

Vyondys 53™ (Golodirsen)

Policy Number: PHARMACY 327.3 T2
Effective Date: September 1, 2020

[➔ Instructions for Use](#)

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Related Policy
<ul style="list-style-type: none"> Provider Administered Drugs - Site of Care

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 Time (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: maximum dosing of 30 mg/kg infused once weekly; and
- Vyondys 53 is not used concomitantly with other exon skipping therapies for DMD; and
- Initial authorization will be for no more than 6 months.

- For continuation 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: maximum dosing of 30 mg/kg infused once weekly; 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.

Prior Authorization Requirements

Prior authorization is required in all sites of service.

Notes:

New Jersey Small Group plan members should refer to their Certificate of Coverage for prior authorization and quantity limit guidelines.

Participating providers in the office setting: Prior authorization is required for services performed in the office of a participating provider.

- Non-participating/out-of-network providers in the office setting: Prior authorization is not required but is encouraged for out-of-network services. If prior authorization is not obtained, Oxford will review for out-of-network benefits and medical necessity after the service is rendered.
- Home infusion of Vyondys 53 requires additional prior authorization for the home care services.
- Additional prior authorization requirements apply to requests for hospital outpatient facility infusion of Vyondys 53™ (golodirsen); refer to the Clinical Policy titled [Provider Administered Drugs - Site of Care](#).

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 may apply.

CPT Code	Description
J1429	Injection, golodirsen, 10 mg

CPT® is a registered trademark of the American Medical Association

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.^{2,4}

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).¹

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.¹

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.⁵

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. See 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.¹

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. The study is ongoing, and results for the primary efficacy endpoint of 6MWT at Week 144 are not yet available. 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%.⁶⁻⁸

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).¹

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

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealth Group National Pharmacy & Therapeutics Committee. [2020D0088A]

Vyondy 53 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, December 2019.

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.

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.

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.

Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, October 2018.

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

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.

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.

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 July 22, 2019.

Institute for Clinical and Economic Review (ICER). Deflazacort, eplirsen, and golodirsen for Duchenne muscular dystrophy: Effectiveness and value: Evidence Report. https://icer-review.org/wp-content/uploads/2018/12/ICER_DMD_Evidence_Report_071119.pdf. Accessed July 22, 2019.

Policy History/Revision Information

Date	Summary of Changes
09/01/2020	<p>Template Update</p> <ul style="list-style-type: none">Reformatted policy; transferred content to new templateRemoved and replaced section titled <i>Conditions of Coverage</i> with <i>Prior Authorization Requirements</i><ul style="list-style-type: none">○ Simplified and relocated language pertaining to prior authorization guidelines○ Removed language addressing benefit type and referral requirements (refer to the member specific benefit plan document)Replaced references to “precertification” with “prior authorization” <p>Supporting Information</p> <ul style="list-style-type: none">• Archived previous policy version PHARMACY 327.2 T2

Instructions for Use

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford 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 Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Oxford Clinical 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.