Exondys 51 (eteplirsen)
PAM – 005

Iowa Medicaid Program	Prior Authorization	**Effective Date**	04/21/2017
Revision Number	8	**Last Reviewed**	10/18/2024
Reviewed By	Medicaid Medical Director	**Next Review**	10/17/2025
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	06/19/2019

Overview

Medication: [1]	eteplirsen
Brand Name:	Exondys 51®
Pharmacologic Category:	Neuromuscular agent; antisense oligonucleotide (ASO)
FDA-Approved Indication(s):	Treatment of Duchenne muscular dystrophy (DMD) in patients with a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. ➢ Accelerated Approval: This indication is approved under accelerated approval based on an increase in dystrophin production 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.
How Supplied:	Single-dose vial, 100 mg/2 mL or 500 mg/10 mL
Dosage and Administration:	Intravenous infusion: 30 mg/kg once weekly
Benefit Category:	Medical

Descriptive Narrative

Duchenne muscular dystrophy (DMD) is a type of dystrophinopathy which occurs as a result of mutations (primarily deletions) in the dystrophin gene. Dystrophin is a protein that is present in skeletal and heart muscles allowing the muscles to function properly. The principal symptom of DMD is weakness, as muscle fiber degeneration is the primary pathologic process.

The dystrophinopathies are inherited as X-linked recessive traits and have varying clinical characteristics, with DMD being associated with the most severe clinical symptoms. In DMD, dystrophin is either absent or found in very small amounts. The majority of mutations of the dystrophin gene are deletions

of one or more exons, which are found in approximately 60 to 65 percent of patients with DMD.[2]

Exon skipping is a form of RNA splicing used to cause cells to "skip" over faulty or misaligned sections of genetic code resulting in a truncated, but still functional protein, despite the genetic mutation. Exondys 51® is an antisense oligonucleotide indicated for the treatment of patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. This type of mutation is present in an estimated 13 percent of patients with DMD.[3]

Definitions

- **Ambulatory:** Able to walk, with or without an assistive device, such as a cane or walker (in contrast to "non-ambulatory": unable to walk and requiring use of a wheelchair on a regular basis).
- **Adeno-associated virus (AAV):** A small virus that infects humans and is not known to cause disease. Modified (non-replicating) AAVs are frequently used as viral vectors for gene therapy.
- **Becker muscular dystrophy (BMD):** A type of muscular dystrophy that is similar to but not as severe as DMD. BMD has a later onset and milder symptoms than DMD but can affect the heart in a manner similar to DMD.
- **Dystrophin:** A protein that is required for muscles to function properly. This protein is missing or found in inadequate amounts in individuals with DMD.
- **Gene replacement therapy:** A medical treatment that introduces or alters genetic material to replace the function of a missing or dysfunctional gene with the goal of lessening or eliminating a disease process that results from genetic dysfunction; also known as gene therapy.
- **Surrogate endpoint:** A marker, such as a physical sign, laboratory measurement, or radiographic image or biomarker that is "reasonably likely" to predict clinical benefit, but in and of itself does not measure clinical benefit (such as changes in survival or symptoms).
- **X-linked recessive trait:** A mutation in the gene on the X-chromosome. The phenotype is always expressed in males (who have only one X chromosome) and in females who have mutations in both of their X chromosomes.

Guidelines

In 2005, the American Academy of Neurology issued guidelines on corticosteroid treatment of Duchenne muscular dystrophy (DMD).[4] The guidelines (updated in 2016 and reaffirmed in 2022) include these recommendations:

Prednisone, offered as an intervention for patients with DMD:
- Should be used to improve strength (Level B) and may be used to improve times motor function (Level C);
- Should be used to improve pulmonary function (Level B);
- May be used to reduce the need for scoliosis surgery (Level C);
- May be used to delay the onset of cardiomyopathy by 18 years of age (Level C).

Deflazacort, offered as an intervention for patients with DMD, may be used to:
- Improve strength and timed motor function and delay age at loss of ambulation by 1.4–2.5 years (Level C);
- Improve pulmonary function (Level C);
- Reduce the need for scoliosis surgery (Level C);
- Delay the onset of cardiomyopathy by 18 years of age (Level C);
- Increase survival at 5 and 15 years of follow-up (Level C).

Care considerations for DMD were last published in April 2018, and while they do mention the implications of emerging genetic and molecular therapies for DMD, exon-skipping therapies had not yet been FDA-approved and so are not a part of the official guidance.[5,6,7]

Criteria

Prior authorization is required.

Exondys 51® may be considered medically necessary when **ALL** of the following are met:

1. Diagnosis of Duchenne muscular dystrophy (DMD), with a mutation in the *DMD* gene amenable to exon 51 skipping (confirmed by genetic testing); **AND**
2. Member is male and is between 7 and 13 years of age at therapy initiation; **AND**
3. Will not be used concomitantly with other exon-skipping therapies for DMD or with gene therapy treatment for DMD (e.g., Elevidys®); **AND**
4. Member must have useful function of upper extremities; **AND**
5. Prescribed concurrently with a corticosteroid, unless clinically significant adverse effects are experienced or therapy is contraindicated; **AND**
6. Prescribed by, or in consultation with, a neurologist with expertise in the management of DMD; **AND**
7. The regimen prescribed does not exceed FDA-approved labeling: 30 mg/kg administered once weekly as an intravenous infusion.

Exondys 51® may be considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Member must have useful function of upper extremities; **AND**
3. Prescribed concurrently with a corticosteroid, unless clinically significant adverse effects are experienced or therapy is contraindicated; **AND**
4. Will not be used concomitantly with other exon-skipping therapies for Duchenne muscular dystrophy (DMD) or with gene therapy treatment for DMD (e.g., Elevidys®); **AND**
5. Prescribed by, or in consultation with, a neurologist with expertise in the management of DMD; **AND**
6. The regimen prescribed does not exceed FDA-approved labeling: 30 mg/kg administered once weekly as an intravenous infusion.

Approval Duration and Quantity Limits

	Approval Duration	Quantity Limits
Initial and Continuation	6 months	30 mg/kg once weekly

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J1428	Injection, eteplirsen, 10 mg

ICD-10	Description
G71.01	Duchenne or Becker muscular dystrophy

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
60923-0363-02 (100 mg/2 mL)	Sarepta Therapeutics, Inc. (60923)	10 mg	1	EA	10
60923-0284-10 (500 mg/10 mL)	Sarepta Therapeutics, Inc. (60923)	10 mg	1	EA	50

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Exondys 51® prescribing information (01/2022). Sarepta Therapeutics, Inc.: Cambridge, MA. Available online: www.sareptadmd.com/exondys51. Accessed July 3, 2024.

[2] Darras BT. Duchenne and Becker muscular dystrophy: Genetics and pathogenesis. Dashe JF, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed August 23, 2024.

[3] McDonald CM, Shieh PB, 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. PMID: 34120909.

[4] Gloss D, Moxley RT 3rd, et al. Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016 Feb 2;86(5):465-72. PMID: 26833937. Reaffirmed in 2022.

[5] Birnkrant, David J et al. “Diagnosis and management of Duchenne muscular dystrophy, part 1: Diagnosis, and neuromuscular, rehabilitation, endocrine, and

gastrointestinal and nutritional management." The Lancet. Neurology vol. 17,3 (2018): 251-267. PMID: 29395989.

[6] Birnkrant, David J et al. "Diagnosis and management of Duchenne muscular dystrophy, part 2: Respiratory, cardiac, bone health, and orthopaedic management." The Lancet. Neurology vol. 17,4 (2018): 347-361. PMID: 29395990.

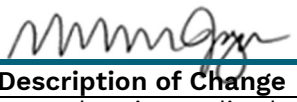
[7] Birnkrant, David J et al. "Diagnosis and management of Duchenne muscular dystrophy, part 3: Primary care, emergency management, psychosocial care, and transitions of care across the lifespan." The Lancet. Neurology vol. 17,5 (2018): 445-455. PMID: 29398641.

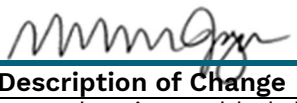
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

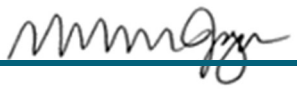
Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]
Signature			

Change Date	Changed By	Description of Change	Version
10/18/2024	CAC	Annual review. Added Definitions to Descriptive Narrative. Updated Guidelines section to include American Academy of Neurology guidelines on corticosteroid treatment of DMD.	8
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Annual review. Edited criteria (added bold portion): "Will not be used concomitantly with other exon-skipping therapies for DMD **or with gene therapy treatment for DMD (e.g., Elevidys®)**." Added same language into continuation criteria.	7
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
04/21/2023	CAC	Annual review. Added dosing regimen into criteria. Updated references.	6
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

Change Date	Changed By	Description of Change	Version
07/15/2022	CAC	Change in ambulatory criterion.	5
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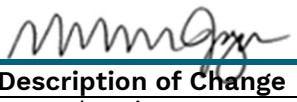
William (Bill) Jagiello, DO			
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04/15/2022	CAC	Annual review.	4
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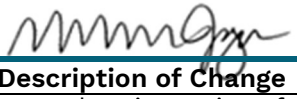
William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/16/2021	CAC	Annual review. Minor formatting changes.	3
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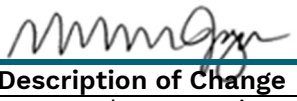
William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
05/15/2020	CAC	Removed age requirement and amended the ambulatory requirement.	2
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William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
08/07/2018	CAC	Wording.	1
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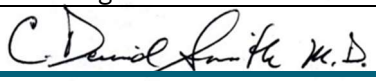
C. David Smith, MD			

CAC = Medicaid Clinical Advisory Committee