## Prior Authorization Review Panel

**CHC-MCO Policy Submission**

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

| | |
|---|---|
| **Plan: PA Health & Wellness** | **Submission Date: 02/01/2023** |
| **Policy Number: PA.CP.PHAR.288** | **Effective Date: 01/01/2018**<br>**Revision Date: 01/2023** |
| **Policy Name: Eteplirsen (Exondys 51)** | |

**Type of Submission – Check all that apply:**

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

**Please provide any changes or clarifying information for the policy below:**

1Q 2023 annual review: no significant changes; references reviewed and updated.

| | |
|---|---|
| **Name of Authorized Individual (Please type or print):**<br><br>**Venkateswara R. Davuluri, MD** | **Signature of Authorized Individual:** |

# Clinical Policy: Eteplirsen (Exondys 51)

Reference Number: PA.CP.PHAR.288
Effective Date: 01/2018
Last Review Date: 01/2023 Revision Log

**Description**
Eteplirsen (Exondys 51™) is an antisense oligonucleotide.

**FDA Approved Indication(s)**
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.

Limitation(s) of use: 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.

**Policy/Criteria**
It is the policy of PA Health & Wellness® that eteplirsen (Exondys 51) is **medically necessary** when the following criteria are met:

**** Exondys 51 was FDA-approved based on an observed increase in dystrophin in skeletal muscle, but it is unknown if that increase is clinically significant. Continued FDA-approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.***

## I. Requirements for Prior Authorization of Exondys 51 (eteplirsen)

**A.** Prescriptions That Require Prior Authorization

All prescriptions for Exondys 51 (eteplirsen) must be prior authorized.

**B.** Review of Documentation for Medical Necessity

In evaluating a request for prior authorization of a prescription for Exondys 51 (eteplirsen), the determination of whether the requested prescription is medically necessary will take into account whether:

1. The beneficiary has a diagnosis that is:
   a. Indicated in the FDA-approved package insert, **OR**

   b. Listed in nationally recognized compendia for the determination of medically-accepted indications for off-label uses for Exondys 51 (eteplirsen)

**AND**

2. Exondys 51 (eteplirsen) is prescribed by or in consultation with a neurologist with experience treating Duchenne muscular dystrophy

**AND**

3. The beneficiary has documentation of a baseline evaluation, including a standardized assessment of motor function, by a neurologist with experience treating Duchenne muscular dystrophy

**AND**

4. The beneficiary will receive concurrent corticosteroids unless contraindicated or intolerant

**AND**

5. Exondys 51 (eteplirsen) is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45™, Viltepso™, Vyondys 53™)

NOTE:The beneficiary does not meet the clinical review guidelines listed above, but, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the beneficiary.

**FOR RENEWALS OF PRESCRIPTIONS FOR Exondys 51 (eteplirsen)** - The determination of medical necessity of requests for prior authorization of renewals of prescriptions for Exondys 51 (eteplirsen) that were previously approved, will take into account whether:

1. Exondys 51 (eteplirsen) is prescribed by or in consultation with a neurologist with experience treating Duchenne muscular dystrophy

**AND**

2. The beneficiary has documentation of an annual evaluation, including an assessment of motor function ability, by a neurologist with experience treating Duchenne muscular dystrophy

**AND**

3. Based on the prescriber's assessment, the beneficiary continues to benefit from Exondys 51 (eteplirsen)

**AND**

4. The beneficiary will receive concurrent corticosteroids unless contraindicated or intolerant

**AND**

5. Exondys 51 (eteplirsen) is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45™, Viltepso™, Vyondys 53™)

NOTE: The beneficiary does not meet the clinical review guidelines listed above, but, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the beneficiary.

## II. Clinical Review Process

Prior authorization personnel will review the request for prior authorization and apply the clinical guidelines in Section I.B. above, to assess the medical necessity of the request for a prescription for Exondys 51 (eteplirsen). If the guidelines in Section I.B are met, the reviewer will prior authorize the prescription. If the guidelines are not met, the prior authorization request will be referred to a physician reviewer for a medical necessity determination. Such a request for prior authorization will be approved when, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the beneficiary.

## III. Approval Duration: 6 months

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

6MWT: 6-minute walk test
DMD: Duchenne muscular dystrophy
FDA: Food and Drug Administration
FVC: forced vital capacity
ICER: Institute for Clinical and Economic Review
LVEF: left ventricular ejection fraction

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| prednisone* | 0.3-0.75 mg/kg/day or 10 mg/kg/weekend PO | Based on weight |
| Emflaza™ (deflazacort) | 0.9 mg/kg PO QD | Based on weight |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*
**Off-label*

*Appendix C: Contraindications/Boxed Warnings*
None reported

*Appendix D: General Information*

- Common mutations amenable to exon 51 skipping include: 3-50, 4-50, 5-50, 6-50, 9-50, 10-50, 11-50, 13-50, 14-50, 15-50, 16-50, 17-50, 19-50, 21-50, 23-50, 24-50, 25-50, 26-50, 27-50, 28-50, 29-50, 30-50, 31-50, 32-50, 33-50, 34-50, 35-50, 36-50, 37-50, 38-50, 39-50, 40-50, 41-50, 42-50, **43-50, 45-50, 47-50, 48-50, 49-50, 50, 52**, 52-61, 52-63, 52-64, 52-66, 52-76. The bolded mutations are deletions which make up > 97% of all mutations amenable to skipping exon 51 according to the DMD registration database.
- Corticosteroids are routinely used in DMD management with established efficacy in slowing decline of muscle strength and function (including motor, respiratory, and cardiac). They are recommended for all DMD patients per the American Academy of Neurology (AAN) and DMD Care Considerations Working Group; in addition, the AAN guidelines have been endorsed by the American Academy of Pediatrics, the American Association of Neuromuscular & Electrodiagnostic Medicine, and the Child Neurology Society.
  - The DMD Care Considerations Working Group guidelines, which were updated in 2018, continue to recommend corticosteroids as the mainstay of therapy while Exondys 51 is mentioned only as an emerging treatment.
  - In an evidence report published August 2019, the Institute for Clinical and Economic Review (ICER) states that current evidence is insufficient to conclude that Exondys 51 has net clinical benefit when added to corticosteroids and supportive care versus corticosteroids and supportive care alone.
- Prednisone is the corticosteroid with the most available evidence. A second corticosteroid commonly used is deflazacort, which was FDA approved for DMD in February 2017.
- The inclusion criteria for Study 201 and Study 202, the pivotal studies used to support the FDA approval of Exondys 51, enrolled patients age 7-13 years old with a 6MWT distance ≥ 200 m, LVEF > 40%, and FVC ≥ 50% at baseline.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| DMD | 30 mg/kg IV once weekly | 30 mg/kg/week |

## VI. Product Availability

Single-dose vial for injection: 100 mg/2 mL (50 mg/mL) and 500 mg/10 mL (50 mg/mL)

## VII. References

1. Exondys 51 Prescribing Information. Cambridge, MA: Sarepta Therapeutics, Inc; January 2022. Available at www.exondys51.com. Accessed November 7, 2022.
2. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol. 2018; 17: 251-267.
3. Gloss D, Moxley RT, Ashwal S, Oskoui M. Practice guideline update summary: corticosteroid treatment of Duchenne muscular dystrophy. Neurology. 2016; 86: 465-472. Reaffirmed on January 22, 2012.

4. Mendell JR, Rodino-Klapac LR, Sahenk Z, et al. Eteplirsen for the treatment of Duchenne muscular dystrophy. Ann Neurol. 2013; 74: 637-647.
5. Mendell JR, Goemans N, Lowes LP, et al. Longitudinal effect of eteplirsen versus historical control on ambulation in Duchenne muscular dystrophy. Ann Neurol. 2016; 79: 257-271.
6. Khan N, Eliopoulos H, Han L, et al. Eteplirsen treatment attenuates respiratory decline in ambulatory and non-ambulatory patients with Duchenne muscular dystrophy. J Neuromuscul Dis. 2019; 6(2): 213-225.
7. Institute for Clinical and Economic Review. Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: Effectiveness and value. Published August 15, 2019. Available at: https://icer-review.org/material/dmd-final-evidence-report. Accessed November 7, 2022.
8. Sarepta Therapeutics. Amenability to exon 51 skipping. Available at: https://www.exondys51hcp.com/amenability. Accessed November 7, 2022.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J1428 | Injection, eteplirsen, 10 mg |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| References reviewed and updated. | | |
| 1Q 2019 annual review: references reviewed and updated. | 01/2019 | |
| 1Q 2020 annual review: references reviewed and updated. | 01/2020 | |
| 1Q 2021 annual review: reformatted policy to match Viltepso and Vyondys 53; references reviewed and update | 01/2021 | |
| 1Q 2022 annual review: added Amondys 45 to examples of exon-skipping therapies; references reviewed and updated. | 01/2022 | |
| 1Q 2023 annual review: no significant changes; references reviewed and updated. | 01/2023 | |