# Drug Coverage Policy

**Effective Date.....4/1/2025**
**Coverage Policy Number.....IP0136**
**Policy Title..... Vyondys 53**

# Muscular Dystrophy – Vyondys 53

- Vyondys 53™ (golodirsen intravenous infusion – Sarepta)

***INSTRUCTIONS FOR USE***
*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

## Cigna Healthcare Coverage Policy

### OVERVIEW
Vyondys 53, an antisense oligonucleotide, 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] Vyondys 53 was approved for this indication under accelerated approval based on an increase in dystrophin observed in the skeletal muscle of patients who received the drug. The Prescribing Information notes that continued FDA-approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

## Disease Overview

DMD is an X-linked recessive disease affecting 1 in 3,600 to 6,000 newborn male infants.[2] The disease is attributed to large frame-shift deletions in the DMD gene (chromosome Xp21) which lead to loss of a structural protein of muscle cells (dystrophin).[3] Over 4,700 mutations on the DMD gene have been identified which lead to a deficiency in production of dystrophin.[2] Therefore, the type of mutation and its effect on the production of dystrophin accounts for the variable phenotypic expression.[4] Female carriers are usually asymptomatic but some may show mild symptoms.[2] There are wide variances in how quickly DMD progresses, but without intervention death is at approximately 19 years of age.[2-4] With respiratory, cardiac, orthopedic and rehabilitative interventions, and use of corticosteroids, children born today can have a life expectancy of up to 40 years.

Vyondys 53 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.[1] These patients represent up to 10% of all patients with DMD.[5] This genetic manipulation intends to restore the reading frame of the resulting mRNA. The result would be production of a shortened, but partially functional dystrophin protein as seen in less severe forms of muscular dystrophy (e.g., Becker muscular dystrophy). Of note, the reading frame of certain deletions (e.g., exon 52 deletions) can be restored by skipping either exon 51 or exon 53.[6] Approximately 8% of mutations are amenable to skipping exon 53 with Vyondys 53 but are not amenable to skipping of exon 51.

## Guidelines

There are guidelines for the diagnosis and management of DMD available from the DMD Care Considerations Working Group (2018).[4] Genetic testing for a DMD mutation in a blood sample is always required. By fully characterizing the mutation, the predicted effect on the reading frame can be identified, which is the major determinant of phenotype and will determine eligibility for mutation-specific clinical trials. In patients with no mutation identified but with signs/symptoms of DMD, a muscle biopsy is clinically indicated. Glucocorticoids slow decline in muscle strength and function in DMD. Use of corticosteroids reduces the risk of scoliosis and stabilizes pulmonary function. Continued treatment after the patient loses ambulation provides a reduction in the risk of progressive scoliosis and stabilization of pulmonary function tests. Therefore, glucocorticoids should be considered for all patients with DMD. Exondys 51 (eteplirsen intravenous infusion) is mentioned as an emerging product, approved by an accelerated pathway for those with a mutation in the dystrophin gene amenable to exon 51 skipping. However, these guidelines do not specifically address exon 53 skipping or mention Vyondys 53.

# Medical Necessity Criteria

**Vyondys 53 is considered medically necessary when the following criteria are met:**

### FDA-Approved Indication

1. **Duchenne Muscular Dystrophy.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A.** Initial Therapy. Approve for 6 months if the patient meets ALL the following (i, ii, iii, iv, and v):
     - **i.** Less than 16 years of age at start of therapy; AND
     - **ii.** Documented diagnosis of Duchenne muscular dystrophy is confirmed by a pathogenic or likely pathogenic variant in the *DMD* gene that is amenable to exon 53 skipping; AND

**iii.** Able to walk a distance of at least 250 meters independently over 6 minutes; AND
**iv.** Rise (Gower's) time less than 7 seconds; AND
**v.** Medication is prescribed by, or in consultation with, a neurologist, neuromuscular specialist, or by a Muscular Dystrophy Association clinic.

**B.** Patient is Currently Receiving Vyondys 53. Approve for 6 months if the patient meets ALL the following (i, ii, and iii):
**i.** The above criteria were met prior to initiation of Vyondys 53; AND
**ii.** Patient has experienced a beneficial clinical response, including the continued ability to walk; AND
**iii.** Medication continues to be prescribed by, or in consultation with, a neurologist, neuromuscular specialist, or by a Muscular Dystrophy Association clinic.

**Dosing.** Approve 30 milligrams per kilogram administered once weekly as a 35 to 60-minute intravenous infusion.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use with Other Exon-skipping DMD Agents.** Currently, there is no clinical evidence to support concurrent use of exon-skipping agents for the treatment of Duchenne muscular dystrophy.

## Coding Information

**Note:**
1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.
**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

| HCPCS Codes | Description |
|---|---|
| J1429 | Injection, golodirsen, 10 mg |

## References


1. Vyondys 53 intravenous infusion [prescribing information]. Cambridge, MA: Sarepta; June 2024.
2. Annexstad EJ, Lund-Petersen I, Rasmussen M. Duchenne muscular dystrophy. *Tidsskr Nor Laegeforen*. 2014;134(14):1361-1364.

3. Wood MJA. To skip or not to skip: that is the question for Duchenne muscular dystrophy. *Mol Ther*. 2013;21(12):2131-2132.
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.
5. van Deutekom JC, Bremmer-Bout M, Janson AA, et al. Antisense-induced exon skipping restores dystrophin expression in DMD patient derived muscle cells. *Hum Mol Genet*. 2001;10(15):1547-1554.
6. Bladen CL, Salgado D, Monges S, et al. The TREAT-NMD DMD Global Database: analysis of more than 7,000 Duchenne muscular dystrophy mutations. *Hum Mutat*. 2015;36(4):395-402.
7. Shimizu-Motohashi Y, Murakami T, Kimura E, et al. Exon skipping for Duchenne muscular dystrophy: a systematic review and meta-analysis. *Orphanet J Rare Dis*. 2018;13(1):93.
8. Frank DE, Schnell FJ, Akana C, et al. Increased dystrophin production with golodirsen in patients with Duchenne muscular dystrophy. *Neurology*. 2020;94(21): e2270-e2282.
9. 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 Feb;32(1):29-39.
10. Sarepta Therapeutics. Study of SRP-4045 (Casimersen) and SRP-4053 (Golodirsen) in participants with Duchenne muscular dystrophy (DMD) (ESSENCE). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2024 December 16]. Available at: https://clinicaltrials.gov/study/NCT02500381?intr=golodirsen&rank=3. NLM Identifier: NCT02500381.

## Revision Details

| Type of Revision | Summary of Changes | Date |
|---|---|---|
| Annual Revision | Updated policy title: previously it was Golodirsen. Added dosing to the policy. | 8/15/2024 |
| Annual Revision | No criteria change. | 4/1/2025 |

The policy effective date is in force until updated or retired.