motor Function Measure (MFM)
    b. **NO** concurrent therapy with another exon skipping therapy for DMD (see Appendix 1)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Duration 24 months

Rationale

Summary

Exondys 51 is an antisense oligonucleotide indicated 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. Exondys 51 is approved under accelerated approval by the FDA based on an increase in dystrophin in skeletal muscle observed in some patients. A clinical benefit of Exondys 51 has not been established (1).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of Exondys while maintaining optimal therapeutic outcomes.

References

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; July 2020.
2. Mendell JR, Rodino-Klapac LR, Sahenk Z, et al; Eteplirsen Study Group. Eteplirsen for the treatment of Duchenne muscular dystrophy. Ann Neurol. 2013; 74(5):637-647.
3. Kole R, Krieg AM. Exon skipping therapy for Duchenne muscular dystrophy. Adv Drug Deliv Rev. 2015; 87:104-107.

Policy History

Date	Action
October 2016	Addition to PA
December 2016	Annual review
March 2017	Annual editorial review Addition of obtain a baseline dystrophin level and patient has had an improvement from baseline in dystrophin levels Addition of obtain a baseline muscle strength score from one of the following: 6-minute walk distance (6MWD), North Star ambulatory assessment, or Motor Function Measure; and the patient has had an improvement from baseline from one of the scoring tools Addition of prescribed by or in consultation with a neurologist specializing in DMD Addition of the age 20 years of age or younger requirement
July 2017	Annual review
February 2018	Removal of the dystrophin level requirements
June 2018	Annual review and reference update
September 2019	Annual review and reference update
June 2020	Annual review and reference update
December 2020	Annual review and reference update. Per FEP, addition of requirement of no concurrent therapy with another exon skipping therapy for DMD
March 2021	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.

Appendix 1 - List of Exon Skipping Therapies for Duchenne Muscular Dystrophy (DMD)

Generic Name	Brand Name
eteplirsen	Exondys 51
golodirsen	Vyondys 53
viltolarsen	Viltepso