Amondys 45™ (Casimersen)

Policy Number: 2021D00105B
Effective Date: July 1, 2021

Instructions for Use

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Related Commercial Policy

- Provider Administered Drugs – Site of Care

Coverage Rationale

See Benefit Considerations

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
  - 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 Amondys 45 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
  - 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) confirming that the patient is ambulatory without needing an assistive device (e.g., without side-by-side assist, cane, walker, wheelchair, etc.); 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 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
C9075	Injection, casimersen, 10 mg
J3490	Unclassified drugs
J3590	Unclassified biologics

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]

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).[1]

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.[1]

Eteplirsen (Exondys 51®) was the first PMO approved by the US Food and Drug Administrationfor 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.[5] Golodirsen (Vyondys 53™) and viltolarsen (Viltepso™) were the second and third exon skipping agents approved by the U.S. Food and Drug Administrationfor 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.

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

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.[1]

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 ≥ 300 m and ≤ 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. [1, 8]

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).[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.

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

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, July 2020.

6. Vyondys 53 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, February 2021.
7. Viltepso [package insert]. Paramus NJ: NS Pharma, Inc, August 2020.
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 26, 2021

Policy History/Revision Information

Date	Summary of Changes
07/01/2021	**Template Update** • Replaced reference to "MCG™ Care Guidelines" with "InterQual® criteria" in *Instructions for Use* **Applicable Codes** • Updated list of applicable HCPCS codes to reflect quarterly edits; replaced C9399 with C9075 **Supporting Information** • Archived previous policy version 2021D00105A

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.