**09-J4000-76**

**Original Effective Date: 04/01/24**

**Reviewed: 02/14/24**

**Revised: 00/00/00**

# Subject: Vamorolone (Agamree)

**THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.**


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## DESCRIPTION:

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. This X-linked recessive disorder is caused by mutations (mainly deletions) in the dystrophin gene that lead to an absence or defect in the dystrophin protein.

Dystrophin is thought to maintain the structural integrity of the muscle cell membrane by connecting the cytoskeleton to the underlying extracellular matrix and acting as a scaffold for several molecules that also contribute to normal muscle physiology. Absence of dystrophin leads to mitochondrial dysfunction and damage, with inflammatory processes also appearing to contribute to muscle pathology. Muscle fibers ultimately undergo necrosis with replacement by adipose and connective tissue. Principal disease manifestations include progressive degeneration of skeletal and cardiac muscle, leading to loss of physical function in childhood and adolescence with premature death from respiratory and/or cardiac failure in the second to fourth decade.

As males have only one X chromosome, and thus 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. DMD has an estimated incidence of 1 in 3,500 male births. Available data suggests around 83% of DMD patients have genotypes amenable to exon skipping, and that 13% of DMD patients have genotypes that are amenable to exon 51 skipping.

Treatment options for DMD predominantly focus on management of symptoms and secondary complications. Corticosteroids are the standard of care of treatment of DMD and have been shown to improve skeletal muscle strength and function in reproducible randomized controlled trials; they also reduce the risk of scoliosis, stabilize pulmonary function, and may also improve cardiac function. Current guidelines recommend initiation of glucocorticoids (such as prednisolone) once patients reach a plateau

of motor skill development, generally at age 4-6 years, but prior to onset of motor decline. Exon-skipping therapy such as eteplirsen, golodirsen, casimersen, and viltolarsen increase dystrophin protein expression with exon deletions – this represents approximately 30% of the DMD population. Gene therapy is available for ambulatory pediatric patients with a mutation in the DMD gene. Both exon-skipping therapy and gene therapy are used in addition to corticosteroids.

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.

Vamorolone (Agamree), an oral dissociative corticosteroid, was approved by the U.S. Food and Drug Administration (FDA) in 2023 for treatment of DMD in patients 2 years of age and older. While vamorolone works as both an anti-inflammatory and immunosuppressant, the exact mechanism of action in patients with DMD is unknown. Vamorolone is administered once daily and is available as an oral suspension.

The approval of vamorolone was based on data from the VISION-DMD trial, a phase 2b, randomized, double-blind, placebo and prednisone-controlled clinical trial.

Participants (n=121) were corticosteroid naïve, ambulatory boys greater than or equal to 4 years of age, but less than 7 years of age. All participants had a genetically confirmed diagnosis of DMD and were able to walk independently without assistive devices and able to complete TTSTAND without assistance in less than 10 seconds. Patients were randomized to receive one of the following for 24 weeks: vamorolone 6 mg/kg/day, vamorolone 2 mg/kg/day, prednisone 0.75 mg/kg/day, or placebo. The primary clinical efficacy endpoint was the change from baseline in TTSTAND velocity for vamorolone 6 mg/kg/day vs placebo.

Vamorolone significantly improved multiple functional/motor outcomes compared with placebo, including time to stand from supine velocity for 6 mg/kg/day (TTSTAND; 0.05 m/s vs -0.01 m/s; primary outcome). Additional significant improvements for vamorolone vs placebo in the hierarchical progression through secondary outcomes included TTSTAND velocity (2 mg/kg/day), 6-minute walk test (6MWT, 6 and 2 mg/kg/day), and time to run/walk 10 meters (TTRW, 6 mg/kg/day only). Exploratory post-hoc analysis suggested similar efficacy of vamorolone 6 mg/kg/day and prednisone for all motor outcomes. Height percentile significantly declined during prednisone treatment, but not with vamorolone 6 mg/kg/day (-1.88 vs 3.86 percentile). All serum biomarkers of bone formation and turnover were significantly diminished by prednisone treatment but not vamorolone treatment.

Table 2. Change from Baseline to Week 24 in TTSTAND, 6MWT, and TTRW Compared to Placebo

| Parameter | Placebo | Vamorolone 2 mg/kg/day | Vamorolone 6 mg/kg/day |
|---|---|---|---|
| | TTSTAND Velocity (Rises/Second) | | |
| Baseline | 0.200 | 0.184 | 0.186 |
| Mean CFB | −0.012 | 0.033 | 0.048 |

| | | | |
|---|---|---|---|
| Difference from placebo (95% CI) | N/A | 0.045 (0.008, 0.082) | 0.060 (0.023, 0.098) |
| P-value | N/A | 0.017 | 0.002b |
| | 6MWT Distance (Meters) | | |
| Baseline | 355 | 316 | 313 |
| Mean CFB | −14 | 27 | 29 |
| Difference from placebo (95% CI) | N/A | 40 (13, 68) | 42 (16, 69) |
| P-value | N/A | 0.004 | 0.002 |
| | TTRW Velocity (Meters/Second) | | |
| Baseline | 1.735 | 1.563 | 1.600 |
| Mean CFB | 0.014 | 0.141 | 0.258 |
| Difference from placebo (95% CI) | N/A | 0.127 (−0.026, 0.281) | 0.244 (0.093, 0.395) |
| P-value | N/A | 0.103 | 0.002 |
| Abbreviations: 6MWT, 6-minute walk test; CFB, change from baseline; CI, confidence interval; TTSTAND, time to stand test; TTRW, time to run/walk | | | |

## POSITION STATEMENT:

**Comparative Effectiveness**

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of vamorolone (Agamree) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with Duchenne Muscular Dystrophy (DMD)
2. Member's DMD diagnosis is confirmed by genetic testing – laboratory results must be provided
3. Member's DMD symptom onset occurred prior to 2 years of age
4. Member meets one of the following:
    a. Member has been receiving treatment with prednisone for at least 6 months and has experienced prednisone-related weight gain of more than 20% from baseline (i.e., prior to initiation of prednisone) – documentation from the medical record must be provided

b. Member was previously approved for vamorolone by another health plan **–** documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for vamorolone must be provided

5. Member provides a baseline score from a 6- minute walk test – documentation from the medical record must be provided
6. Vamorolone will not be used in combination with deflazacort (Emflaza)
7. Member is 2 years of age or older
8. Dose does not exceed 6 mg/kg/day, up to a maximum daily dosage of 300 mg

**Approval duration**: 6 months

Continuation of vamorolone (Agamree) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of DMD (if another health plan, documentation of a health plan-paid claim for vamorolone during the 90 days immediately before the request must be submitted), OR the member has previously met all indication-specific initiation criteria
2. Member meets **ONE** of the following
    a. Member demonstrates a clinically meaningful response to treatment with vamorolone as evidenced by any of the following:
        i. Improvement or maintenance of score from 6-minute walk test compared to baseline (i.e., immediately prior to initiation of vamorolone) – documentation from the medical record must be provided
        ii. Weight loss of approximately 10% from baseline (i.e., prior to initiation of vamorolone) – documentation from the medical record must be provided
    b. Member has been receiving treatment for a minimum of 1 year and demonstrates a clinically meaningful response to treatment with vamorolone as evidenced by any of the following:
        i. Improvement or maintenance of score from 6-minute walk test compared to baseline (i.e., immediately prior to initiation of vamorolone) – documentation from the medical record must be provided
        ii. Weight or body mass index (BMI) for age falls below the 85$^{th}$ percentile based on CDC growth charts– documentation from the medical record must be provided
3. Vamorolone will not be used in combination with deflazacort (Emflaza)
4. Dose does not exceed 6 mg/kg/day, up to a maximum daily dosage of 300 mg

**Approval duration**: 1 year

## DOSAGE/ADMINISTRATION:

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

### FDA-approved

- The recommended dosage is 6 mg/kg taken orally once daily preferably with a meal, up to a maximum daily dosage of 300 mg for patients weighing more than 50 kg

### Dose Adjustments

- In patients with mild to moderate hepatic impairment, the recommended dosage is 2 mg/kg taken orally once daily preferably with a meal, up to a maximum daily dosage of 100 mg for patients weighing more than 50 kg

### Drug Availability

- Oral Suspension: 40 mg/mL

## PRECAUTIONS:

### Boxed Warning

- None

### Contraindications

- Hypersensitivity to vamorolone or any of the inactive ingredients in AGAMREE

### Precautions/Warnings

- Alterations in Endocrine Function: Hypothalamic-pituitary-adrenal axis suppression, cushingoid features, and hyperglycemia can occur. Monitor patients for these conditions with chronic use of AGAMREE.
- Immunosuppression and Increased Risk of Infection: Increased risk of new infections, exacerbation, dissemination, or reactivation of latent infections, which can be severe and at times fatal; signs and symptoms of infections may be masked.
- Alterations in Cardiovascular/Renal Function: Monitor for elevated blood pressure and monitor sodium and potassium levels in patients chronically treated with AGAMREE.
- Gastrointestinal Perforation: Increased risk in patients with certain GI disorders; signs and symptoms may be masked.
- Behavioral and Mood Disturbances: May include euphoria, insomnia, mood swings, personality changes, severe depression, and psychosis.
- Effects on Bones: Monitor for decreases in bone mineral density with chronic use of AGAMREE.
- Ophthalmic Effects: May include cataracts, infections, and glaucoma; monitor intraocular pressure in patients chronically treated with AGAMREE.

- Vaccination: Do not administer live or live attenuated vaccines to patients receiving immunosuppressive doses of corticosteroids. Administer live-attenuated or live vaccines at least 4 to 6 weeks prior to starting AGAMREE.

## BILLING/CODING INFORMATION:

The following codes may be used to describe:

### HCPCS Coding

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|---|---|
| J3490 | Unclassified drugs |

### ICD-10 Diagnosis Codes That Support Medical Necessity

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|---|---|
| G71.01 | Duchenne or Becker muscular dystrophy |

## REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Part D:** Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

**Medicare Advantage:** No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

## DEFINITIONS:

**6 minute walk test:** assesses distance walked over 6 minutes as a sub-maximal test of aerobic capacity/endurance

**9 Hole Peg Test:** a brief, standardized quantitative test of upper extremity function

**Maximum Voluntary Isometric Contraction Test:** assesses muscle strength

**North Star Ambulatory Assessment**: a functional scale designed for ambulant boys affected by DMD

## RELATED GUIDELINES:

**Deflazacort (Emflaza), 09-J2000-76**

**Exon-Skipping Therapy for Duchenne Muscular Dystrophy, 09-J3000-93**

## OTHER:

None

## REFERENCES:


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## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/14/24.

## GUIDELINE UPDATE INFORMATION:

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|---|---|
| 04/01/24 | New Medical Coverage Guideline. |