

# Amondys 45® (Casimersen) (for Ohio Only)

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Related Policies
None

## Application

This Medical Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

## Coverage Rationale

Amondys 45 (casimersen) 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 45 skipping; and
  - Submission of medical records (e.g., chart notes, laboratory values) confirming that the patient is ambulatory prior to beginning Amondys 45 therapy; and
  - Amondys 45 is prescribed by, or in consultation with, a neurologist with expertise in the treatment of DMD; and
  - Amondys 45 dosing for DMD is in accordance with the United States Food and Drug Administration approved labeling; and
  - Amondys 45 is not used concomitantly with other exon skipping therapies for DMD; and
  - Initial authorization will be for no more than 6 months
- For continuation of therapy, all of the following:
  - Amondys 45 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) demonstrating that the patient continues to remain ambulatory; and
  - Amondys 45 dosing for DMD is in accordance with the United States Food and Drug Administration approved labeling; and
  - Amondys 45 is not used concomitantly with other exon skipping therapies for DMD; and
  - Reauthorization will be for no more than 12 months

Amondys 45 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 federal, state, or contractual requirements 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
J1426	Injection, casimersen, 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 to 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>

Amondys 45 (casimersen) 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>

Casimersen is designed to bind to exon 45 of dystrophin pre-mRNA, resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 45 skipping. Approximately 8% of DMD patients have out-of-frame deletion mutations amenable to exon 45 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.<sup>1</sup>

Eteplirsen (Exondys 51<sup>®</sup>) was 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.<sup>5</sup> Golodirsen (Vyondys 53<sup>™</sup>) and viltolarsen (Viltepso<sup>™</sup>) were the second and third exon skipping agents approved by the U.S. Food and Drug Administration for treatment of DMD patients with confirmed genetic mutations amenable to exon 53 skipping. Approximately 8% of DMD patients have out-of-frame deletion mutations amenable to exon 53 skipping. Both of these agents were also approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in treated patients.

## Clinical Evidence

Casimersen 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 45 skipping.<sup>1</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 ambulatory 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. Following the 96-week double-blind period, all patients began or are to begin an additional 48 week open-label treatment period. Interim efficacy was assessed based on change from baseline in the dystrophin protein level (measured as % of the dystrophin level in healthy

subjects, i.e., % of normal determined by Western Blot) at Week 48. Interim results from 43 evaluable patients (n = 27, casimersen; n = 16, placebo) who had a muscle biopsy at Week 48 of the double-blind period have been reported. Patients randomized to casimersen had a baseline mean dystrophin level of 0.93% of normal. At week 48, the mean dystrophin level increased 0.81% to 1.74% of normal. Patients randomized to placebo had a baseline mean dystrophin level of 0.54% of normal. At week 48, the mean dystrophin level increased 0.22% to 1.15% of normal. 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.<sup>1,8</sup>

Casimersen has not been studied in DMD that is not amenable to exon 45 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.

Amondys 45 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 45 skipping. This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in patients treated with Amondys 45. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.<sup>1</sup>

## References

1. Amondys 45 [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. Vyondys 53 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, February 2021.
7. Viltepso [package insert]. Paramus NJ: NS Pharma, Inc, March 2021.
8. 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.

## Policy History/Revision Information

Date	Summary of Changes
06/01/2023	<p><b>Template Update</b></p> <ul style="list-style-type: none"> <li>Created state-specific policy version</li> </ul> <p><b>Coverage Rationale</b></p> <ul style="list-style-type: none"> <li>Revised coverage criteria: <ul style="list-style-type: none"> <li><i>Initial Therapy</i> <ul style="list-style-type: none"> <li>Replaced criterion requiring “submission of medical records (e.g., chart notes, laboratory values) confirming that the patient <i>has a 6-Minute Walk Time (6MWT) ≥ 300 meters while walking independently (e.g., without side-by-side assist, cane, walker, wheelchair, etc.)</i> prior to beginning Amondys 45 therapy” with “submission of medical records (e.g., chart notes, laboratory values) confirming that the patient <i>is ambulatory</i> prior to beginning Amondys 45 therapy”</li> </ul> </li> </ul> </li> </ul>

Date	Summary of Changes
	<ul style="list-style-type: none"> <li>○ Removed criterion requiring both of the following: <ul style="list-style-type: none"> <li>▪ 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</li> <li>▪ One of the following: <ul style="list-style-type: none"> <li>– Patient has achieved a score of greater than 17 on the North Star Ambulatory Assessment (NSAA); or</li> <li>– Patient has achieved a time to rise from the floor (Gower’s test) of less than 7 seconds</li> </ul> </li> </ul> </li> </ul> <p><i>Continuation of Therapy</i></p> <ul style="list-style-type: none"> <li>○ Replaced criterion requiring “submission of medical records (e.g., chart notes) <i>confirming that the patient is ambulatory without needing an assistive device (e.g., without side-by-side assist, cane, walker, wheelchair, etc.)</i>” with “submission of medical records (e.g., chart notes) <i>demonstrating that the patient continues to remain ambulatory</i>”</li> </ul> <p><b>Supporting Information</b></p> <ul style="list-style-type: none"> <li>● Updated <i>Background</i> and <i>References</i> sections to reflect the most current information</li> <li>● Archived previous policy version CS2022D0105G</li> </ul>

## Instructions for Use

This Medical Benefit Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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.