

Clinical Policy: Golodirsen (Vyondys 53)

Reference Number: ERX.SPA.375

Effective Date: 03.01.20

Last Review Date: 02.22

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Golodirsen (Vyondys 53™) is an antisense oligonucleotide.

FDA Approved Indication(s)

Vyondys 53 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 53 skipping.

Limitation(s) of use: This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Vyondys 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Vyondys 53 may be **medically necessary** when the following criteria are met:

*** Vyondys 53 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 53 skipping (see *Appendix D*) confirmed by genetic testing;
2. Age ≤ 15 years at therapy initiation;
3. Prescribed by or in consultation with a neurologist;
4. Member has 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 ≥ 250 m;
 - b. Stable cardiac function with left ventricular ejection fraction (LVEF) ≥ 50%;
 - 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;
**Prior authorization is required for Emflaza*
6. Vyondys 53 is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
7. Vyondys 53 is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45™, Exondys 51®, Viltepso®);
8. Dose does not exceed 30 mg/kg per week.

Approval duration: 6 months

II. Continued Therapy

A. Duchenne Muscular Dystrophy (must meet all):

1. Currently receiving medication for DMD with mutation amenable to exon 53 skipping or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
 - a. All of the following assessed within the last 6 months (i, ii, and iii):
 - i. Ambulatory function (e.g., ability to walk with or without assistive devices, not wheelchair dependent) with a 6MWT distance \geq 250 m;
 - ii. Stable cardiac function with LVEF \geq 50%;
 - iii. Stable pulmonary function with predicted FVC \geq 50%;
 - b. Member has received this medication via a healthcare insurer without meeting the requirements above (see criterion 2a), and medical record shows improved or stable LVEF and FVC, assessed within the last 6 months;
3. Member has been assessed by a neurologist within the last 6 months;
4. Vyondys 53 is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
5. Vyondys 53 is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45, Exondys 51, Viltepso);
6. If request is for a dose increase, new dose does not exceed 30 mg/kg per week.

Approval duration: 6 months

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. 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 for all relevant lines of business 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/day PO QD	Based on weight

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 53 skipping include: 3-52, 4-52, 5-52, 6-52, 9-52, 10-52, 11-52, 13-52, 14-52, 15-52, 16-52, 17-52, 19-52, 21-52, 23-52, 24-52, 25-52, 26-52, 27-52, 28-52, 29-52, 30-52, 31-52, 32-52, 33-52, 34-52, 35-52, 36-52, 37-52, 38-52, 39-52, 40-52, 41-52, 42-52, 43-52, 45-52, 47-52, 48-52, 49-52, 50-52, 52, 54-58, 54-61, 54-64, 54-66, 54-76, 54-77.
- 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.
- In an evidence report published August 2019, the Institute for Clinical and Economic Review (ICER) states that current evidence is insufficient to conclude that Vyondys 53 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 4053-US-101 (NCT02310906) used to support the FDA approval of Vyondys 53 enrolled male patients age 6-15 years old with a mean 6MWT distance of 250 m or more at screening and baseline visits, LVEF ≥ 50% based on screening echocardiogram (ECHO), and stable pulmonary function with FVC ≥ 50%.

V. Dosage and Administration

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

VI. Product Availability

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

VII. References

1. Vyondys 53 Prescribing Information. Cambridge, MA: Sarepta Therapeutics, Inc.; February 2021. Available at: <https://www.vyondys53.com>. Accessed September 14, 2021.
2. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *Lancet Neurol.* 2010; 9(1): 77-93.
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 26, 2019.
4. Frank D, Mercuri E, Servais L, et al. Golodirsén induces exon skipping leading to sarcolemmal dystrophin expression in patients with genetic mutations amenable to exon 53 skipping. Paper presented at: Annual Clinical Genetics Meeting of the American College of Medical Genetics and Genomics; April 2-6, 2019; Seattle, WA.
5. Chamberlain JS. Dystrophin levels required for genetic correction of Duchenne muscular dystrophy. *Basic Appl. Myol.* 1997; 7(3&4): 251-255.
6. Neri M, Torelli S, Brown S, et al. Dystrophin levels as low as 30% are sufficient to avoid muscular dystrophy in the human. *Neuromuscul Disord.* 2007; doi:10.1016/j.nmd.2007.07.005.
7. Institute for Clinical and Economic Review. Deflazacort, eteplirsén, and golodirsén for Duchenne muscular dystrophy: Effectiveness and value. Published August 15, 2019. Available at: <https://icer-review.org/material/dmd-final-evidence-report/>. Accessed September 14, 2021.
8. Vyondys 53 Formulary Submission Dossier V1.0. Sarepta Therapeutics, Inc, December 2019.
9. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.21.20	02.20
PA criteria added for coverage consideration when medically necessary.	02.13.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added option for continuation of therapy for patients who have been receiving the medication through another healthcare insurer and/or has been responding positively to therapy with stable disease; modified time frame for positive response parameters from within the last 30 days to within the last 6 months; added requirement for neurologist assessment within the last 6 months.	09.24.20	11.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	10.09.20	02.21
1Q 2022 annual review: no significant changes; clarified that LVEF is inclusive of 50% per pivotal study design; references reviewed and updated.	09.14.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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