



## Clinical Edit Criteria Proposal

Drug/Drug Class: **Exondys 51<sup>®</sup> (Eteplirsen) Clinical Edit**

Date: **April 19, 2017**

Prepared for:

Prepared by: **MO HealthNet**

**New Criteria**

**Revision of Existing Criteria**

### Executive Summary

**Purpose:**

To establish MO HealthNet (MHD) Program policy regarding authorization of Exondys 51<sup>®</sup> (Eteplirsen) as a treatment for Duchenne muscular Dystrophy (DMD).

**Why was this Issue Selected:**

Duchenne muscular dystrophy (DMD) is a genetic disorder characterized by progressive muscle degeneration and weakness. It is one of nine types of muscular dystrophy. The prevalence of this disease in the United States is approximately 18,000 cases with an incidence rate of 1 in 3,600 births. DMD is caused by an absence of dystrophin, a protein that helps keep muscle cells intact. The disease primarily affects boys, but in rare cases, it can affect girls. Muscle weakness can begin as early as age 3, first affecting the muscles of the hips, pelvic area, thighs and shoulders, and later the skeletal (voluntary) muscles in the arms, legs and trunk. The calves often are enlarged. By the early teens, the heart and respiratory muscles also are affected. Historically, patients with DMD had short life expectancies (10 to 20 years). With the advancement in medical technology, it is becoming more common to see these patients live into their 30s; some cases into their 40s and 50s. Mobility is a large focus area for future researches in this disease. There are many molecules that are currently being studied that either help repair muscles or prevent muscle damages, and the 6-minute walking distance (6MWD) is commonly used to assess the effectiveness of treatment in clinical trials.

**Exondys 51<sup>®</sup>** is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD), targeting dystrophin deficiency. About 13% of DMD patients have the genetic mutation of the dystrophin gene amenable to exon 51 skipping. Treatment involves a once weekly IV infusion of 30mg/kg. This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with eteplirsen. **A clinical benefit of eteplirsen has not been established.** Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

All requests for therapy will be reviewed by a Clinical Consultant.

<b>Program-specific information:</b>	<b>Drug</b> <ul style="list-style-type: none"> <li>• Exondys 51<sup>®</sup> (Eteplirsen)</li> </ul>	<b>Claims</b> None	<b>Cost Information</b> \$ 300,000 annually per participant
<b>Setting &amp; Population:</b>	MHD participants with confirmed mutation of the dystrophin gene amenable to exon 51 skipping.		
<b>Type of Criteria:</b>	<input type="checkbox"/> Increased risk of ADE	<input type="checkbox"/> Non-Preferred Agent	
	<input checked="" type="checkbox"/> Appropriate Indications	<input type="checkbox"/> Dose Optimization	
<b>Data Sources:</b>	<input type="checkbox"/> Only administrative databases	<input checked="" type="checkbox"/> Databases + Prescriber-supplied	

## Setting & Population

- Drug for review: Exondys 51<sup>®</sup> (Eteplirsen)
- Age range: Patients 4 years of age and older
- Gender: Male and female

## Approval Criteria

### INITIAL 6-MONTH APPROVAL (MUST MEET ALL CRITERIA)

- Appropriate age of patient (4 years of age or older)
- Documentation of a confirmed diagnosis of Duchenne muscular dystrophy (DMD)
  - Genetic testing is required to demonstrate a mutation on the DMD gene that is amenable to exon 51 skipping; **AND**
- Patient is under the supervision and monitoring of a Neurology Specialist; **AND**
- Maintained on stable dose of corticosteroids for ≥ 6 months; **AND**
- Patient retains meaningful voluntary motor function (e.g. patient is able to speak, manipulate objects using upper extremities, ambulate, etc.); **AND**
- Patient should be receiving physical therapy; **AND**
- Clinical Baseline Documentation Received:
  - BMI/Weight
  - Forced Vital Capacity (FVC) ≥ 30%
  - Brooke Score ≤ 5 (e.g. some useful hand function present for use of adaptive technology)
  - Baseline urinalysis showing absence of proteinuria
  - Blood urea nitrogen (BUN) / Serum Creatinine (SCr)
  - Baseline 6-minute walking test (6MWT)

## Approval Criteria (continued)

### RENEWAL APPROVAL (MUST MEET ALL CRITERIA)

- Patient retains meaningful voluntary motor function (e.g. patient is able to speak, manipulate objects using upper extremities, ambulate, etc.); **AND**
- Patient continues to receive physical therapy; **AND**
- Documentation that patient has received benefit from therapy, which may include an increase in dystrophin, an improvement in 6-minute walk test (6MWT), improvement in quality of life, etc.
- Renewal request, including documentation, is required every 6-months
- Documented compliance on current therapy regimen

## Denial Criteria

- Lack of appropriate diagnosis of Duchenne muscular dystrophy (DMD)
- Less than 4 years of age
- Lack of documented genetic testing confirming mutation of dystrophin gene that is amenable to exon 51 skipping
- Lack of documentation of clinical benefit from treatment
- Failure to meet approval criteria
- Dose exceeds FDA approved indication
- Adverse reaction or drug toxicity to therapy

## Required Documentation

Laboratory results:   
MedWatch form:

Progress notes:   
Other:

## Disposition of Edit

- **Denial:** Edit 682 "Clinical Edit"

## References

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7. Drug Topics Red Book 2009. Thomson Medical Economics. Synagis.
8. American Academy of Pediatrics Committee on ID and Comm on Fetus and Newborn-Prevention of RSV Infections: Indications for the use of palivizumab and update on the use of RSV-IGIV. *Pediatrics* 1998;102(5):1211-1215.
9. RSV Guidelines Evaluation-A Comparison Study. Mark Roaseau, BS Pharmacy, MD. July 2003.

## References (continued)

10. American Academy of Pediatrics. Summaries of Infectious Diseases, Respiratory SyncytialVirus. RedBook 2009.
11. Meissner HC and Bocchini JA. Reducing RSV hospitalizations. AAP modifies recommendations for use of palivizumab in high-risk infants, young children. American Academy of Pediatrics News. July 2009. Volume 30 (7):1-2.
12. **Committee On Infectious Diseases and Bronchiolitis Guidelines Committee, American Academy of Pediatrics, Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. 2014;134;415**