PRIOR AUTHORIZATION POLICY

POLICY: Testosterone Injectable Products Prior Authorization Policy
- Depo®-Testosterone (testosterone cypionate intramuscular injection – Pfizer, generic)
- Delatestryl® (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: 10/19/2022

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] The prescribing information define those 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 Delatestryl (testosterone enanthate) are also indicated for **delayed puberty**.[2,3] Delatestryl (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 that 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 clinical 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.

Documentation: Documentation is required for use of injectable testosterones as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory reports, prescription claims records, prescription receipts, and/or other information. For patient cases in which documentation is required, if this documentation has been previously received upon a prior coverage review, the documentation requirement is considered to be met.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of injectable testosterone is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Hypogonadism (Primary or Secondary) in Males* [Testicular Hypofunction/Low Testosterone with Symptoms].** Approve for 1 year if the patient meets the following criteria (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 the following criteria (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 **[documentation required]**, 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 **[documentation required]**.
   - **B)** Patient Currently Receiving Testosterone Therapy. Approve if the patient meets the following criteria (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 **[documentation required]**, which was low, as defined by the normal laboratory reference values **[documentation required]**.

* 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), Delatestryl (testosterone enanthate), or Testopel for 6 months.

   *Refer to the Policy Statement

3. **Breast Cancer in Females*.** Approve Delatestryl (testosterone enanthate) 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 RECOMMENDED FOR APPROVAL

Coverage of injectable testosterone is not recommended in the following situations:

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.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Depo®-Testosterone [prescribing information]. New York, NY: Pfizer; August 2018.
2. Testosterone enanthate inection [prescribing information]. Berkeley Heights, NJ: Hikma; January 2021.
3. Testopel® [prescribing information]. Malvern, PA: Endo; August 2018.
4. Aveed™ [prescribing information]. Malvern, PA: Endo; August 2021.
5. Xyosted [prescribing information]. Ewing, NJ: Antares; November 2019
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. Available at: Testosterone Deficiency Guideline - American Urological Association (auanet.org). Accessed on October 12, 2022.
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.