POLICY Document for EXONDYS 51

The overall objective of this policy is to support the appropriate and cost effective use of the medication, lower cost site of care and overall clinically appropriate use. This document provides specific information to each section 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
Administration of Exondys 51

POLICY

I. 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:

A. 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.
B. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
C. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
D. 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.
E. The member is less than 21 years of age or is 65 years of age or older.

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.

II. REQUIRED DOCUMENTATION

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

A. 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
B. Medical records supporting the member is medically unstable
C. Medical records supporting the member has severe venous access issues that requires specialized interventions only available in the outpatient hospital setting
D. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver

Section 2: Clinical Criteria

SPECIALTY GUIDELINE MANAGEMENT

EXONDYS 51 (eteplirsen)

POLICY

I. 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
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. 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.

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

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
Laboratory confirmation of DMD diagnosis with a *DMD* gene mutation that is amenable to exon 51 skipping (refer to examples in Appendix)

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with a physician who specializes in treatment of DMD.

IV. CRITERIA FOR INITIAL APPROVAL

Duchenne Muscular Dystrophy
Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:
1. Genetic testing was conducted to confirm the diagnosis of DMD and to identify the specific type of *DMD* gene mutation.
2. The *DMD* gene mutation is amenable to exon 51 skipping (refer to examples in Appendix).
3. Treatment with Exondys 51 is initiated before the age of 14.
4. Member is able to achieve an average distance of at least 180 meters while walking independently over 6 minutes.

V. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members requesting continuation of therapy when 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).

VI. APPENDIX

Examples of *DMD* gene mutations (exon deletions) amenable to exon 51 skipping

1. Deletion of exon 50
2. Deletion of exon 52
3. Deletion of exons 45-50
4. Deletion of exons 47-50
5. Deletion of exons 48-50
6. Deletion of exons 49-50

REFERENCES:

SECTION 1

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics Inc; October 2018.

SECTION 2

2. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; October 2018.
3. Mendell JR, Rodino-Klapac LR, Sahenk Z, et al. Eteplirsen for the treatment of Duchenne muscular dystrophy. *Ann Neurol*. 2013;74(5):637-47.
4. 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.
5. 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.
6. Randeree L, Eslick GD. Eteplirsen for pediatric patients with Duchenne muscular dystrophy: A pooled-analysis. J Clin Neurosci. 2018;49:1-6.