# PRIOR AUTHORIZATION POLICY

**POLICY:** Testosterone (Injectable) Products Prior Authorization Policy
- Depo®-Testosterone (testosterone cypionate intramuscular injection – Pfizer, generics)
- Azmiro™ (testosterone cypionate intramuscular injection – Azurity)
- testosterone enanthate intramuscular injection – Hikma, generic only
- Aveed™ (testosterone undecanoate intramuscular injection – Endo)
- Testopel® (testosterone subcutaneous pellet – Endo)
- Xyosted™ (testosterone enanthate subcutaneous injection – Antares)

**REVIEW DATE:** 09/11/2024; selected revision 12/04/2024

---

***INSTRUCTIONS FOR USE***

*THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.*

## CIGNA NATIONAL FORMULARY COVERAGE:

### OVERVIEW

Testosterone regimens can be administered orally, parenterally, or transdermally. All of the injectable agents are indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.[1-5,10] The prescribing information define these patients and/or conditions for which use of testosterone replacement products are indicated:
- **Primary hypogonadism (congenital or acquired),** for testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.
- **Hypogonadotropic hypogonadism (congenital or acquired),** for gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation.

The diagnosis of male hypogonadism is based on both signs/symptoms and low testosterone levels. By restoring normal levels of testosterone, the replacement

regimens correct symptoms of hypogonadism, which can include malaise, loss of muscle strength, depressed mood, and decreased libido.[6]

Testopel and testosterone enanthate are also indicated for **delayed puberty**.[2,3] Testosterone enanthate (per the product labeling) may also be used secondarily in **advanced inoperable metastatic mammary cancer** in women who are 1 to 5 years postmenopausal.[2] The goal of therapy is ablation of ovaries. Per labeling, it also can be used in premenopausal women with breast cancer who have benefited from oophorectomy and are considered to have hormone-responsive tumors.

## Guidelines

- **Hypogonadism:** Guidelines from the American Urological Association (2018) note that clinicians should use a total testosterone level below 300 ng/dL as a reasonable cut-off in support of the diagnosis of low testosterone.[7] The guidelines additionally note that a diagnosis of low testosterone should be made only after two total testosterone measurements are taken on separate occasions with both conducted in an early morning fashion and that a clinical diagnosis should be made when patients have low testosterone levels combined with signs and symptoms. The Endocrine Society guidelines on testosterone therapy in men with hypogonadism (2018) recommend diagnosing hypogonadism in men with symptoms and signs of testosterone deficiency and unequivocally and consistently low serum total testosterone and/or free testosterone concentrations (when indicated).[8]
- **Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Female-To-Male (FTM) Gender Reassignment (i.e., Endocrinologic Masculinization):** A clinical practice guideline published by the Endocrine Society (2017) recommends that, prior to initiation of hormonal therapy, the treating endocrinologist should confirm the diagnostic criteria of gender dysphoria/gender incongruence and the criteria for the endocrine phase of gender transition.[9] The clinician should also evaluate and address medical conditions that can be exacerbated by hormone depletion and treatment with sex hormones of the affirmed gender before beginning treatment. Guidelines mention that clinicians can use either parenteral or transdermal preparations to achieve appropriate testosterone values.

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of injectable testosterone. All approvals are provided for the duration noted below. In the clinical criteria, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: males are defined as individuals with the biological traits of a male, regardless of the individual's gender identity or gender expression; females are defined as individuals with the biological traits of a female, regardless of the individual's gender identity or gender expression. Because of the specialized skills required for evaluation and diagnosis of some patients treated with testosterone, certain approval requires testosterone to be prescribed by or in consultation with a physician who specializes in the conditions being treated.

- **Depo®-Testosterone (testosterone cypionate intramuscular injection – Pfizer, generics)**
- **Azmiro™ (testosterone cypionate intramuscular injection – Azurity)**
- **testosterone enanthate intramuscular injection – Hikma, generic only**
- **Aveed™ (testosterone undecanoate intramuscular injection – Endo)**
- **Testopel® (testosterone subcutaneous pellet – Endo)**
- **Xyosted™ (testosterone enanthate subcutaneous injection – Antares)**

**is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

**FDA-Approved Indications**

1. **Hypogonadism (Primary or Secondary) in Males* [Testicular Hypofunction/Low Testosterone with Symptoms].** Approve for 1 year if the patient meets ONE of the following (A or B):
   Note: The pre-treatment timeframe refers to sign and symptoms of androgen deficiency and serum testosterone levels prior to the initiation of any testosterone therapy.
   **A)** Initial Therapy. Approve in a patient with hypogonadism as confirmed by ALL of the following (i, ii, and iii):
      **i.** Patient has had persistent signs and symptoms of androgen deficiency (pre-treatment); AND
      Note: Signs and symptoms of androgen deficiency include depressed mood, decreased energy, progressive decrease in muscle mass, osteoporosis, and loss of libido.
      **ii.** Patient has had two pre-treatment serum testosterone (total or bioavailable) measurements, each taken in the morning, on two separate days; AND
      **iii.** The two serum testosterone levels are both low, as defined by the normal laboratory reference values.
   **B)** Patient Currently Receiving Testosterone Therapy. Approve if the patient meets BOTH of the following (i and ii):
      **i.** Patient has had persistent signs and symptoms of androgen deficiency (pre-treatment); AND
      Note: Signs and symptoms of androgen deficiency include depressed mood, decreased energy, progressive decrease in muscle mass, osteoporosis, and loss of libido.
      **ii.** Patient has had at least one pre-treatment serum testosterone (total or bioavailable) level, which was low, as defined by the normal laboratory reference values.

   * Refer to the Policy Statement

2. **Delayed Puberty or Induction of Puberty in Males* 14 years of Age or Older.** Approve Depo-Testosterone (testosterone cypionate intramuscular

injection, generics), Azmiro, testosterone enanthate intramuscular injection, or Testopel for 6 months.

*Refer to the Policy Statement

3. **Breast Cancer in Females*.** Approve testosterone enanthate intramuscular injection for 6 months if prescribed by or in consultation with an oncologist.

   *Refer to the Policy Statement.

**Other Uses with Supportive Evidence**

4. **Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Female-to-Male (FTM) Gender Reassignment (i.e., Endocrinologic Masculinization).** Approve for 1 year if prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender patients.
   Note: For a patient who has undergone gender reassignment, use this FTM criterion for hypogonadism indication.

## CONDITIONS NOT COVERED

- **Depo®-Testosterone (testosterone cypionate intramuscular injection – Pfizer, generics)**
- **Azmiro™ (testosterone cypionate intramuscular injection – Azurity)**
- **testosterone enanthate intramuscular injection – Hikma, generic only**
- **Aveed™ (testosterone undecanoate intramuscular injection – Endo)**
- **Testopel® (testosterone subcutaneous pellet – Endo)**
- **Xyosted™ (testosterone enanthate subcutaneous injection – Antares)**

**is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

1. **To Enhance Athletic Performance.** Injectable testosterone products are not recommended for approval because this indication is excluded from coverage in a typical pharmacy benefit.

## REFERENCES


1. Depo®-Testosterone [prescribing information]. New York, NY: Pfizer; September 2018.
2. Testosterone enanthate injection [prescribing information]. Berkeley Heights, NJ: Hikma; January 2021.
3. Testopel® [prescribing information]. Malvern, PA: Endo; March 2024.
4. Aveed™ [prescribing information]. Malvern, PA: Endo; August 2021.
5. Xyosted [prescribing information]. Ewing, NJ: Antares; August 2023
6. Lee M. Erectile Dysfunction. Urologic Disorders. In: Dipiro JT, Talbert RL, Yee GC, et al, eds. Pharmacotherapy: A pathophysiologic approach. 8th ed. New York: McGraw Hill Medical; 2008: 1437-1454.

7. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and Management of Testosterone Deficiency. American Urological Association. 2018. Reaffirmed 2024. Available at: Testosterone Deficiency Guideline - American Urological Association (auanet.org). Accessed on September 3, 2024.
8. 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;103(5):1715-1744.
9. Hembree WC, Cohen-Kettenis P, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2017;102(11)::3869-3903.
10. Azmiro™ [prescribing information]. Woburn, MA: Azurity; May 2024.

## HISTORY

| Type of Revision | Summary of Changes | Review Date |
|---|---|---|
| Early Annual Revision | **Documentation:** Removal of the documentation requirement from the policy. | 09/06/2023 |
| Annual Revision | No criteria changes. | 09/11/2024 |
| Selected Revision | Added Azmiro to the policy; the same criteria apply as for testosterone cypionate products. | 12/04/2024 |