Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Eteplirsen (Exondys 51®)	**MP-RX-FP-182-26**	☒ **MMM MA** ☒ **MMM MultiHealth**	**5/6/2026** **Last Review Date:** **5/6/2026**	**5/6/2026** **Frequently Revision:** **Annual**

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

This document addresses the use of Exondys 51® (eteplirsen), an antisense oligonucleotide drug used to treat Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping. DMD is a genetic disorder characterized by decrease in muscle mass over time, including progressive damage and weakness of facial, limb, respiratory and heart muscles.

Background Information:

In Duchenne muscular dystrophy (DMD) patients, dystrophin, a protein that is present in skeletal and heart muscles allowing the muscles to function properly, is either absent or found in very small amounts. Exon 51 skipping allows for the creation of a shorter-than-normal, but partially functional, dystrophin protein in patients with a specific type of DMD mutation. The clinical benefit of increased dystrophin has not been established.

The presence of exon 51 in the dystrophin gene and the deletion of one or more exons contiguous with exon 51, resulting in an out-of frame deletion in which the reading frame is potentially restorable by the skipping (removing) of exon-51 (e.g., deletions of exons 45-50, 47-50, 48-50, 49-50, 50, 52, 52-63), as confirmed in a Clinical Laboratory Improvement Act-accredited laboratory by any of the peer reviewed and published methodology that evaluates all exons (including, but not limited to, multiplex ligation-dependent probe, comparative genomic hybridization, and single condition amplification/internal primer analysis).

Exondys 51 was FDA approved against FDA advisory committee recommendations. Exondys 51 was granted priority review as well as accelerated approval, allowing for a surrogate endpoint to be used. FDA approval was based on the increase in dystrophin in study participants. The label states the following:

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. This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with EXONDYS 51 [see Clinical Studies (14)]. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials. (Exondys 51 label)

FDA determined the differences in 6-minute walk test (6MWT) for Exondys 51 vs. historical controls were not considered reliable based on study design and flaws, including post-hoc analysis and failure to meet primary endpoints in one RCT and one open-label trial. FDA labeling states there is no difference in 6MWT for Exondys 51 vs. placebo. Continued FDA approval of Exondys 51 (eteplirsen) may be contingent on results from a confirmatory Phase III study. Results are expected in 2024.

The recommended dose of Exondys 51 is 30 mg per kilogram administered once weekly as a 35-60 minute infusion.

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Approved Indications

A. 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.

Other Uses

A. None.

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Exondys 51® (Eteplirsen)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Initial requests for Exondys 51 (eteplirsen) may be approved if the following criteria are met:

i. Individual has a diagnosis of Duchenne muscular dystrophy (DMD); **AND**
ii. Documentation is provided that individual has a genetic mutation that is amenable to exon 51 skipping; **AND**
iii. Individual is age 7-13 years of age (NCT01396239 [Study 201] and NCT01540409 [Study 202]); **AND**
iv. Individual is using a corticosteroid; **AND**
v. Documentation is provided that shows individual must be able to walk an average distance between 200 and 400 meters (+/- 10%) while walking independently during 6MWT (NCT01396239 [Study 201] and NCT01540409 [Study 202]).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Exondys 51 therapy medically necessary in members requesting reauthorization for an indication listed in Section A Above (Criteria for Initial Approval) if the following criterion are met:
   A. Criteria above were met at initiation of therapy; **AND**
   B. Documentation is provided that individual remains ambulatory (with or without needing an assistive device, such as a cane or walker)

C. Authorization Duration

i. Initial Approval Duration: 6 months
ii. Reauthorization Approval Duration: 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Exondys 51may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.
   a. Concomitant use with another exon-skipping agent for DMD (including but not limited to Exondys 51, Vyondys 53).

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Dosage Form & Strengths	Recommended Dosing/Limits
Exondys 51 injection 100 mg/2 mL (50 mg/mL) 500 mg/10 mL (50 mg/mL) single-dose vial	• 30 mg/kg once weekly
Exceptions	
None	

Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
G71.01	Duchenne or Becker muscular dystrophy

HCPCS Codes:

Codes	Description
J1428	Injection, eteplirsen, 10 mg [Exondys 51]

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Reference Information:

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. Charleston JS, Schnell FJ, Dworzak J, et.al. Eteplirsen treatment for Duchenne muscular dystrophy: Exon skipping and dystrophin production. Neurology. 2018; 90:e2146-e2154.
5. Cirak S, Arechavala-Gomeza V, Guglieri M, et.al. Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligometer treatment: an open-label, phase 2, dose-escalation study. Lancet. 2011; 378:595-605.
6. Kole R, Krieg AM. Exon skipping therapy for Duchenne muscular dystrophy. Ad Drug Del Rev. 2015; 87:140-107.
7. McDonald CM, Shieh PB, Abdel-Hamid HZ, et al. Open-Label Evaluation of Eteplirsen in Patients with Duchenne Muscular Dystrophy Amenable to Exon 51 Skipping: PROMOVI Trial. J Neuromuscul Dis. 2021;8(6):989-1001. doi:10.3233/JND-210643
8. Mendell JR, Rodino-Klapac LR, Sahenk Z, et.al. Eteplirsen for the treatment of Duchenne muscular dystrophy. Ann Neurol. 2013; 74:631-647.
9. 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.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	5/1/2026	5/6/2026