Medical Policy:

Aveed® (testosterone undecanoate) Intramuscular

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.134	February 18, 2025	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines 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. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Aveed is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

1. Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
2. Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Length of Authorization

Coverage will be provided for 6 months initially and may be renewed for 12 thereafter

Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

Primary/Secondary hypogonadotropic hypogonadism: 750 billable units at week 0 and 4 initially, then every 10 weeks thereafter.

Gender Dysphoria: 1500 billable units at weeks 0 and 6 initially, then every 12 weeks thereafter

Guideline

I. Initial Approval Criteria

Aveed *may be considered medically necessary if the below conditions are met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

Universal Criteria:

1. The prescriber is enrolled in the AVEED REMS Program **AND**
2. The patient will be receiving only one androgen or anabolic agent; **AND**
3. Patient hemoglobin, hematocrit, and lipid concentrations are measured at baseline and monitored periodically, during treatment.

1. **Primary and Hypogonadotropic Hypogonadism**
   - A. Member is at least 18 years of age; **AND**
   - B. Prescribed by, or in consultation with, an endocrinologist or urologist; **AND**
   - C. Patient does not have "age-related hypogonadism"; **AND**
   - D. Patient does not have a prostate specific antigen (PSA) level of > 4.0 ng/mL, at baseline; **AND**
   - E. Pre-treatment morning total testosterone of less than 300 ng/dL (or below lower limit of normal by the testing laboratory); **AND**
   - F. Patient has signs and symptoms consistent with hypogonadism (e.g., low libido, decreased morning erections, loss of body hair, low bone mineral density, gynecomastia, small testes, etc.); **AND**
   - G. Diagnosis is confirmed by one of the following:
     - i. Repeat morning total testosterone test (as above); **OR**
     - ii. Pre-treatment free testosterone of less than 50 pg/mL (or below lower limit of normal by the testing laboratory); **AND**
   - H. Patient had an inadequate response (or contraindication or intolerance) to a 3 or more-month trial with a topical agent such as testosterone gel, testosterone patch, bio-adhesive buccal testosterone, testosterone nasal gel, testosterone topical solution, etc.; **AND**
   - I. Patient had an inadequate response (or contraindication or intolerance) to a 3 or more-month trial with an alternative injectable agent (i.e., testosterone cypionate or testosterone enanthate)

Other Uses with Supportive Evidence

2. **Gender-Dysphoria/Gender-Incongruent Persons**
   - A. Patient has experienced puberty development to at least Tanner stage 2 (*Note: this applies only to patients <18 years of age);* **AND**
   - B. Patient has a diagnosis of gender dysphoria as confirmed by a qualified mental health professional (MHP**) OR the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-V-TR) Criteria §; **AND**
   - C. A qualified MHP** has confirmed all of the following:
     - i. The persistence of gender dysphoria; **AND**
     - ii. Any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the

patient's situation and functioning are stable enough to start treatment; **AND**

iii. Patient has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment; **AND**

D. Patient has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility); **AND**

E. Patient has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretaker or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process; **AND**

F. Adolescent patients have undergone treatment to suppress pubertal development (i.e., have initially received treatment with gonadotropin-releasing hormone [GnRH] analogues where indicated); **AND**

G. For adolescent patients, a pediatric endocrinologist or other clinician experienced in pubertal induction has confirmed all of the following:

i. Agreement in the indication for treatment; **AND**

ii. There are no medical contraindications to treatment.

Limitations/Exclusions

Aveed is not considered medically necessary for when any of the following selection criteria is met:

1. Men with carcinoma of the breast or known or suspected carcinoma of the prostate
2. Safety and efficacy of Aveed in men with "age-related hypogonadism"
3. Safety and efficacy of Aveed in males less than 18 years old have not been established
4. Women who are or may become pregnant, or who are breastfeeding. Testosterone can cause fetal harm when administered to a pregnant woman. Aveed may cause serious adverse reactions in nursing infants. Exposure of a female fetus or nursing infant to androgens may result in varying degrees of virilization

II. Renewal Criteria

1. Patient continues to meet INITIAL APPROVAL CRITERIA; **AND**
2. Absence of unacceptable toxicity from the drug. *Examples of unacceptable toxicity include the following: serious pulmonary oil microembolism (POME) reactions and anaphylaxis, prostatic hypertrophy/carcinoma, polycythemia, venous thromboembolism, azoospermia, myocardial infarction and stroke, edema with/without congestive heart failure in those with preexisting cardiac/renal/hepatic disease, gynecomastia, hepatic dysfunction (e.g., jaundice), sleep apnea, severe changes in lipid profile, hypercalcemia, signs of abuse or dependence, etc.*; **AND**
3. Patient's testosterone levels (within the preceding 28 days) do not exceed the upper limit of the normal range for the testing laboratory (generally mid-range is targeted); **AND**
4. Patient has an improvement in signs and symptoms; **AND**
5. Patient has not had a PSA increase of > 1.4 ng/mL above baseline or an absolute level > 4.0 ng/mL

**** Definition of a qualified health care professional**

- Are licensed by their statutory body and hold, at a minimum, a master's degree or equivalent training in a clinical field relevant to this role and granted by a nationally accredited statutory institution; AND
- For countries requiring a diagnosis for access to care, the health care professional should be competent using the latest edition of the World Health Organization's International Classification of Diseases (ICD) for diagnosis. In countries that have not implemented the latest ICD, other taxonomies may be used; efforts should be undertaken to utilize the latest ICD as soon as practicable; AND

- Are able to identify co-existing mental health or other psychosocial concerns and distinguish these from gender dysphoria, incongruence, and diversity; AND
- Are able to assess capacity to consent for treatment; AND
- Have experience or be qualified to assess clinical aspects of gender dysphoria, incongruence, and diversity; AND
- Undergo continuing

§ DSM-V-TR Criteria for Gender Dysphoria in Adolescents and Adults
• A marked incongruence between one's experienced/expressed gender and their assigned gender, lasting at least 6 months, as manifested by at least TWO of the following: o A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics) • A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics) • A strong desire for the primary and/or secondary sex characteristics of the other gender • A strong desire to be of the other gender (or some alternative gender different from one's assigned gender) • A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender) • A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender); **AND** • The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Dosage/Administration

Indication	Dose
Primary and Hypogonadotropic Hypogonadism, Male	Aveed is for intramuscular use only. Dosage titration is not necessary. The recommended dose of Aveed is 3 mL (750 mg) injected intramuscularly, followed by 3 mL (750 mg) injected after 4 weeks, then 3 mL (750 mg) injected every 10 weeks thereafter.
Gender Dysphoria	The recommended dose of Aveed is 4 mL (1000mg) injected intramuscularly at week 0, week 6, and then every 12 weeks thereafter.

Applicable Procedure Codes

Code	Description
J3145	Injection, testosterone undecanoate, 1 mg, 1 billable unit = 1 mg

Applicable NDCs

Code	Description
67979-0511-43	Aveed single use vial; 250 mg/ml solution

ICD-10 Diagnoses

Code	Description

E23.0	Hypopituitarism
E29.1	Testicular hypofunction
E89.3	Postprocedural hypopituitarism
E89.5	Postprocedural testicular hypofunction
F64.0	Transsexualism
F64.1	Dual role transvestism
F64.2	Gender identity disorder of childhood
F64.8	Other gender identity disorders
F64.9	Gender identity disorder, unspecified

Revision History

<table>
<tr><th>Company(ies)</th><th>DATE</th><th>REVISION</th></tr>
<tr><td>EmblemHealth &
ConnectiCare</td><td>2/18/2025</td><td>Annual Review:
Addition to ICD Codes:
<table>
<tr><td>F64.0</td><td>Transsexualism</td></tr>
<tr><td>F64.1</td><td>Dual role transvestism</td></tr>
<tr><td>F64.2</td><td>Gender identity disorder of childhood</td></tr>
<tr><td>F64.8</td><td>Other gender identity disorders</td></tr>
<tr><td>F64.9</td><td>Gender identity disorder, unspecified</td></tr>
</table>
Addition of dosing limits: Gender Dysphoria: 1500 billable units at weeks 0 and 6 initially, then every 12 weeks thereafter.

Addition of universal criteria: Universal Criteria: 1.The prescriber is enrolled in the AVEED REMS Program AND 2.The patient will be receiving only one androgen or anabolic agent; AND 3.Patient hemoglobin, hematocrit, and lipid concentrations are measured at baseline and monitored periodically, during treatment.

Addition to primary/secondary hypogonadotropic hypogonadism in males: Prescribed by, or in consultation with, an endocrinologist or urologist; AND Patient does not have “age-related hypogonadism”; AND Patient does not have a prostate specific antigen (PSA) level of > 4.0 ng/mL, at baseline.

Addition of <u>Gender-Dysphoria/Gender-Incongruent Persons</u>
A. Patient has experienced puberty development to at least Tanner stage 2 (Note: this applies only to patients <18 years of age); AND
B. Patient has a diagnosis of gender dysphoria as confirmed by a qualified mental health professional (MHP) OR the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-V-TR) Criteria §; AND
C. A qualified MHP has confirmed all of the following:
i. The persistence of gender dysphoria; AND
ii. Any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the patient’s situation and functioning are stable enough to start treatment;</td></tr>
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		AND iii. Patient has sufficient mental capacity (which most adolescents have by age 16 years) to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment; **AND** D. Patient has been informed of the (irreversible) effects and side effects of treatment (including potential loss of fertility and options to preserve fertility); **AND** E. Patient has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretaker or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process; **AND** F. Adolescent patients have undergone treatment to suppress pubertal development (i.e., have initially received treatment with gonadotropin-releasing hormone [GnRH] analogues where indicated); **AND** G. For adolescent patients, a pediatric endocrinologist or other clinician experienced in pubertal induction has confirmed all of the following: i. Agreement in the indication for treatment; **AND** ii. There are no medical contraindications to treatment.
EmblemHealth & ConnectiCare	4/2/2024	Annual Review: Added dosing limits, removed E23.6, added E89.3 and E89.5. Initial Criteria: Primary and Hypogonadotropic Hypogonadism: Removed: "Members have at least 2 confirmed low morning serum total testosterone concentrations based on the reference laboratory range." Updated to read: "Pre-treatment morning total testosterone of less than 300 ng/dL (or below lower limit of normal by the testing laboratory); AND Patient has signs and symptoms consistent with hypogonadism (e.g., low libido, decreased morning erections, loss of body hair, low bone mineral density, gynecomastia, small testes, etc.); AND Diagnosis is confirmed by one of the following: Repeat morning total testosterone test (as above); OR Pre-treatment free testosterone of less than 50 pg/mL (or below lower limit of normal by the testing laboratory); AND Patient had an inadequate response (or contraindication or intolerance) to a 3 or more-month trial with a topical agent such as testosterone gel, testosterone patch, bio-adhesive buccal testosterone, testosterone nasal gel, testosterone topical solution, etc.; AND Patient had an inadequate response (or contraindication or intolerance) to a 3 or more-month trial with an alternative injectable agent (i.e., testosterone cypionate or testosterone enanthate)" Renewal Criteria: Removed: "Patient achieved and/or maintained a positive clinical response to therapy." Added: "Absence of unacceptable toxicity from the drug. *Examples of unacceptable toxicity include the following: serious pulmonary oil microembolism (POME) reactions and anaphylaxis, prostatic hypertrophy/carcinoma, polycythemia, venous thromboembolism, azoospermia, myocardial infarction and stroke, edema with/without congestive heart failure in those with preexisting cardiac/renal/hepatic disease, gynecomastia, hepatic dysfunction (e.g., jaundice), sleep apnea, severe changes in lipid profile, hypercalcemia, signs of abuse or dependence, etc.*; AND Patient's testosterone levels (within the preceding 28 days) do not exceed the upper limit of the normal range for the testing

		laboratory (generally mid-range is targeted); AND Patient has an improvement in signs and symptoms; AND Patient has not had a PSA increase of > 1.4 ng/mL above baseline or an absolute level > 4.0 ng/mL"
EmblemHealth & ConnectiCare	7/28/2023	Annual Review: No Criteria Changes
EmblemHealth & ConnectiCare	3/30/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	06/01/2020	Annual Review: Highlighted covered indications for Primary and Hypogonadotropic Hypogonadism
EmblemHealth & ConnectiCare	04/07/2020	Added under Limitations: -Men with carcinoma of the breast or known or suspected carcinoma of the prostate -Safety and efficacy of Aveed in men with "age-related hypogonadism" -Safety and efficacy of Aveed in males less than 18 years old have not been established -Women who are or may become pregnant, or who are breastfeeding. Testosterone can cause fetal harm when administered to a pregnant woman. Aveed may cause serious adverse reactions in nursing infants. Exposure of a female fetus or nursing infant to androgens may result in varying degrees of virilization -Updated Dosing per FDA label

References

1. Aveed [package insert]. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; May 2015.