# Medical Drug Clinical Criteria

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| **Subject:** | Vyondys 53 (golodirsen) | | |
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## Overview

This document addresses the use of Vyondys 53 (golodirsen), a phosphorodiamidate morpholino oligomer (PMO) in the treatment of Duchenne muscular dystrophy (DMD) with a mutation amenable to exon 53 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. In theory, exon 53 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 presence of exon 53 in the dystrophin gene and the deletion of one or more exons contiguous with exon 53, resulting in an out-of-frame deletion in which the reading frame is potentially restorable by the skipping (removing) of exon-53 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).

Vyondys 53 is FDA approved for the treatment of DMD with a mutation amenable to exon 53 skipping. Vyondys 53 was approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed. Golodirsen was studied in Phase I/II trials in 39 patients. Patients were all male and age 6-15 years. Inclusion criteria included the requirement of a minimum performance on 6MWT (6-minute walk test), North Star Ambulatory Assessment and rise (Gowers) test. Results were presented at the 2018 American Academy of Neurology conference as an abstract. The results showed an increase in dystrophin in the study participants, with an increase from 0.095% at baseline to 1.019% at week 48. It is yet to be determined whether the increase in dystrophin production translates into clinical benefit. Continued approval for Vyondys 53 may be contingent upon verification of a clinical benefit in confirmatory trials. The recommended dose of Vyondys 53 is 30 mg per kilogram administered once weekly as a 35–60-minute infusion.

Vyondys 53 was FDA-approved four months after receiving a complete response (denial) letter from the FDA. A Phase 3 confirmatory trial (ESSENCE) is ongoing. The FDA initially denied the new drug application due to safety concerns including infection at the infusion site and pre-clinical renal toxicity. The manufacturer responded to safety concerns noting that the signal for renal toxicity came from pre-clinical trials at high doses. The Phase I/II clinical trial has not demonstrated renal toxicity in patients taking Vyondys 53 over 48 weeks. Because animal data showed a possible increase in the risk of renal toxicity, renal function should be monitored. Per the label for Vyondys 53, the measurement of renal function should be done via measurement of glomerular filtration rate (GFR) by 24-hour urine collection prior to initiation of therapy. Monitoring should be done monthly for proteinuria and every three months for serum cystatin C. If proteinuria of 2+ or greater or elevated serum cystatin C is found, a 24-hour urine collection to quantify proteinuria and assess GFR should be performed.

## 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.

**Vyondys 53 (golodirsen)**

Initial requests for Vyondys 53 (golodirsen) 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 53 skipping; **AND**

III. Individual is age 6-15 years (NCT02310906, Study 4053-101; Frank 2020); **AND**
IV. Individual is using a corticosteroid; **AND**
V. Documentation is provided that individual has a 6MWT (6 minute walk test) ≥ 250m (NCT02310906, Study 4053-101; Frank 2020); **AND**
VI. One of the following:
    A. NorthStar Ambulatory Assessment (NSAA) total > 17 (NCT02310906, Study 4053-101, Frank 2020), and documentation is provided; **OR**
    B. Rise (Gowers) time of < 7 seconds (NCT02310906, Study 4053-101, Frank 2020).

Continuation of therapy with Vyondys 53 (golodirsen) 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, including but not limited to a cane or walker).

Vyondys 53 (golodirsen) may not be approved for the following:

I. Individual is using another exon skipping agent for DMD (including but not limited to Exondys 51, Amondys 45); **OR**
II. When the above criteria are not met and for all other indications.

**Approval Duration:** 6 months

## Quantity Limits

**Vyondys 53 (golodirsen) Quantity Limits**

| Drug | Limit |
|---|---|
| Vyondys 53 (golodirsen) | 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**

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|---|---|
| J1429 | Injection, golodirsen 10 mg [Vyondys 53] |

**ICD-10 Diagnosis**

| | |
|---|---|
| G71.01 | Duchenne or Becker muscular dystrophy |
| Z14.8 | Genetic carrier of other disease |

## Document history

Reviewed: 08/18/2023
Document History:

- 08/18/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: Removed all diagnoses pend for NOC codes.
- 08/19/2022 – Annual Review: No changes. Coding reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 08/21/2020 – Annual Review: Updated criteria to include Rise (Gowers) time of < 7 seconds as an alternative to NSAA score > 17 per published trial inclusion criteria (Frank 2020) NCT02310906; updated to include requirement for corticosteroid use. Coding reviewed: No changes.
- 05/15/2020 – Select Review: Updated Vyondys 53 clinical criteria to indicate it will not be used with any other exon skipping agent for DMD; added approval duration of 6 months; added may not be approved criteria; added quantity limit per label. Coding Review: Added HCPCS J1429 (Effective 7/1/2020), Removed J3590, J3490, C9399 (Effective 6/30/2020), Delete ALL Dx pend 6/30/2020

- 02/21/2020 – Select Review: No changes. Coding Reviewed: Added HCPCS J3590, C9399. All Diagnosis codes when using NOC codes.
- 12/20/2019 – Select Review: First review of Vyondys 53; new prior authorization for Vyondys 53. Coding Reviewed: Added HCPCS code J3490, added ICD-10 DX G71.01, Z14.8

## References


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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
4. Frank, DE, Schnell FJ, Akana C, et.al. Increased dystrophin production with golodirsen in patients with Duchenne muscular dystrophy. *Neurology*. 2020;94:e2270-e2282. Doi:10.1212/WNL.0000000000009233. Available from: https://n.neurology.org/content/neurology/94/21/e2270.full.pdf.
5. Kole R, Krieg AM. Exon skipping therapy for Duchenne muscular dystrophy. *Ad Drug Del Rev*. 2015; 87:140-107.
6. Muntoni F, Frank D, Sarone V, et.al. Golodirsen Induces Exon Skipping Leading to Sarcolemmal Dystrophin Expression in Duchenne Muscular Dystrophy Patients With Mutations Amenable to Exon 53 Skipping (S22.001). Neurology Apr 2018, 90 (15 Supplement) S22.001.
7. Shieh PB. Golodirsen Induces Exon Skipping Leading to Sarcolemmal Dystrophin Expression in Patients With Genetic Mutations Amenable to Exon 53 Skipping. Presented at: Carrell-Krusen Neuromuscular Symposium, February 22–23, 2018; Dallas, TX.



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

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