Clinical Policy: Eteplirsen (Exondys 51)

Reference Number: PA.CP.PHAR.288
Effective Date: 01/2018
Last Review Date: 01/2025

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. 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. Member has documentation of a baseline evaluation, including a standardized assessment of motor function, by a neurologist with experience treating Duchenne muscular dystrophy;
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. Dose does not exceed 30 mg/kg per week.

Approval duration: 6 months

NOTE: The member 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 member.

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member has been assessed by a neurologist within the last 12 months;
3. Member has documentation of an annual evaluation, including an assessment of motor function ability;
4. Member continues to benefit based on prescriber's assessment;
5. Exondys 51 is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
6. Exondys 51 is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45, Vyondys 53, Viltepso);
7. If request is for a dose increase, new dose does not exceed 30 mg/kg per week.

Approval duration: 6 months

NOTE: The member 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 member.

III. 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 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
Agamree® (vamorolone)	6 mg/kg/day PO QD (up to a maximum of 300 mg/day) • 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) If co-administered with strong CYP3A4 inhibitors (e.g., itraconazole): 4 mg/kg/day PO QD (up to a maximum of 200 mg/day)	See regimen

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.

IV. Dosage and Administration

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

V. Product Availability

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

VI. References

1. Exondys 51 Prescribing Information. Cambridge, MA: Sarepta Therapeutics, Inc; January 2022. Available at www.exondys51.com. Accessed October 25, 2024.
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.org/wp-content/uploads/2020/10/Corrected_ICER_DMD-Final-Report_042222.pdf. Accessed October 31, 2024.

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
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
1Q 2024 annual review: updated format to match standard PAHW structure; added Agamree to list of corticosteroids in Appendix B; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025