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POLICY Document for EXONDYS 51 (eteplirsen)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall, clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Site of Care

- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 2: Clinical Criteria

- Policy information specific to the clinical appropriateness for the medication

Section 1: Site of Care

Site of Care Criteria
Exondys 51

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated.

Brand Name	Generic Name	Dosage Form
Exondys 51	eteplirsen	intravenous

Criteria For Approval For Administration In Outpatient Hospital Setting

This policy provides coverage for administration of Exondys 51 in an outpatient hospital setting for up to 45 days when a member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months.

This policy provides coverage for administration of Exondys 51 in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:

- The member has experienced an adverse reaction to the drug that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids, other

pre-medications or slowing of infusion rate) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
- The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
- The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
- The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
- Alternative infusion sites (pharmacy, physician office, ambulatory care, etc.) are greater than 30 miles from the member's home.
- The member is less than 14 years of age.

For situations where administration of Exondys 51 does not meet the criteria for outpatient hospital infusion, coverage for Exondys 51 is provided when administered in alternative sites such as physician office, home infusion or ambulatory care.

Required Documentation

The following information is necessary to initiate the site of care prior authorization review (where applicable):

- Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
- Medical records supporting the member is medically unstable
- Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
- Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
- Records supporting alternative infusion sites are greater than 30 miles from the member's home
- Medical records supporting the member is new to therapy

Section 2: Clinical Criteria

Specialty Guideline Management
Exondys 51

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Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Exondys 51	eteplirsen

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1]

Exondys 51 is 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.

This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Initial requests:

- Laboratory confirmation of Duchenne muscular dystrophy (DMD) diagnosis with a DMD gene mutation that is amenable to exon 51 skipping (refer to examples in Appendix).
- If applicable, medical records confirming a worsening in clinical status since receiving gene replacement therapy.

Continuation requests:

Documentation (e.g., chart notes) of response to therapy

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Prescriber Specialties

This medication must be prescribed by or in consultation with a physician who specializes in treatment of Duchenne muscular dystrophy (DMD).

Coverage Criteria

Duchenne Muscular Dystrophy[1-5]

Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:

- Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of DMD gene mutation.
- The DMD gene mutation is amenable to exon 51 skipping (refer to examples in Appendix).
- Treatment with Exondys 51 is initiated before the age of 14.
- Member is able to achieve an average distance of at least 180 meters while walking independently over 6 minutes.
- Member meets one of the following criteria:
  - Member has not previously received gene replacement therapy for DMD (e.g., Elevidys).
  - Member has previously received gene replacement therapy for DMD (e.g., Elevidys) and has experienced a worsening in clinical status since receiving gene replacement therapy (e.g., decline in ambulatory function).
- Member will not exceed a dose of 30 mg/kg once weekly.

Continuation of Therapy

Note: Members who were previously established on Exondys 51 and subsequently administered gene replacement therapy (e.g., Elevidys) must meet all requirements in the coverage criteria section prior to re-starting Exondys 51.

Authorization of 12 months may be granted for members requesting continuation of therapy when both of the following criteria are met:

- The member has demonstrated a response to therapy as evidenced by remaining ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).
- The member will not exceed a dose of 30 mg/kg once weekly.

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Appendix[2,3]

Examples of DMD gene mutations (exon deletions) amenable to exon 51 skipping (not an all-inclusive list):

- Deletion of exon 50
- Deletion of exon 52
- Deletion of exons 45-50
- Deletion of exons 47-50
- Deletion of exons 48-50
- Deletion of exons 49-50

REFERENCES

SECTION 1

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics Inc; December 2024

SECTION 2

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; January 2022.
2. Mendell JR, Rodino-Klapac LR, Sahenk Z, et al. Eteplirsen for the treatment of Duchenne muscular dystrophy. Ann Neurol. 2013;74(5):637-47.
3. Cirak S, Arechavala-Gomeza V, Guglieri M, et al. Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligomer treatment: an open-label, phase 2, dose-escalation study. Lancet. 2011;378(9791):595-605.
4. Mendell JR, Goemans N, Lowes LP, et al. Eteplirsen Study Group and Telethon Foundation DMD Italian Network. Longitudinal effect of eteplirsen versus historical control on ambulation in Duchenne muscular dystrophy. Ann Neurol. 2016;79(2):257-271.
5. Randeree L, Eslick GD. Eteplirsen for paediatric patients with Duchenne muscular dystrophy: A pooled-analysis. J Clin Neurosci. 2018;49:1-6.