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Last P&T Approval/Version: 04/26/2023
Next Review Due By: 04/2023
Policy Number: C21154-A

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 (DMD)

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. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. DUCHENNE MUSCULAR DYSTROPHY (DMD):
1. Documented Diagnosis of Duchenne muscular dystrophy (DMD) with mutation amenable to exon 45 skipping confirmed by genetic testing [DOCUMENTATION REQUIRED]

AND

2. Documentation of baseline evaluation of physical function as documented by BOTH of the following evaluations completed in the past 30 days [DOCUMENTATION REQUIRED]:
    a. Documentation that member is ambulatory as evidenced by ONE of the following:
        - 6-minute walk test (6MWT) ≥ 300 meters while walking independently without assistance or devices (without side-by-side assist, cane, walker, wheelchair, etc.)
        - North Star Ambulatory Assessment (NSAA) score >17
        - Achieved rise time (Gower's test) < 7 seconds

    AND
    b. Documentation of ONE or more of the following measurable evaluations to assess physical function or the rate of disease progression (not an all inclusive list):
        - Dystrophin level
        - Brooke Upper Extremity Scale
        - Forced Vital Capacity assessment

    NOTE: The same assessment should be used in the follow-up evaluation for re-authorization for continuation of therapy. 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
3. Documentation of baseline lab results (within the past 30 days) and prescriber attests to obtain routine follow-up tests as indicated:
    a. Urine dipstick (follow-up monthly), and
    b. Serum cystatin C (follow-up every 3 months), and
    c. Urine protein-to-creatinine ratio (follow-up every 3 months), and
    d. GFR using exogenous filtration marker (baseline)

    AND
4. 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.

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

    AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity including: severe infusion-related reactions, interference with automated platelet counts (platelet clumping)

    AND
3. Documentation of positive or stable response to therapy as evidenced by BOTH of the following evaluations completed within the past 30 days [DOCUMENTATION REQUIRED]:
    a. Documentation member remains ambulatory as evidenced by ONE of the following:
        - Results of 6-Minute Walk Test (6MWT), while walking independently without assistance or devices (without side-by-side assist, cane, walker, wheelchair, etc.)
        - North Star Ambulatory Assessment (NSAA) score >17
        - Achieved rise time (Gower's test) < 7 seconds

    AND

    b. Documentation of ONE or more of the following measurable evaluations to assess physical function or the rate of disease progression (not an all-inclusive list):
        - Increase in dystrophin level
        - Brooke Upper Extremity Scale
        - 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. Documentation member continues to receive concurrent corticosteroids, unless contraindicated or history of severe adverse reactions

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified neurologist, neuromuscular disorder specialist, orthopedic specialist, physical medicine and rehabilitation specialist, neurodevelopmental disability specialist, or physician experienced in the treatment of Duchenne muscular dystrophy (DMD). [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
7 years of age and 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.

Note: Site of Care Utilization Management Policy applies for Amondys 45 (casimersen). For information on site of care, see Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

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 may be 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.

- 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)[A]
  - 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 Duchenne muscular dystrophy (DMD) cardiac function
- 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 Multi-Center Study with an Open-Label Extension; also known as Study 4045-301), The study will enroll 222 boys from 6 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.

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	Amondys 45
Dystrophin by Sarepta Western blot	n = 16	n = 27
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

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. Contraindications to Amondys 45 (casimersen) include: No labeled contraindications.

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:

Amondys 45 SOLN 100MG/2ML single dose vial

REFERENCES

1. Amondys 45 (casimersen) [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
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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
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9. Viltepso [package insert]. Paramus NJ: NS Pharma, Inc, March 2021.
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.
11. Gloss, D., Moxley, R. T., Ashwal, S., & Oskoui, M. (2016). Practice guideline update summary: Corticosteroid treatment of duchenne muscular dystrophy. Neurology, 86(5), 465-472. doi:10.1212/wnl.0000000000002337

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Place of Administration Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q2 2023
REVISION- Notable revisions: Required Medical Information Duration of Approval	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file