Clinical Policy: Golodirsen (Vyondys 53)

Reference Number: CP.PHAR.453
Effective Date: 03.01.20
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.

All requests reviewed under this policy may **require medical director review.**

It is the policy of health plans affiliated with Centene Corporation® 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 ≥ 250 m;
      ii. Stable cardiac function with LVEF ≥ 50%;
      iii. Stable pulmonary function with predicted FVC ≥ 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. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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. Golodirsen 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 Apply. 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, eteplirsen, and golodirsen 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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1429	Injection, golodirsen, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.05.20	02.20
PA criteria added for coverage consideration when medically necessary.	02.13.20	02.20 (ad hoc)

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Removed examples of positive response from Appendix D since specific measures are required in II.A.2.	05.04.20	
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 to HIM.PHAR.21 revised to HIM.PA.154; added coding implications; references reviewed and updated.	10.09.20	02.21
Added disclaimer under Policy/Criteria "All requests reviewed under this policy **require medical director review."**	05.04.21	
1Q 2022 annual review: no significant changes; clarified that LVEF is inclusive of 50% per pivotal study design; added that the review "may" require medical director review; 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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.