

## **Clinical Policy: Eteplirsen (Exondys 51)**

Reference Number: CP.PHAR.288

Effective Date: 01.01.17

Last Review Date: 02.24

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)  
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Eteplirsen (Exondys 51<sup>®</sup>) 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. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

### **Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

All requests reviewed under this policy may **require medical director review**.

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Exondys 51 may be **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. Initial Approval Criteria**

#### **A. Duchenne Muscular Dystrophy (must meet all):**

1. Diagnosis of DMD with mutation amenable to exon 51 skipping (*see Appendix D*) confirmed by genetic testing;
2. Prescribed by or in consultation with a neurologist;
3. Age  $\leq$  13 years at therapy initiation;
4. Member has all of the following assessed within the last 30 days (a, b, and c):
  - a. Ambulatory function (e.g., ability to walk with or without assistive devices, not wheelchair dependent) with a 6-minute walk test (6MWT) distance  $\geq$  200 m;
  - b. Stable cardiac function with left ventricular ejection fraction (LVEF)  $>$  40%;
  - c. Stable pulmonary function with predicted forced vital capacity (FVC)  $\geq$  50%;

5. Inadequate response (as evidenced by a significant decline in 6MWT, LVEF, or FVC) despite adherent use of an oral corticosteroid (e.g., prednisone, Emflaza<sup>®</sup>, Agamree<sup>®</sup>) for  $\geq 6$  months, unless contraindicated or clinically significant adverse effects are experienced;

*\*Prior authorization is required for Emflaza and Agamree*

6. Exondys 51 is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
7. Exondys 51 is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45<sup>™</sup>, Vyondys 53<sup>™</sup>, Viltepso<sup>®</sup>);
8. Member has not previously received gene replacement therapy for DMD (e.g., Elevidys);
9. Dose does not exceed 30 mg/kg per week.

**Approval duration: 6 months**

## II. Continued Therapy

### A. Duchenne Muscular Dystrophy (must meet all):

1. Currently receiving medication for DMD with mutation amenable to exon 51 skipping or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
  - a. All of the following assessed within the last 6 months (i, ii, and iii):
    - i. Ambulatory function (e.g., ability to walk with or without assistive devices, not wheelchair dependent) with a 6MWT distance  $\geq 200$  m;
    - ii. Stable cardiac function with LVEF  $> 40\%$ ;
    - iii. Stable pulmonary function with predicted FVC  $\geq 50\%$ ;
  - b. Member has received this medication via a healthcare insurer without meeting the requirements above (see criterion 2a), and medical record shows improved or stable LVEF and FVC, assessed within the last 6 months;
3. Member has been assessed by a neurologist within the last 6 months;
4. Exondys 51 is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
5. Exondys 51 is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45, Vyondys 53, Viltepso);
6. Member has not previously received gene replacement therapy for DMD (e.g., Elevidys);
7. If request is for a dose increase, new dose does not exceed 30 mg/kg per week.

**Approval duration: 6 months**

## III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

**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 <sup>®</sup> (deflazacort)	0.9 mg/kg/day PO QD	Based on weight
Agamree <sup>®</sup> (vamorolone)	6 mg/kg/day PO QD (up to a maximum of 300 mg/day) <ul style="list-style-type: none"> <li>• If member has mild (Child-Pugh A) to moderate (Child-Pugh B) hepatic impairment: 2 mg/kg/day PO QD (up to a maximum of 100 mg/day)</li> <li>• If co-administered with strong CYP3A4 inhibitors (e.g., itraconazole): 4 mg/kg/day PO QD (up to a maximum of 200 mg/day)</li> </ul>	See regimen

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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. On October 2023, a third corticosteroid, vamorolone, was approved by the FDA for DMD.
- 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  $\geq 200$  m, LVEF  $> 40\%$ , and FVC  $\geq 50\%$  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 vials for injection: 100 mg/2 mL (50 mg/mL), 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](http://www.exondys51.com). Accessed October 13, 2023.
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, 2022.
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.org/wp-content/uploads/2020/10/Corrected\\_ICER\\_DMD-Final-Report\\_042222.pdf](https://icer.org/wp-content/uploads/2020/10/Corrected_ICER_DMD-Final-Report_042222.pdf). Accessed November 7, 2023.

**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	P&T Approval Date
1Q 2020 annual review: no significant changes; references reviewed and updated.	10.07.19	02.20
PA criteria added for coverage consideration when medically necessary.	02.18.20	02.20 (ad hoc)
Removed examples of positive response from Appendix D since specific measures are required in II.A.2.	05.04.20	
Removed the following language from the FDA-approved indication: “A clinical benefit of Exondys 51 has not been established.” per an FDA-approved label update.	08.15.20	
Added option for continuation of therapy for patients who have been receiving the medication through another healthcare insurer and/or has been responding positively to therapy with stable disease; modified time frame for positive response parameters from within the last 30 days to within the last 6 months; added requirement for neurologist assessment within the last 6 months.	09.24.20	11.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; added coding implications; references reviewed and updated.	10.09.20	02.21
Added disclaimer under Policy/Criteria “All requests reviewed under this policy <b>require medical director review.</b> ”	05.04.21	
1Q 2022 annual review: no significant changes; added that the review “may” require medical director review; references reviewed and updated.	09.14.21	02.22
1Q 2023 annual review: no significant changes; updated Section III to match template; references reviewed and updated.	11.07.22	02.23
1Q 2024 annual review: added criteria, member has not previously received gene replacement therapy for DMD (e.g., Elevidys); added Agamree to list of corticosteroids in Appendix B; references reviewed and updated.	10.13.23	02.24

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program

approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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