Corporate Medical Policy: Testosterone Cypionate (Azmiro®) **"Notification"** **POLICY EFFECTIVE JULY 1, 2026**

Restricted Product(s):

- testosterone cypionate (Azmiro®) intramuscular injection for administration by a healthcare professional

Indications for Use:

- For testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone
- For primary hypogonadism (congenital or acquired): Testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, Klinefelter syndrome, chemotherapy, or toxic damage from alcohol or heavy metals
- For hypogonadotropic hypogonadism (congenital or acquired): Idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation
- For delayed puberty: To stimulate puberty in carefully selected males with clearly delayed puberty
- For metastatic mammary cancer in women: Used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal
- Limitations of use:
    - Safety and efficacy in men with age-related hypogonadism or late-onset hypogonadism have not been established
    - Safety and effectiveness in pediatric patients below the age of 12 years have not been established

*Coverage may vary by state. Check applicable state laws for more information.

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. ONE of the following:
    a. The patient has an established diagnosis of hypogonadism with androgen deficiency; **AND**
        i. The diagnosis has been confirmed by BOTH of the following:
            1. ONE of the following:
                a. The patient is NOT currently receiving testosterone replacement therapy and has persistently low testosterone levels as demonstrated by the following:

i. The patient has TWO pretreatment early morning testosterone levels, drawn on subsequent days, that meet one of the following **[medical record documentation required]**:
1. Total serum testosterone level that is below the testing laboratory's lower limit of the normal range OR less than 300 ng/dL; **OR**
2. Free serum testosterone level that is below the testing laboratory's lower limit of the normal range; **OR**

b. The patient has a diagnosis of hypogonadism and is currently receiving testosterone replacement therapy; **AND**
i. The patient has had a total serum or free serum testosterone level checked in the past year; **AND**

2. Presence of symptoms of hypogonadism or symptoms at the time of diagnosis, including at least ONE of the following more specific symptoms:
a. Incomplete or delayed sexual development; **OR**
b. Decreased libido; **OR**
c. Decreased spontaneous erections; **OR**
d. Breast discomfort, gynecomastia; **OR**
e. Loss of axillar and/or pubic body hair; **OR**
f. Very small (< 5 mL) or shrinking testes; **OR**
g. Infertility due to low sperm count; **OR**
h. Height loss due to vertebral fractures, low trauma fractures, low bone density; **OR**
i. Hot flushes, sweats; **OR**

b. The patient has a diagnosis of human immunodeficiency virus (HIV) with unexplained weight loss or low bone mineral density AND has low testosterone levels; **AND**
i. ONE of the following:
1. The patient is NOT currently receiving testosterone replacement therapy and has persistently low testosterone levels as demonstrated by the following:
a. The patient has TWO pretreatment early morning testosterone levels, drawn on subsequent days, that meet one of the following **[medical record documentation required]**:
i. Total serum testosterone level that is below the testing laboratory's lower limit of the normal range OR less than 300 ng/dL; **OR**
ii. Free serum testosterone level that is below the testing laboratory's lower limit of the normal range; **OR**
2. The patient has a diagnosis of hypogonadism and is currently receiving testosterone replacement therapy; **AND**

a. The patient has had a total serum or free serum testosterone level checked in the past year; **OR**

c. The patient is using the requested agent for the palliative treatment of metastatic inoperable breast cancer; **OR**

d. The patient has a diagnosis of delayed puberty; **OR**

e. The patient has a diagnosis of gender dysphoria; **AND**

i. The patient has coverage for sex trait modification[1]; **AND**

ii. The patient is 18 years of age or older; **AND**

1. The patient has persistent, well-documented gender dysphoria; **AND**
2. The patient has the capacity to make a fully informed decision and to consent for treatment; **AND**
3. Mental health concerns, if present, are reasonably well-controlled; **OR**

iii. The patient is 12 to less than 18 years of age; **AND**

1. ALL of the following

a. A qualified mental health provider[2] has confirmed:

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 adolescent's situation and functioning are stable enough to start sex hormone treatment; **AND**

iii. The patient has sufficient mental capacity to estimate the consequences of this (partly) irreversible treatment, weigh the benefits and risks, and give informed consent to this (partly) irreversible treatment; **AND**

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

c. The patient has given informed consent and the parents or other caretakers, or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process; **OR**

2. The treating clinician must submit information indicating why it would be clinically inappropriate to require the candidate to meet these criteria **[medical record documentation required]**; **AND**

2. The patient will NOT be treated for age-related or late-onset hypogonadism; **AND**
3. The patient has a physical or cognitive limitation that makes utilization of a self-administered formulation of testosterone unsafe or otherwise not feasible, as demonstrated by BOTH of the following **[medical record documentation required]**:
   a. Inability to self-administer the medication; **AND**
   b. Lack of caregiver or support system for assistance with administration of self-administered products; **AND**
4. ONE of the following:

   a. The patient has tried and had an inadequate response to testosterone cypionate (Depo-Testosterone) **[medical record documentation required]**; **OR**
   b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to testosterone cypionate (Depo-Testosterone) **[medical record documentation required]**; **AND**
5. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
6. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

[1] Drugs used for sex trait modification for gender affirming care may be specifically excluded under some health benefit plans. Please refer to the Member's Benefit Booklet for availability of benefits.

[2] Qualified mental health provider, including but not limited to: psychiatrist (M.D., D.O.), Psy.D, Ph.D, psychiatric physician assistant, psychiatric nurse practitioner, D.S.W., LCSW, or LCMHC.

Duration of Approval: 365 days (1 year)

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. The patient has demonstrated a positive clinical response while using the medication; **AND**
4. ONE of the following:
   a. The patient has a diagnosis of hypogonadism; **AND**
      i. The patient has had a total serum or free serum testosterone level checked in the past year; **OR**
   b. The patient is using the requested agent for the palliative treatment of metastatic inoperable breast cancer; **OR**
   c. The patient has a diagnosis of delayed puberty; **OR**
   d. The patient has a diagnosis of gender dysphoria; **AND**
      i. The patient has coverage for sex trait modification; **AND**
5. The patient will NOT be treated for age-related or late-onset hypogonadism; **AND**
6. The patient has a physical or cognitive limitation that makes utilization of a self-administered formulation of testosterone unsafe or otherwise not feasible, as demonstrated by BOTH of the following **[medical record documentation required]**:
   a. Inability to self-administer the medication; **AND**
   b. Lack of caregiver or support system for assistance with administration of self-administered products; **AND**

7. ONE of the following:
    a. The patient has tried and had an inadequate response to testosterone cypionate (Depo-Testosterone) **[medical record documentation required]**; **OR**
    b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to testosterone cypionate (Depo-Testosterone) **[medical record documentation required]**; **AND**
8. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
7. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting,** Site of Care Criteria applies (outlined below)*

Duration of Approval: 365 days (1 year)

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
testosterone cypionate (Azmiro®) intramuscular (IM) injection	Testosterone replacement therapy for conditions associated with a deficiency or absence of endogenous testosterone	IM: 50 mg to 400 mg every 2 to 4 weeks (individualized dose and schedule based on the patient's age, diagnosis, response to treatment, and the appearance of adverse reactions)	J1072	10,400

***Maximum units allowed for duration of approval**

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
    b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**

   c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
   d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
   e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
   f. Re-initiation of therapy, defined as ONE of the following:
      i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
      ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
   g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Bhasin S, Brito JP, Cunningham GR, et al. Testosterone Therapy in Men With Hypogonadism: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2018 May 1;103(5):1715-1744.
2. Coleman E, Radix AE, Bouman WP, et al. World Professional Association for Transgender Health: Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. *Int J Transgend Health*. 2022 Sep 6;23(Suppl 1):S1-S259.
3. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017;102:3869.
4. Horberg M, Thompson M, Agwu A, et al, on behalf of the HIV Medicine Association, Primary Care Guidance for Providers of Care for Persons With Human Immunodeficiency Virus: 2024 Update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2024 Oct 12:ciae479.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q1 annually.

July 2026: Original medical policy criteria issued. Added to initial and continuation criteria: the requirement for use of a self-administered formulation of testosterone unless certain criteria are met, the requirement for trial and failure of testosterone cypionate (Depo-Testosterone), and the requirement that the patient will not be treated for age-related or late-onset hypogonadism. Added maximum units and Site of Care medical necessity criteria. **Policy notification given 4/2/2026 for effective date 7/1/2026**.
* Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.