Utilization Review Policy 142

POLICY: Muscular Dystrophy – Exondys 51™ (eteplirsen intravenous infusion – Sarepta)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: All UCare Plans

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. However, 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.

Disease Overview
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 (2018).[4] Genetic testing for a DMD mutation in a blood sample is always required. 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. In patients with no mutation identified but with

signs/symptoms of DMD, a muscle biopsy is clinically indicated. Glucocorticoids 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. Exondys 51 is mentioned as an emerging product, approved by an accelerated pathway for those with a mutation in the dystrophin gene amenable to exon 51 skipping.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Exondys 51. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by an Express Scripts clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Exondys 51, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Exondys 51 to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the durations noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Duchenne Muscular Dystrophy (DMD).** Approve Exondys 51 if the patients meets the following criteria. (A or B).
   - **A)** Initial Therapy. Approve Exondys 51 for 6 months if the patient meets the following criteria (i, ii, iii, iv, and v).
     - **i.** Patient must have a diagnosis of Duchene muscular dystrophy (DMD) AND
     - **ii.** Patient must have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping and provide documentation [documentation required] AND
     - **iii.** Must be prescribed by a physician specializing in genetics or neurology AND
     - **iv.** Provider's specialty must be provided at time of request AND
     - **v.** At time of request, prescriber must confirm whether or not the patient is currently enrolled in clinical trials for Exondys 51
   - **B)** Patients Continuing Exondys 51 Therapy. Approve Exondys 51 for 6 months if the patient meets the following criteria (i, ii, and iii).
     - **i.** Renewals must be prescribed by a physician specializing in genetics or neurology AND
     - **ii.** Provider's specialty must be provided at time of request AND
     - **iii.** Chart notes must be supplied at time of request showing patient is responsive to treatment defined as [documentation required]:
       - **a)** Maintain or increase in physical function from baseline OR
       - **b)** Progression has been slower than otherwise would have been expected in this patient population

Dosing in DMD. *Dosing must meet the following weight-based dosing*:

A) 30 mg/kg once weekly - Patient's most current weight (rounded to the nearest kg) must be provided at time of request.

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. Patient is currently enrolled in clinical trials for Exondys 51.
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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OTHER REFERENCES UTILIZED

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	04/21/2021
Annual Revision	No criteria changes.	04/27/2022
Annual Revision	No criteria changes.	04/26/2023
Annual Revision	No criteria changes.	06/20/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024