

## Amondys 45 (casimersen)-MNR

### PRODUCTS AFFECTED

Amondys 45 (casimersen)

### COVERAGE POLICY

*Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.*

*This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines*

#### **Documentation Requirements:**

*Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes.*

*Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive*

#### **DIAGNOSIS:**

Duchenne muscular dystrophy

#### **REQUIRED MEDICAL INFORMATION:**

*This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review*

#### **A. DUCHENNE MUSCULAR DYSTROPHY(DMD):**

1. Diagnosis of Duchenne muscular dystrophy (DMD) with mutation amenable to exon 45 skipping confirmed by genetic testing

*NOTE: Lab results from genetic testing is required for authorization review. Members who do not have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping will not be authorized.*

**AND**

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## Drug and Biologic Coverage Criteria

2. Documentation that member is ambulatory as evidenced by ONE the following completed in the previous 30 days: 6-minute walk test (6MWT)  $\geq 300$  meters while walking independently without assistance or devices (without side-by-side assist, cane, walker, wheelchair, etc.) OR North Star Ambulatory Assessment (NSAA) score  $> 17$  OR achieved rise time (Gower's test)  $< 7$  seconds  
AND
3. Documentation of member's weight (in kilograms) (within the last 30 days)  
AND
4. Documentation of member's baseline disease activity evaluation, recent (within 30 days) and goals for treatment to be used to evaluate efficacy of therapy at renewal  
AND
5. Documentation member is currently stable on an oral corticosteroid regimen for at least 6 months, unless contraindicated or member has experienced clinically significant adverse effects.  
AND
6. Documentation of ONE (1) or more of the following measurable evaluations to assess (evaluation done within the last 30 days) physical function or the rate of disease progression (not an all-inclusive list):
  - a. Dystrophin level
  - b. Brooke Upper Extremity Scale
  - c. Forced Vital Capacity assessment

**NOTE:** The same assessment should be what was provided on initial review. If the initial assessment tool is not appropriate (i.e., due to change in member's status or age range of the assessment), submit the rationale for change in assessment tool.

### CONTINUATION OF THERAPY:

#### A. DUCHENNE MUSCULAR DYSTROPHY (DMD):

1. Adherence to therapy at least 85% of the time as confirmed by Prescriber or member's claims history  
**NOTE:** Therapy may be discontinued due to poor adherence upon recommendation of the Molina Medical Director when adherence  $< 85\%$  has been demonstrated in at least two months during the course of therapy  
AND
2. Documentation of absence of unacceptable adverse effects or complications from Amondys 45 (casimersen) including: severe infusion-related reactions, interference with automated platelet counts (platelet clumping)  
AND
3. Documentation of positive response to therapy, defined as member remaining ambulatory, as evidenced by ALL of the following evaluations completed within the past 30 days:
  - (a) Results of 6-Minute Walk Test (6MWT), while walking independently without assistance or devices (without side-by-side assist, cane, walker, wheelchair, etc.) OR North Star Ambulatory Assessment (NSAA) score  $> 17$  OR achieved rise time (Gower's test)  $< 7$  seconds  
AND
  - (b) ONE (1) or more of the following measurable evaluations to assess physical function or the rate of disease progression (not an all-inclusive list). Evaluation must be within the past 30 days.
    - i. Increase in dystrophin level†, OR
    - ii. Brooke Upper Extremity Scale, OR
    - iii. Respiratory parameters: Forced Vital Capacity (FVC %) predicted and peak cough flow

**NOTE:** The same assessment should be what was provided on initial review. If the initial assessment tool is not appropriate (i.e., due to change in member's status or age range of the assessment), submit the rationale for change in assessment tool.  
AND

4. Member continues to receive concurrent corticosteroids, unless contraindicated or intolerant (severe adverse reactions)

## Drug and Biologic Coverage Criteria

### **DURATION OF APPROVAL:**

Initial authorization: 6 months, Continuation of therapy: 12 months

### **PRESCRIBER REQUIREMENTS:**

Prescribed by, or in consultation with, a board-certified physician who specializes in treatment of Duchenne muscular dystrophy in one of the following specialties: neurology, orthopedic, physical medicine and rehabilitation, neuromuscular medicine, or neurodevelopmental disabilities. Submit consultation notes if applicable.

NOTE: Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually

### **AGE RESTRICTIONS:**

7 years of age or older

### **QUANTITY:**

30 mg/kg administered once weekly as a 35 to 60-minute intravenous (IV) infusion,

### **PLACE OF ADMINISTRATION:**

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

## **DRUG INFORMATION**

### **ROUTE OF ADMINISTRATION:**

Intravenous infusion

### **DRUG CLASS:**

Muscular Dystrophy Agents

### **FDA-APPROVED USES:**

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 production in skeletal muscle observed in patients treated with AMONDYS 45. Continued approval for this indication maybe contingent upon verification of a clinical benefit in confirmatory trials.*

### **COMPENDIAL APPROVED OFF-LABELED USES:**

None

## **APPENDIX**

### **APPENDIX:**

None

## **BACKGROUND AND OTHER CONSIDERATIONS**

### **BACKGROUND:**

Muscular dystrophy includes a group of genetic disorders that cause muscle weakness and progressive disability. Duchenne muscular dystrophy (DMD) is the most common and progresses most rapidly.

## Drug and Biologic Coverage Criteria

### Duchenne muscular dystrophy (DMD)

- A rare genetic disorder characterized by progressive muscle deterioration and weakness
  - An X-chromosome-linked disease recessive disorder caused by mutations (mainly deletions) in the dystrophin gene that lead to an absence or defect in the dystrophin protein, dystrophin is essential for maintenance of myocyte integrity and helps keep muscle cells intact
  - As males have only one X chromosome, and therefore one single copy of the dystrophin gene, they have a much higher probability of developing DMD. A small number of females are also affected but remain asymptomatic and only rarely present with a mild form of the disease.
  - It is the most common type of muscular dystrophy. DMD is caused by an absence of dystrophin, a protein that helps keep muscle cells intact.
  - In United States, estimated prevalence of DMD is 1.51-2.05 per 10,000 boys aged 5-9 years
  - Associated with complete inability to produce functional dystrophin protein
  - Affected children with DMD typically develop symptoms in early childhood around 3-5 years old, experiencing progressive muscle weakness and deterioration. Patients with DMD progressively lose the ability to perform activities independently and usually become non-ambulatory by their early teenage years and require the use of a wheelchair.
  - As the disease progresses, life-threatening heart and respiratory conditions can occur. Patients typically succumb to the disease in their 20s or 30s; however, disease severity and life expectancy vary.
  - In absence of treatment, the patient experiences:
    - wheelchair dependence before age 13 years
    - death occurs by, or around, age 20
- years Prognosis of DMD
- Death occurs around age 20 in absence of treatment and is usually due to cardiac or respiratory failure
  - Disease progression in patients with DMD
    - ♦ Scoliosis is frequent after loss of ambulation
    - ♦ Risk for cardiomyopathy increases with age in absence of ventilatory intervention

### **Treatment Overview: Pharmacologic Agents/Conventional Therapy**

There is no curative therapy, but management of disease manifestations can prolong survival and improve quality of life. A multidisciplinary team is required for management of patient with DMD and treatment options for DMD predominantly focus on management of symptoms and secondary complications.

Goals of management for DMD include:

- Preserve strength, ambulation, and ventilatory and cardiac function
- Minimize of steroid complications where applicable
- Prevent and treat complications including contractures, scoliosis, ventilatory function impairment or failure, and cardiomyopathy
- Determine and arrange appropriate school environment and manage family stressors

Other pharmacologic therapies for DMD are primarily aimed at the management of comorbidities such as cardiomyopathy, osteoporosis, pain management, and respiratory failure. These treatment options include: angiotensin-converting-enzyme (ACE) inhibitors, beta-blockers, calcium and vitamin D supplements, muscle relaxants, and non-steroidal anti-inflammatory drugs.

#### ◆ Corticosteroids

- DMD Care Considerations Working Group consensus guidelines urge consideration of glucocorticoid therapy (prednisone or deflazacort) for all patients with DMD (optimal dose ranges not established)<sup>A</sup>
  - Goal in the ambulatory child is to preserve ambulation and minimize later respiratory, cardiac, and orthopedic complications
  - Goal of continuing glucocorticoid therapy after loss of ambulation is to preserve upper limb strength, reduce scoliosis progression, and delay declines in respiratory and cardiac function

## Drug and Biologic Coverage Criteria

- Generally used to preserve ambulation and minimize complications in patients with DMD
- In ambulatory patients, recommended if motor skills have plateaued or begun to decline
- In non-ambulatory patients, glucocorticoids often continued if already started while ambulatory, but limited evidence regarding starting glucocorticoids
- Daily dosing preferred over alternative regimens (alternate day, high-dose weekend, or 10-day cycles)
- Monitor and manage side effects associated with chronic steroid therapy

### Clinical Evidence

The FDA approved Amondys 45 based on interim efficacy at Week 48 of the Phase 3 ESSENCE trial, which is still ongoing and expected to conclude in 2024 as the confirmatory trial for Amondys 45 and Vyondys 53.

Phase 3 ESSENCE trial (NCT02500381)- global, randomized, double-blind, placebo-controlled; also known as Study 4045-301), 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

### Study Population

Interim results from 43 evaluable male patients with Duchenne muscular disease (DMD) who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping were included in an interim analysis and are presented in this table.

- Patients who provided muscle biopsy data had a median age of 9 years (range, 7–13 years) and 86% were White.
- Key inclusion criteria: Patients were required to have been on a stable dose of oral corticosteroids for at least 24 weeks prior to dosing with Amondys 45 or placebo

**Interventions** 43 male patients 7 to 13 years of age were randomized 2:1 to receive one of the following every week for up to 96 weeks, although interim results at 48 weeks were reviewed for the FDA accelerated approval:

- Placebo (n = 16)
- Amondys 45 (30 mg/kg/week) via IV infusion (n = 27)

Following the 96-week double-blind period, all patients began or will begin an additional 48-week open-label treatment period

### Endpoints

- Interim efficacy was assessed based on a change from baseline in the dystrophin protein level (measured as percentage of the dystrophin level in healthy subjects, i.e. percentage of normal) at Week 48.
- Interim results at Week 48:

*Dystrophin Levels (% of Normal) at Baseline and at Week 48 from Muscle Biopsy: Interim Results*

	Placebo n = 16	Amondys 45 n = 27
Dystrophin by Sarepta Western blot		
Baseline Mean (SD)	0.54 (0.79)	0.93 (1.67)
Week 48 Mean (SD)	0.76 (1.15)	1.74 (1.97)
Change from Baseline Mean (SD)	0.22 (0.49)	0.81 (0.70)
P Value Change from Baseline to Week 48	0.09	<0.001
Between-Group Mean Difference	0.59	
P Value Between Groups	0.004	

## Drug and Biologic Coverage Criteria

### Efficacy and Safety Results

- Patients who received Amondys 45 showed a significantly greater increase in dystrophin protein levels from baseline to Week 48 of treatment compared to those who received placebo.
- Although kidney toxicity was not observed in the Amondys 45 clinical studies, kidney toxicity was observed in the nonclinical studies. Kidney toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Kidney function should be monitored in patients taking Amondys 45.
  - The most common side effects observed in DMD patients treated with Amondys 45 were upper respiratory tract infections, cough, fever, headache, joint pain, and throat pain.
- Other adverse reactions that occurred in at least 10% of patients treated with Amondys 45, and that were reported at a rate at least 5% more frequently in the Amondys 45 group than in the placebo group, were ear pain, nausea, ear infection, posttraumatic pain, and dizziness and light-headedness.

### CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Amondys 45 (casimersen)-are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

Authorization will not be granted if ANY of the following conditions apply:

- Member is wheelchair dependent,
- Requested dose and frequency is not in accordance with FDA-approved labeling, nationally recognized compendia, and/or evidence-based practice guidelines
- Non-FDA approved indications

### OTHER SPECIAL CONSIDERATIONS:

None

## CODING/BILLING 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*

HCPCS CODE	DESCRIPTION
J1426	Injection, casimersen, 10 mg

### AVAILABLE DOSAGE FORMS:

Casimersen IV Solution: Single-dose vials containing 100 mg/2 mL (50 mg/mL)

## REFERENCES

1. Amondys 45 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, February 2021.
2. Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan. *Lancet Neurol*. 2018;17(5):445-455. doi:10.1016/S1474-4422(18)30026-7
3. Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopedic management. *Lancet Neurol*. 2018;17(4):347-361. doi:10.1016/S1474-4422(18)30025-5
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. American Academy of Neurology. Evidence-Based Guideline Summary: Evaluation, Diagnosis,

## Drug and Biologic Coverage Criteria

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6. National Institutes of Health, Genetic and Rare Diseases Information Center. Duchenne muscular dystrophy. Updated November 2, 2020. Accessed March 4, 2021. <https://rarediseases.info.nih.gov/diseases/6291/duchenne-musculardystrophy>
7. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, July 2020.
8. Vyondys 53 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc, February 2021.
9. Vilepso [package insert]. Paramus NJ: NS Pharma, Inc, August 2020.
10. 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>.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Duration of Approval	Quarter 2 2022
Q2 2022 Established tracking in new format	Historical changes on file