

# Vyondys 53® (Golodirsen)

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[Instructions for Use](#)

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Related Commercial Policy
<ul style="list-style-type: none"> <li><a href="#">Provider Administered Drugs – Site of Care</a></li> </ul>
Community Plan Policy
<ul style="list-style-type: none"> <li><a href="#">Vyondys 53® (Golodirsen)</a></li> </ul>

## Coverage Rationale

[See Benefit Considerations](#)

Vyondys 53 (golodirsen) may be covered for the treatment of Duchenne muscular dystrophy (DMD) in patients who meet all of the following criteria:

- For **initial therapy**, all of the following:
  - Diagnosis of Duchenne muscular dystrophy by, or in consultation with, a neurologist with expertise in the diagnosis of DMD; **and**
  - Submission of medical records (e.g., chart notes, laboratory values) confirming the mutation of the DMD gene is amenable to exon 53 skipping; **and**
  - One** of the following:
    - Submission of medical records (e.g., chart notes, laboratory values) confirming that the patient has a 6-Minute Walk Test (6MWT) ≥ 300 meters while walking independently (e.g., without side-by-side assist, cane, walker, wheelchair, etc.) prior to beginning Vyondys 53 therapy; **or**
    - Both** of the following:
      - Submission of medical records (e.g., chart notes) confirming that the patient is ambulatory **without** needing an assistive device (e.g., without side-by-side assist, cane, walker, wheelchair, etc.); **and**
      - One** of the following:
        - Patient has achieved a score of greater than 17 on the North Star Ambulatory Assessment (NSAA); **or**
        - Patient has achieved a time to rise from the floor (Gower’s test) of less than 7 seconds
  - and**
  - Vyondys 53 is prescribed by, or in consultation with, a neurologist with expertise in the treatment of DMD; **and**
  - Vyondys 53 dosing for DMD is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Vyondys 53 is not used concomitantly with other exon skipping therapies for DMD; **and**
  - Initial authorization will be for no more than 12 months.
- For **continuation of therapy**, all of the following:
  - Vyondys 53 is prescribed by, or in consultation with, a neurologist with expertise in the treatment of DMD; **and**
  - Submission of medical records (e.g., chart notes) confirming that the patient is ambulatory **without** needing an assistive device (e.g., without side-by-side assist, cane, walker, wheelchair, etc.); **and**
  - Vyondys 53 dosing for DMD is in accordance with the United States Food and Drug Administration approved labeling; **and**

- Vyondys 53 is not used concomitantly with other exon skipping therapies for DMD; **and**
- Reauthorization will be for no more than 12 months.

**Vyondys 53 will not be covered for other forms of muscular dystrophy.**

## Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1429	Injection, golodirsen, 10 mg

Diagnosis Code	Description
G71.01	Duchenne or Becker muscular dystrophy

## Background

Duchenne muscular dystrophy (DMD) is an X-linked disease that affects 1 in 3,600 – 6,000 live male births. DMD occurs as a result of mutations (mainly deletions) in the dystrophin gene. These mutations lead to an absence or a defect of the protein, dystrophin, resulting in progressive muscle degeneration, leading to loss of ambulation and additional respiratory, orthopedic, and cardiac complications. If left untreated, mean age of death is approximately 19 years of age.<sup>2-4</sup>

Vyondys 53 (golodirsen) is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. PMOs are synthetic molecules in which the five-membered ribofuranosyl rings found in natural DNA and RNA are replaced by a six-membered morpholino ring. Each morpholino ring is linked through an uncharged phosphorodiamidate moiety rather than the negatively charged phosphate linkage that is present in natural DNA and RNA. Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine).<sup>1</sup>

Golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA, resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Approximately 8% of DMD patients have out of frame deletion mutations amenable to exon 53 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.<sup>1</sup>

Eteplirsen (Exondys 51) is the first PMO approved by the US Food and Drug Administration for treatment of DMD patients with confirmed genetic mutations amenable to exon 51 skipping. Approximately 13% of DMD patients have out of frame deletion mutations amenable to exon 51 skipping. This indication was approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with eteplirsen. A clinical benefit of eteplirsen has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.<sup>5</sup>

## Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

## Clinical Evidence

Golodirsen 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.<sup>1</sup>

The SKIP-NMD trial of golodirsen is a US-based, blinded, placebo-controlled, dose-escalation two-part Phase I/II RCT of male patients aged six to 15 years with a DMD diagnosis and DMD gene amenable to exon 53 skipping. Patients age 6 to 15 years with stable cardiac and pulmonary function, and on a stable dose of corticosteroids for at least six months were included. Additional inclusion criteria included a baseline six-minute walk test (6MWT) of greater than 250m, a North Star Ambulatory Assessment (NSAA) score of greater than 17 or a rise time of less than 7 seconds. In part one, 12 patients were randomized to receive once-weekly intravenous infusions at escalating doses of 4, 10, 20, 30 mg/kg of golodirsen or matching placebo for 12 weeks. Part two consists of an open-label period of all patients from part one and 13 newly recruited patients who are receiving once-weekly infusions of 30 mg/kg of golodirsen for up to 168 weeks.

Part one of the SKIP-NMD trial assessed safety and tolerability. In part two, the primary endpoints are change from baseline in 6MWT at 144 weeks and change in dystrophin protein levels at 48 weeks. Secondary endpoints include drug pharmacokinetics, change from baseline in FVC percent predicted, and change from baseline in dystrophin intensity at 144 weeks.

At the time of pre-planned interim analysis, data from baseline and Week 48 muscle biopsies, exon 53 skipping, and dystrophin localization were available for 25 patients on golodirsen. Mean 6MWT distance at baseline was 405.8 m for golodirsen-treated patients and declined by 26.1, 64.6, and 99.0 m at weeks 48, 96, and 144, respectively.<sup>11</sup> Per a *post hoc* ambulation analysis, control patients' 6MWT distance declined by a mean of 181.4 m [standard deviation (SD), 151.6; range, -401 to 56] after 3 years compared with baseline. In contrast, golodirsen-treated patients had a mean decline from baseline of 99.0 m (SD, 123.8; range, -368 to 144) after 3 years ( $p = 0.067$  between groups). This difference emerged over time, as no difference between treated and untreated patients was observed at the time points before year 3. Among natural history controls, 5 of 19 patients (26%) had lost ambulation over 3 years, compared with 2 of 25 (9%) of those who received golodirsen ( $p = 0.21$ ). Mean baseline of dystrophin in the trial was reported to be 0.095% of normal. At 48 weeks, the mean level of dystrophin had increased to 1.019% of normal resulting in an absolute increase of 0.918% of normal ( $p < 0.001$ ). A clinically meaningful change in level of dystrophin has not yet been established in humans. As such, the clinical significance of these results is not clear. Among individual patients, dystrophin levels at Week 48 ranged from 0.09% to 4.30%.<sup>6-8</sup>

ESSENCE is an ongoing 96-week, Phase 3, double-blind, placebo controlled, randomized clinical trial that will evaluate the efficacy of golodirsen and casimersen in DMD patients with out-of-frame deletion mutations amenable to skipping exon 53 and exon 45, respectively. The study will enroll 222 boys from 7 to 13 years of age with genotypically confirmed DMD and 6MWT  $\geq 300$  m and  $\leq 450$  m. The primary endpoint is the change from baseline to Week 96 in 6MWT.

Golodirsen has not been studied in DMD that is not amenable to exon 53 skipping, nor in other forms of muscular dystrophy (e.g., Becker muscular dystrophy).<sup>1</sup>

## U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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

## References

1. Vyondys 53 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, February 2021.
2. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *Lancet Neurol*; 2010 Jan; 9(1):77-93.

3. Bushby K, Finkel R, Birnkrant DJ, et al. (2010) Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. *Lancet Neurol*; 2010 Jan; 9(2):177-189.
4. 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(3):251-267. doi: 10.1016/S1474-4422(18)30024.
5. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, January 2022.
6. Frank DE, 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. Poster presented at: Annual Clinical Genetics Meeting of the American College of Medical Genetics and Genomics; April 2-6, 2019; Seattle, WA.
7. Muntoni F, Frank DE, Morgan J, et al. Golodirsen induces exon skipping leading to sarcolemmal dystrophin expression in patients with genetic mutations amenable to exon 53 skipping [abstract]. *Neuromuscul Disord*. 2018;28:S5. Abstract D01.
8. Muntoni F, Frank DE, Sardone V, et al. SRP-4053 induces exon skipping leading to sarcolemmal dystrophin expression in Duchenne muscular dystrophy patients amenable to exon 53 skipping. Poster presented at: 22nd International Annual Congress of the World Muscle Society; October 3-7 2017; Saint Malo, France.
9. Study of SRP-4045 and SRP-4053 in DMD Patients (ESSENCE) <https://clinicaltrials.gov/ct2/show/NCT02500381?term=golodirsen&cond=Duchenne+Muscular+Dystrophy&rank=3>. Accessed February 4, 2023.
10. Institute for Clinical and Economic Review (ICER). Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: Effectiveness and value: Evidence Report. [ICER DMD-Final-Report 081519-2.pdf](#) . April 22, 2022. Accessed February 4, 2023.
11. Servais L, Mercuri E, Straub V, et al. Long-Term Safety and Efficacy Data of Golodirsen in Ambulatory Patients with Duchenne Muscular Dystrophy Amenable to Exon 53 Skipping: A First-in-human, Multicenter, Two-Part, Open-Label, Phase 1/2 Trial. *Nucleic Acid Ther*. 2022;32(1):29-39. doi:10.1089/nat.2021.0043.

## Policy History/Revision Information

Date	Summary of Changes
12/01/2024	<b>Template Update</b> <ul style="list-style-type: none"> <li>Modified font style; no change to policy content</li> </ul>
05/01/2024	<b>Coverage Rationale</b> <ul style="list-style-type: none"> <li>Changed duration for initial authorization from “no more than 6 months” to “no more than 12 months”</li> </ul> <b>Supporting Information</b> <ul style="list-style-type: none"> <li>Archived previous policy version 2023D0088E</li> </ul>

## Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence ([Medicare IOM Pub. No. 100-16, Ch. 4, §90.5](#)).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.