Clinical Policy Title:	eteplirsen
Policy Number:	RxA.605
Drug(s) Applied:	Exondys 51™
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2021
Line of Business Policy Applies to:	All lines of business

Background

Eteplirsen (Exondys 51™) is an antisense oligonucleotide. 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
eteplirsen (Exondys 51™)	DMD	30 mg/kg Intravenously once weekly	30 mg/kg Intravenously once weekly

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Duchenne Muscular Dystrophy (must meet all):

1. Diagnosis of DMD with mutation amenable to exon 51 skipping confirmed by genetic testing;
2. Prescribed by or in consultation with a neurologist;
3. Member must be at least 7 years of age at therapy initiation;
4. Member has all 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 ≥ 200 m;

b. Stable cardiac function with left ventricular ejection fraction (LVEF) > 40%;
c. Stable pulmonary function with predicted forced vital capacity (FVC) ≥ 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™) for ≥ 6 months, unless contraindicated or clinically significant adverse effects are experienced;
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., Vyondys 53™);
8. Dose does not exceed 30 mg/kg per week.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Duchenne Muscular Dystrophy (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance, or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by 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 ≥ 200 m;
   b. Stable cardiac function with LVEF > 40%;
   c. Stable pulmonary function with predicted FVC ≥ 50%;
3. Exondys 51™ is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
4. Exondys 51™ is not prescribed concurrently with other exon-skipping therapies (e.g., Vyondys 53);
5. If request is for a dose increase, new dose does not exceed 30 mg/kg per week.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

Appendices

APPENDIX A: Abbreviation/Acronym Key
6MWT: 6-minute walk test
DMD: Duchenne muscular dystrophy
FDA: Food and Drug Administration
LVEF: Left ventricular ejection fraction
FVC: Forced vital capacity

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
prednisone*	0.75 mg/kg/day orally. If side effects (e.g., weight gain and Cushingoid facial appearance) outweigh benefits on muscle strength and function, gradual	Based on weight

	dose reduction to as low as 0.3 mg/kg/day orally can still be beneficial	
Emflaza™	0.9 mg/kg orally once daily	0.9 mg/kg/dose

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

- Hypersensitivity reactions, including rash and urticaria, pyrexia, flushing, cough, dyspnea, bronchospasm, and hypotension, have occurred in patients who were treated with Exondys 51™. If a hypersensitivity reaction occurs, institute appropriate medical treatment and consider slowing the infusion or interrupting the Exondys 51™ therapy.

References

1. Exondys 51™ Prescribing Information. Cambridge, MA: Sarepta Therapeutics, Inc; July 2020. Available at: www.exondys51.com. Accessed October 13, 2021.
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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	03/2019	03/06/2020
Policy was reviewed: 1. Policy title table was updated: Line of business policy applies was updated to All lines of business. 2. Background was updated. 3. Clinical criteria (both initial and continued) were added. 4. Appendix A: LVEF and FVC were added. 5. Appendix B was updated: Pre table phrase was updated to “Below are suggested therapeutic alternatives..”. 6. Appendix D: General Information was added. 7. References were updated.	10/02/2020	12/07/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial Approval Criteria I.A.3 age criteria was changed from “at least 13 years of age” to at least 7 years”. 3. Appendix B was updated to remove “deflazacort” generic as it was not available in US. 4. Appendix B was updated to include max dose for Emflaza™ from “Based on weight” to “0.9 mg/kg/dose”. 5. Appendix B was updated to include dosing regimen of prednisone from “0.3-0.75 mg/kg/day or 10 mg/kg/weekend orally” to “0.75 mg/kg/day orally. If side effects (e.g., weight gain and Cushingoid facial appearance) outweigh benefits on muscle strength and function, gradual dose reduction to as low as 0.3 mg/kg/day orally can still be beneficial”. 6. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name®	10/13/2021	12/07/2021

when the drug is available by brand only and generic name when the drug is available by generic only". 7. References were reviewed and updated.		