

Medical Drug Clinical Criteria

Subject:	Exondys 51 (eteplirsen)		
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Overview

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. In 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.

Clinical Criteria

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)

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]).

Continuation of therapy with Exondys 51 (eteplirsen) may be approved if the following criterion are met:

- I. Criteria above were met at initiation of therapy; **AND**
- II. Documentation is provided that individual remains ambulatory (with or without needing an assistive device, such as a cane or walker).

Exondys 51 (eteplirsen) may not be approved for the following:

- I. Individual is using another exon skipping agent for DMD (including but not limited to Exondys 51, Vyondys 53); **OR**
- II. When the above criteria are not met and for all other indications.

Approval Duration: 6 months

Quantity Limits

Exondys 51 (eteplirsen) Quantity Limits

Drug	Limit
Exondys 51 (eteplirsen)	30 mg/kg once weekly

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J1428 Injection, eteplirsen, 10 mg [Exondys 51]

ICD-10 Diagnosis

G71.01 Duchenne or Becker muscular dystrophy

Document History

Reviewed: 08/16/2024

Document History:

- 08/16/2024 – Annual Review: No changes. Coding Reviewed: No changes.
- 08/20/2021 – Annual Review: No changes. Coding review: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 08/21/2020 – Annual Review: Updated Exondys 51 criteria to include requirement for use of corticosteroid. Coding reviewed: No changes.
- 05/15/2020 – Selected Review: Updated Exondys 51 criteria to align with initial clinical trial inclusion data (NCT01396239 [Study 201] and NCT01540409 [Study 202]); added may not be approved criteria to explicitly indicate it will not be used with any other exon skipping therapy; added initial and continuation of therapy approval duration; added may not be approved criteria; added quantity limit per label. Coding Reviewed: No changes
- 02/21/2020 – Selected Review: Selected Review. No changes. Coding Reviewed: No changes.
- 08/16/2019 – Annual Review: Annual review. No changes.
- 11/16/2018 – Annual Review: Initial P&T review of Exondys 51. No changes. HCPCS and ICD-10 coding review: No changes.

References

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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.

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

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