Drug Coverage Policy

Effective Date.....11/15/2025
Coverage Policy Number.....IP0351
Policy Title.....Testosterone (Injectable) Products

Testosterone (Injectable) Products

- Aveed™ (testosterone undecanoate intramuscular injection – Endo)
- Azmiro™ (testosterone cypionate intramuscular injection – Azurity)
- Testopel® (testosterone subcutaneous pellet – Endo)
- Xyosted™ (testosterone enanthate subcutaneous injection – Antares)

Coverage for treatment of gender dysphoria varies across plans. Coverage of drugs for hormonal therapy, as well as whether the drug is covered as a medical or a pharmacy benefit, varies across plans. Refer to the customer's benefit plan document for coverage details. In addition, coverage for treatment of gender dysphoria, including gender reassignment surgery and related services may be governed by state and/or federal mandates.

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 where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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.

Overview
Testosterone regimens can be administered orally, parenterally, or transdermally. All 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 defines those patients and/or conditions for which 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 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 between 1 and 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 that have benefited from oophorectomy and are considered to have hormone-responsive tumors.

Dosing Information
Testosterone injections are used in clinical practice as intramuscular or subcutaneous injections. For Depo-Testosterone, Azmiro, and testosterone enanthate, as replacement therapy for male hypogonadism, the suggested dose is 50 to 400 mg every 2 to 4 weeks.[1,2,10] In general, total doses of above 400 mg per month are not required because of prolonged action of the preparation.[2] For delayed puberty, various dosage regimens have been used, but dosage is generally within the range of 50 to 200 mg every 2 to 4 weeks.[2] The suggested dosage for testosterone injection varies depending on the age, sex, and diagnosis of the individual patient; dosage is adjusted according to the patient's response and the appearance of adverse reactions.[1-3,10] 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.[4] The suggested dose for Testopel (testosterone pellet) is 150 mg to 450 mg subcutaneously every 3 to 6 months; dosages for delayed puberty are generally in the lower range.[3] Xyosted is administered subcutaneously once weekly[5] and dosages above 100 mg per week have not been studied.

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. 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 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. Testosterone regimens for transgender males include testosterone enanthate or cypionate of 100 mg to 200 mg intramuscularly every 2 weeks or subcutaneously at 50% (of the intramuscular dosage) per week.

Coverage Policy

Policy Statement
Prior Authorization is required for benefit coverage of injectable testosterone. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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 patients treated with injectable testosterone as well as the monitoring required for adverse events and long-term efficacy, some approvals require injectable testosterone to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Injectable Testosterone is considered medically necessary when ONE of the following is met (1, 2, or 3):

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, iii and iv):

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 early morning, on two separate days; AND

iii. The two serum testosterone levels are both low, as defined by the normal laboratory reference values; AND

iv. Preferred product criteria is met for the products listed in the below table(s)

B. Patients Currently Receiving Testosterone Therapy. Approve is 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

Employer Plans:

Product	Criteria
Azmiro (testosterone cypionate intramuscular injection)	Patient has tried and, according to the prescriber, the patient has had inadequate efficacy or significant intolerance to **ONE** of the following: 1. Testosterone cypionate intramuscular injection (Depo-testosterone) 2. Testosterone enanthate intramuscular injection (Delatestryl)
Xyosted (testosterone enanthate subcutaneous injection)	**Standard/Performance/Value/Advantage/Total Savings Drug List Plans:** Patient has tried and, according to the prescriber, the patient has had inadequate efficacy or significant intolerance to **ONE** of the following: 1. Testosterone cypionate intramuscular injection (Depo-testosterone) 2. Testosterone enanthate intramuscular injection (Delatestryl)

Individual and Family Plans:

Product	Criteria
Azmiro (testosterone cypionate intramuscular injection)	Patient has tried and, according to the prescriber, the patient has had inadequate efficacy or significant intolerance to **ONE** of the following: 1. Testosterone cypionate intramuscular injection (Depo-testosterone)

Product	Criteria
	2. Testosterone enanthate intramuscular injection (Delatestryl)
Xyosted (testosterone enanthate subcutaneous injection)	Patient has tried and, according to the prescriber, the patient has had inadequate efficacy or significant intolerance to **ONE** of the following: 1. Testosterone cypionate intramuscular injection (Depo-testosterone) 2. Testosterone enanthate intramuscular injection (Delatestryl)

Dosing. Patient meets ONE of the following dosing regimens (A, B, C, or D):
A. Aveed: 750 mg administered intramuscularly, followed by 750 mg injected after 4 weeks, then 750 mg injected every 10 weeks thereafter; OR
B. Azmiro: Up to 400 mg administered subcutaneously or intramuscularly every 1 to 4 weeks, not to exceed 400 mg every 2 weeks; OR
C. Testopel: Up to 150 mg to 450 mg subcutaneously up to every 3 to 6 months; OR
D. Xyosted: Up to 100 mg subcutaneously once weekly.

2. **Delayed Puberty or Induction of Puberty in Males* 14 years of age or older.** Approve Azmiro or Testopel for 6 months.

   *Refer to the Policy Statement

   Dosing. Patient meets ONE of the following dosing regimens (A or B):
   A. Azmiro: Up to 400 mg administered subcutaneously or intramuscularly every 1 to 4 weeks, not to exceed 400 mg every 2 weeks; OR
   B. Testopel: Up to 150 mg to 450 mg subcutaneously up to every 3 to 6 months.

Other Uses with Supportive Evidence

3. **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.

   Dosing. Patient meets ONE of the following dosing regimens (A, B, C, or D):
   A. Aveed: 750 mg administered intramuscularly, followed by 750 mg injected after 4 weeks, then 750 mg injected every 10 weeks thereafter; OR
   B. Azmiro: Up to 400 mg administered subcutaneously or intramuscularly every 1 to 4 weeks, not to exceed 400 mg every 2 weeks; OR
   C. Testopel: Up to 150 mg to 450 mg subcutaneously up to every 3 to 6 months; OR
   D. Xyosted: Up to 100 mg subcutaneously once weekly

Conditions Not Covered

Injectable Testosterone for any other use is considered not medically necessary, 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.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
11980	Subcutaneous hormone pellet implantation (implantation of estradiol and/or testosterone pellets beneath the skin)

HCPCS Codes	Description
J3145	Injection, testosterone, undecanoate, 1 mg
S0189	Testosterone pellet, 75 mg

References

1. Depo®-Testosterone [prescribing information]. New York, NY: Pfizer; June 2024.
2. Testosterone enanthate injection [prescribing information]. Berkeley Heights, NJ: Hikma; January 2021.
3. Testopel® [prescribing information]. Malvern, PA: Endo; July 2025.
4. Aveed™ [prescribing information]. Malvern, PA: Endo; July 2025.
5. Xyosted [prescribing information]. Ewing, NJ: Antares; July 2025.
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 9, 2025.
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; July 2025.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	No criteria changes; minor policy format updates and addition of dosage form to products in the preferred product table.	12/01/2024
Selected Revision	**Updated** policy title. **Added** Azmiro to the policy; with the same criteria apply as for other testosterone products.	03/01/2025
Annual Revision	**Updated** the policy statement. **Hypogonadism (Primary or Secondary) in Males* [Testicular Hypofunction/Low Testosterone with Symptoms].** Initial Therapy **Updated** Employer Plans and Individual and Family plans preferred product criteria. **Updated** the Conditions Not Covered statement.	11/15/2025

The policy effective date is in force until updated or retired.