Original Effective Date: 06/27/2024
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Policy Number: C27685-A

Agamree (vamorolone)

PRODUCTS AFFECTED

Agamree (vamorolone)

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. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. DUCHENNE MUSCULAR DYSTROPHY (DMD):
   1. Documented diagnosis of Duchenne muscular dystrophy (DMD) confirmed by ONE of the following:
      a. Genetic testing (e.g., dystrophin deletion or duplication mutation found)

b. Absence of dystrophin protein confirmed by muscle biopsy
AND

2. Documentation of baseline motor milestone score from ONE of the following assessments [DOCUMENTATION REQUIRED]:
NOTE: Reauthorization requires a positive response to therapy from the same baseline motor milestone score
   a. 6-minute walk test (6MWT)
   b. North Star Ambulatory Assessment (NSAA)
   c. Motor Function Measure (MFM)
   d. Hammersmith Functional Motor Scale (HFMS)
   AND
3. Documentation member experienced clinically significant adverse effects on prednisone as evidenced by ONE of the following:
   a. Cushingoid appearance
   b. Central (truncal) obesity
   c. Undesirable weight gain, defined as ≥ 10% of body weight gain increase over 6 months
   d. Diabetes and/or hypertension that is difficult to manage per the prescribing physician
   e. Neuropsychiatric side effects (abnormal behavior, aggression) while on prednisone therapy, that has or would require a prednisone dose reduction.
   AND
4. Prescriber attests to the absence of active infection [i.e., active ocular herpes simplex, tuberculosis or Hepatitis B virus (HBV)]
   AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA-labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Agamree (vamorolone) include: patients with known hypersensitivity to vamorolone or any of the inactive ingredients, do not administer live or live attenuated vaccines.]

CONTINUATION OF THERAPY:

A. DUCHENNE MUSCULAR DYSTROPHY (DMD):
1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Prescriber attests to ongoing monitoring for development of infection (e.g., tuberculosis, Hepatitis B reactivation, etc.) according to the FDA label
   AND
4. Documentation of positive response to therapy confirmed by stabilization, or less than expected decline, in baseline motor milestone score from ONE of the following assessments [DOCUMENTATION REQUIRED]:
   a. 6-minute walk test (6MWT)
   b. North Star Ambulatory Assessment (NSAA)
   c. Motor Function Measure (MFM)
   d. Hammersmith Functional Motor Scale (HFMS)

   NOTE: Prescriber may submit additional supporting documentation of objective assessment of ambulation or other muscle function, including pulmonary or cardiac function. This may include improvement in muscle strength tests (e.g., Medical Research Council [MRC] scale for muscle strength with 0 being no movement and 5 being normal strength), Pulmonary function tests e.g., forced vital capacity [FVC] and maximal expiratory pressure), Timed functional tests (e.g., standing from lying position, climbing 4 stairs, running/walking 30 feet, propelling a wheelchair 30 feet)

AND

5. Documentation of improvement in the symptom(s) or side effect(s) associated with prednisone use including but not limited to:
   a. If neuropsychiatric side effects while on prednisone, the member has shown improvement in neuropsychiatric symptoms
   b. If excessive weight gain with prednisone, the member has experienced a return to baseline growth curve expectations or remained on the same

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 rehab 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:
2 years of age and older

QUANTITY:
6 mg/kg taken orally once daily

Maximum Quantity Limits – Maximum daily dosage of 300 mg for members weighing more than 50 kg

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Glucocorticosteroids

FDA-APPROVED USES:
Indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
The effectiveness of AGAMREE for the treatment of Duchenne muscular dystrophy (DMD) was evaluated in a multicenter, randomized, double-blind, parallel-group, placebo- and active-controlled, multinational 24-

week study (Study 1; NCT03439670). The study randomized 121 male patients with DMD to one of the following treatment groups: AGAMREE 6 mg/kg/day (n=30), AGAMREE 2 mg/kg/day (n=30), prednisone 0.75 mg/kg/day (n=31), or placebo (n=30) for 24 weeks. After 24 weeks, patients on prednisone and placebo received either AGAMREE 6 mg/kg/day (n=29) or AGAMREE 2 mg/kg/day (n=29) for an additional 20 weeks. The study included patients 4 to less than 7 years of age at time of enrollment in the study who were corticosteroid naïve and ambulatory, with a confirmed diagnosis of DMD. At baseline, patients had a mean age of 5.4 years, 83% were Caucasian, 10% were Asian, and 96% were not Hispanic or Latino.

The primary endpoint was the change from baseline to Week 24 in Time to Stand Test (TTSTAND) velocity for AGAMREE 6 mg/kg/day compared to placebo. TTSTAND velocity is a measure of muscle function that measures the time required for the patient to stand to an erect position from a supine position (floor). The key secondary endpoints consisted of change from baseline to Week 24 in TTSTAND velocity (AGAMREE 2 mg/kg/day vs placebo), 6 Minute Walk Test (6MWT) distance (AGAMREE 6 mg/kg/day vs placebo and 2 mg/kg/day vs placebo) and Time to Run/Walk 10 meters (TTRW) velocity (AGAMREE 6 mg/kg/day vs placebo and 2 mg/kg/day vs placebo). The 6MWT measures the distance that a patient can walk on a flat, hard surface in a period of 6 minutes and TTRW measures the time that it takes a patient to run or walk 10 meters. The fixed sequential testing process was applied to the key secondary endpoints in the order listed above. The primary endpoint and key secondary endpoints were met for the AGAMREE 6 mg/kg/day treatment group. The AGAMREE 2 mg/kg/day treatment group was statistically significant vs. placebo for TTSTAND and 6MWT, but was not statistically significant vs. placebo for TTRW.

In the VISION-DMD study, Agamree met the primary endpoint, TTSTAND velocity at 6 mg/kg/day versus placebo at 24 weeks of treatment (P = 0.002), and key secondary endpoints were also met for the Agamree 6 mg/kg/day group. The Agamree 2 mg/kg/day treatment group showed statistically significant improvements versus placebo in TTSTAND and 6MWT but not TTRW. Hierarchical testing ended prior to the sixth- and seventh-ranked secondary efficacy endpoints, which compared Agamree to prednisone.
In addition to the previously listed most common adverse reactions (see Drug Information section), other clinical and biomarker safety endpoints, including growth, bone biomarkers, and a corticotropin (adrenocorticotropic hormone; ACTH) challenge test were also assessed in VISION-DMD.
- Height percentile declined in prednisone-treated, but not vamorolone-treated participants (changes from baseline [standard deviation (SD)]: prednisone, −1.88 [8.81] percentile; vamorolone 6 mg/kg/day, +3.86 [6.16] percentile; P = 0.02).
- Serum biomarkers of bone formation (osteocalcin, procollagen 1 intact N-terminal propeptide [P1NP]) and bone turnover (type 1 collagen cross-linked C-telopeptide [CTX1]) showed a statistically significant decline in the prednisone group and not in the vamorolone group. There were two treatment-emergent vertebral fractures at Week 24; one participant in the prednisone group had a total of four incident vertebral fractures, and one participant in the placebo group had a single incident vertebral fracture.
- Boys with DMD at baseline showed low ACTH-stimulated cortisol and a high incidence of adrenal insufficiency.

All three treatments led to increased adrenal insufficiency. Additionally, one participant receiving prednisone 0.75 mg/kg/day, withdrew from the study owing to an adverse event (AE) (personality change, Common Terminology Criteria for AEs [CTCAE] grade 2) that was viewed by the investigator as possibly related to the drug and abated after cessation of the drug. Another single TEAE in the study considered by the investigator to be severe (aggression, CTCAE grade 3) was experienced by a participant receiving prednisone 0.75 mg/kg/day; the participant remained in the study.

VBP15-LTE was a 24-month, Phase 2, open-label long-term extension (LTE) study (NCT03038399) to evaluate the long term safety and efficacy of vamorolone in young boys with DMD who participated in the Phase 2a, 2-week VBP15-002 (NCT02760264) and Phase 2a, 24-week, VBP15-003 (NCT02760277) open-label core studies. Participants with DMD treated with corticosteroids from the Cooperative International Neuromuscular Research Group Duchenne Natural History Study (CINRG DNHS) and NorthStar United Kingdom (NSUK) Network were matched and compared with participants in the LTE study receiving vamorolone (2 and 6 mg/kg/day). Results, published in JAMA Open, 2022, showed there were no statistically significant differences between participants receiving vamorolone and matched

participants in the CINRG DNHS or NSUK groups receiving corticosteroid treatment (75 patients in DNHS and 110 patients in NSUK) over a 2-year period in NorthStar Ambulatory Assessment (NSAA) total score change (0.22 units vs. NSUK; 95% CI, −4.48 to 4.04]; P = 0.92), body mass index (BMI) z score change (0.002 vs. DNHS SD/month; 95% CI, −0.006 to 0.010; P = 0.58), or timed function test change. The NSAA is a 17-item rating scale used to measure functional motor abilities in ambulatory children with DMD. It is used to monitor the progression of the disease and its treatment effects.

Among 41 participants receiving vamorolone at 6 mg/kg/day, ten participants (24.4%) deescalated to 2 mg/kg/day due to a treatment-emergent AE of weight gain. The AE abated in six participants after dose reduction. Among the 46 LTE participants, six participants (13.0%) were observed to have a total of seven clinical fracture events. Participants in the DNHS treated with corticosteroids had significant growth delay in comparison with participants treated with vamorolone, who had stable height percentiles (0.37 percentile/month; 95% CI, 0.23 to 0.52 percentile/month) over time.

Efficacy: Vamorolone treatment showed comparable efficacy and maintenance of muscle function to corticosteroid treatment in historical cohorts of patients with DMD after 30 months.

Safety: Patients treated with vamorolone showed an improved linear growth trajectory compared with the DNHS cohort treated with corticosteroids. Although there was no significant change in BMI z score compared to the DNHS cohort, 24.4% of participants receiving vamorolone at 6 mg/kg/day experienced a TEAE of weight gain.

Results of the LTE study that suggest vamorolone has similar efficacy and results in an improved growth trajectory compared to other corticosteroids should be interpreted with caution due to the open-label study design, the use of prospectively collected real-world observational control data sets that include varying corticosteroid treatments (i.e., prednisone or deflazacort), dose, and regimen use in clinical practice (i.e., daily or intermittent). Patients with DMD in the comparator data sets had been on corticosteroid treatment for different amounts of time before the baseline comparator visits. Lastly, the investigators in the study noted a significant amount of attrition in the data of participants in comparator groups over time (e.g., 91.3% of participants in LTE vs. 40.0% of participants in DNHS had >18 months of follow-up data for TTSTAND velocity.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Agamree (vamorolone) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Agamree (vamorolone) include: hypersensitivity to vamorolone or to any of the inactive ingredients of Agamree, do not administer live or live attenuated vaccines.

OTHER SPECIAL CONSIDERATIONS:

The recommended dosage of AGAMREE 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.

- Some patients may respond to a dose of 2 mg/kg daily.
- Doses may be titrated down to 2 mg/kg/day as needed, based on individual tolerability.
- recommended dosage of AGAMREE in patients with mild (Child-Pugh A) to moderate (Child-Pugh B) hepatic impairment 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
- recommended dosage of AGAMREE when administered with strong CYP3A4 inhibitors is 4 mg/kg taken orally once daily preferably with a meal, up to a maximum daily dosage of 200 mg for patients weighing more than 50 kg

Shake AGAMREE oral suspension well for about 30 seconds before administration. Discard any unused AGAMREE oral suspension remaining after 3 months of first opening the bottle.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not*

effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Agamree SUSP 40MG/ML

REFERENCES

1. Agamree (vamorolone) oral suspension [prescribing information]. Coral Gables, FL: Catalyst Pharmaceuticals, Inc; June 2024.
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3. Guglieri M, et al. Efficacy and safety of vamorolone vs placebo and prednisone among boys with Duchenne muscular dystrophy: a randomized clinical trial. JAMA Neurol. 2022;79(10):1005-1014. doi:10.1001/jamaneurol.2022.2480
4. Mah JK, et al. Efficacy and safety of vamorolone in Duchenne muscular dystrophy: a 30-month nonrandomized controlled open-label extension trial. JAMA Netw Open. 2022;5(1):e2144178. Published January 4, 2022. doi:10.1001/jamanetworkopen.2021.44178
5. Grounds MD, Lloyd EM. Considering the promise of vamorolone for treating Duchenne muscular dystrophy. J Neuromuscul Dis. 2023;10(6):1013-1030. doi:10.3233/JND-230161
6. Smith EC, Conklin LS, Hoffman EP, et al. Efficacy and safety of vamorolone in Duchenne muscular dystrophy: an 18-month interim analysis of a non-randomized open-label extension study. PLoS Med. 2020;17(9):e1003222. doi:10.1371/journal.pmed.1003222
7. Gloss, D., Moxley, R. T., Ashwal, S., & Oskoui, M. (2016, reaffirmed 2022). Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology, 86(5), 465–472. https://doi.org/10.1212/WNL.0000000000002337

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Quantity References	Q4 2025
REVISION- Notable revisions: Coding/Billing Information Template Update Continuation of Therapy References	Q4 2024
NEW CRITERIA CREATION	Q2 2024