MEDICAL MUTUAL

Drug Policy

Policy:	**201616**	**Initial Effective Date: 12/01/2016**
Code(s):	**HCPCS J1428**	**Annual Review Date: 02/21/2019**
SUBJECT:	**Exondys 51 ™ (eteplirsen infusion)**	**Last Revised Date: 02/21/2019**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

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.[1] Exondys 51 was approved for this indication under accelerated approval based on an increase in dystrophin observed in the skeletal muscle of some patients who received the drug. A clinical benefit of Exondys has not been established. The prescribing information notes that continued FDA-approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

DMD is an X-linked recessive disease affecting 1 in 3,600 to 6,000 newborn male infants.[2] The disease is attributed to large frame-shift deletions in the DMD gene (chromosome Xp21) which lead to loss of a structural protein of muscle cells (dystrophin).[3] Over 4,700 mutations on the DMD gene have been identified which lead to a deficiency in production of dystrophin.[2] Therefore, the type of mutation and its effect on the production of dystrophin accounts for the variable phenotypic expression.[4] Females carriers are usually asymptomatic but some may show mild symptoms.[2] There are wide variances in how quickly DMD progresses, but without intervention death is at approximately 19 years of age.[2-4] With respiratory, cardiac, orthopedic and rehabilitative interventions and use of corticosteroids, children born today can have a life expectancy of up to 40 years.

Exondys 51 is an antisense oligonucleotide designed to bind to exon 51 of dystrophin pre-mRNA, resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 51 skipping.[1] These patients represent approximately 13% of all patients with DMD.[5] This genetic manipulation intends to restore the reading frame of the resulting mRNA. The result would be production of a shortened, but partially functional dystrophin protein as seen in less severe forms of muscular dystrophy (e.g., Becker muscular dystrophy).

Guidelines

There are guidelines for the diagnosis and management of DMD available from the DMD Care Considerations Working Group (2010).[4] Genetic testing for a DMD mutation in a blood sample is always required. If deletion/duplication testing is negative, dystrophin gene sequencing should be done to look for point mutations or small deletions or insertions. By fully characterizing the mutation, the predicted effect on the reading frame can be identified, which is the major determinant of phenotype and will determine eligibility for mutation-specific clinical trials. Muscle biopsy may be done to provide information on the amount and molecular size of dystrophin but is not necessary if the genetic diagnosis has been confirmed. In patients with no mutation identified but with increased CK levels and other signs/symptoms of DMD,

a muscle biopsy is clinically indicated. At the time the guidelines were written, glucocorticoids were the only medication available to slow decline in muscle strength and function in DMD. Use of corticosteroids reduces the risk of scoliosis and stabilizes pulmonary function. Continued treatment after the patient loses ambulation provides a reduction in the risk of progressive scoliosis and stabilization of pulmonary function tests. Therefore, glucocorticoids should be considered for all patients with DMD.

POLICY STATEMENT

This policy involves the use of Exondys 51. Prior authorization is recommended for pharmacy and medical benefit coverage of Exondys 51. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Exondys 51 as well as the monitoring required for AEs and long-term efficacy, initial approval requires Exondys 51 be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Exondys 51 is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Duchenne Muscular Dystrophy (DMD)-** ***Initial Therapy.*** Approve for 6 months if the patient meets the following criteria:
   - **A)** The patients has a confirmed mutation of the Duchenne muscular dystrophy (DMD) gene that is amenable to exon 51 skipping [documentation required]; AND
   - **B)** The medication is prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy (DMD) and/or neuromuscular disorders; AND
   - **C)** The patient is 7 years of age or older; AND
   - **D)** The patient has been on a stable dose of corticosteroids for at least 6 months or has a documented contraindication to corticosteroids; AND
   - **E)** The patient is ambulatory (with or without needing an assistive device, such as a cane or walker); AND
   - **F)** Patient has baseline muscle strength score: 6-minute walk test, North Star Ambulatory assessment or Motor function measure. [Documentation required]; AND
   - **G)** Site of care medical necessity is met*

2. **Duchenne Muscular Dystrophy (DMD)- *Continuation Therapy.*** Approve for 1 year if the patient meets the following criteria:
   - **A)** The patient has a confirmed mutation of the Duchenne muscular dystrophy (DMD) gene that is amenable to exon 51 skipping [documentation required]; AND
   - **B)** The medication is prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy (DMD) and/or neuromuscular disorders; AND
   - **C)** The patient is 7 years of age or older; AND
   - **D)** The patient remains ambulatory (with or without needing an assistive device, such as a cane or walker); AND
   - **E)** Patient has had an improvement or stabilization in muscle strength score: 6-minute walk test, North Star Ambulatory assessment or Motor function measure[Documentation required]; AND
   - **F)** Site of care medical necessity is met*

Dosing in DMD. *Dosing must meet the following (medical benefit only):* IV: 30 mg/kg once weekly

Initial Approval/ Extended Approval.
A) *Initial Approval:6 months*
B) *Extended Approval: 1 year*

Duration of Therapy in DMD. Until disease progression, loss of ambulation, or unacceptable toxicity.

Labs/Diagnostics. Genetic testing confirming mutation of the Duchenne muscular dystrophy (DMD) gene that is amenable to exon 51 skipping

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Waste Management for All Indications.

Solution, Intravenous [preservative free]:

Exondys 51: 50 mg/mL (2 mL, 10 mL)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Exondys 51 has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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MEDICAL MUTUAL®

Drug Policy

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

MMO Site of Care Medical Necessity Criteria:

- Medications in this policy will be administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless *at least one* of the following are met[†]:

1. Age less than 18 years*; or
2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
3. History of a severe adverse event from previous administration of the prescribed medication; or
4. Requested medication is being administered as follows:
   - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
   - administered with dialysis; or
5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
6. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.
7. Allowed doses at HOP: up to 1 dose of medication or re-initiation after at least 12 months

* Effective 01/01/2019, age criterion applies to 18 years of older. Age at original effective date (03/01/2016) was 21 years or older.
[†]This criterion does not apply to Medicare or Medicare Advantage members.

Prior approval is required for HCPCS Codes J1428

HCPCS Code(s):	
J1428	Injection, eteplirsen, 10 mg (Exondys) (Effective date 1/1/2018)