BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.75.014

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Neuromuscular Agents	**Original Policy Date:**	October 7, 2016
Subject:	Exondys 51	**Page:**	1 of 6

Last Review Date: March 7, 2025

Exondys 51

Description

Exondys 51 (eteplirsen)

Background
Exondys 51 (eteplirsen) 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 (1).

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).

Monitoring motor changes in patients with DMD requires functional evaluation along with measurement of muscle strength. The need for a reliable outcome measure in diseases of rapid deterioration such as DMD has led to the use of motor functional tests. In a large, multicenter, international clinical trial, the six minute walk test (6MWT) proved to be feasible and highly reliable. Also used are the Motor Function Measure (MFM) and North Star Ambulatory Assessment (NSAA) to help predict loss of ambulation 1 year before its occurrence in order to

allow time to adapt rehabilitation, change the patient's environment, and consider acquisition of assistive aids or the use of medications (2-4).

Related policies
Agamree, Amondys 45, Duvyzat, Elevidys, 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** if the conditions indicated below are met.

Exondys 51 may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 20 years of age or younger

Diagnosis

Patient must have **ALL** of 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. Patient will be advised to monitor for hypersensitivity reactions
    d. 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)
    e. **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 **ALL** of 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. Patient will be advised to monitor for hypersensitivity reactions
    c. **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 (eteplirsen) 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. Dystrophin levels should be measured at baseline to evaluate pretreatment dystrophin-positive fibers and sometime during therapy to evaluate the effect of Exondys 51 dose (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Exondys 51 while maintaining optimal therapeutic outcomes.

References

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; December 2024.
2. Mcdonald C, Henricson E, et al. The 6-Minute Walk test and Other Clinical Endpoints in Duchenne Muscular Dystrophy: Reliability, Concurrent Validity, and Minimal Clinically Important Differences from a Multicenter Study. Muscle Nerve. 2013 Sep; 48(3): 357‑368.
3. Mcdonald C, Henricson E, et al. The 6-Minute Walk test and Other Endpoints in Duchenne Muscular Dystrophy: Longitudinal Natural History Observations Over 48 weeks from a Multicenter Study. Muscle Nerve. 2013 Sep; 48(3): 343‑356.
4. Vuillerot C, Girardot F, et al. Monitoring changes and predicting loss of ambulation in Duchenne muscular dystrophy with the Motor Function Measure. *Developmental Medicine & Child Neurology* 2010, 52: 60–65.

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

June 2021	Annual editorial review. Updated Appendix 1.
March 2022	Annual review and reference update
March 2023	Annual review. Changed policy number to 5.75.014
December 2023	Annual review. Per SME, added requirements to monitor for hypersensitivity reactions
March 2024	Annual review
June 2024	Annual review
September 2024	Annual editorial review
December 2024	Annual review
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.

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

Generic Name	Brand Name
casimersen	Amondys 45
eteplirsen	Exondys 51
golodirsen	Vyondys 53
viltolarsen	Viltepso