PRIOR AUTHORIZATION POLICY

POLICY: Testosterone (Oral, Topical, and Nasal) Products Prior Authorization Policy

Oral Testosterone Products

- Jatenzo® (testosterone undecanoate capsules – Clarus/Tolmar)
- Kyzatrex™ (testosterone undecanoate capsules – Marius)
- Tlando® (testosterone undecanoate capsules – Antares)

Transdermal Patch

- Androderm® (testosterone transdermal system [2,4 mg/day] – Allergan)

Transdermal Gels

- AndroGel® (testosterone 1% gel (generics only), 1.62% gel – AbbVie, generic)
- Fortesta™ (testosterone 2% gel – Endo, generic)
- Testim® (testosterone 1% gel – Endo, generic)
- Vogelxo™ (testosterone 1% gel – Upsher-Smith, generic)

Transdermal Solution

- testosterone 2% solution – Actavis, generics only

Nasal Gel

- Natesto™ (testosterone nasal gel – Acerus)

REVIEW DATE: 11/08/2023

OVERVIEW

The oral, topical, and nasal testosterone replacement products are all indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.[1-10,15] The labels for the FDA-approved products define those patients and/or conditions for which use of testosterone replacement products is indicated:

- **Primary hypogonadism (congenital or acquired):** testicular failure due to conditions such as 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 above-normal gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]).
- **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 serum testosterone concentrations, but have gonadotropins in the normal or low range.

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.[12]

All of the oral, topical, and nasal testosterone replacement product labeling states that due to the lack of controlled evaluations in women and potential virilizing effects, the products are not indicated for use in women.[1-10,15]

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 cutoff in support of the diagnosis of low testosterone.[13] A clinical diagnosis requires low testosterone levels (two separate levels, both conducted in the early morning) 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).[11]
- **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.[14] 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 oral, topical, and nasal testosterone products. In the approval indications, 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 individuals' gender identity or gender expression. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of some patients treated with testosterone, certain approval conditions require testosterone to be prescribed by or in consultation with a physician who specializes in the conditions being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of oral, topical, and nasal testosterone products is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Hypogonadism (Primary or Secondary) in Males* [Testicular Hypofunction/Low Testosterone with Symptoms].** Approve for 1 year if the patient meets the following (A or B):
   Note: The pretreatment timeframe refers to signs and symptoms of androgen deficiency and serum testosterone levels prior to the initiation of any testosterone therapy.
   A) Initial Therapy. Patient with hypogonadism as confirmed by the following (i, ii, and iii):
      i. Patient has had persistent signs and symptoms of androgen deficiency (pretreatment); 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 pretreatment 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 is Currently Receiving Testosterone Therapy. Approve if the patient meets the following (i and ii):
- **i.** Patient has had persistent signs and symptoms of androgen deficiency (pretreatment); 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 pretreatment serum testosterone (total or bioavailable) level, which was low, as defined by the normal laboratory reference values.

*Refer to the Policy Statement.

Other Uses with Supportive Evidence

2. **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 oral, topical, and nasal testosterone products is not recommended in the following situations:

1. **To Enhance Athletic Performance.** Topical 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. Androderm® transdermal patch [prescribing information]. Madison, NJ: Allergan; May 2020.
2. Testim® topical gel [prescribing information]. Malvern, PA: Endo; August 2021.
3. Testosterone topical 1% gel [prescribing information]. Chestnut Ridge, NY: Par; January 2022.
4. AndroGel® topical 1.62% gel [prescribing information]. North Chicago, IL: AbbVie; November 2020.
5. Kyzatrex® capsules [prescribing information]. Raleigh, NC: Marius; September 2022
6. Testosterone topical solution [prescribing information]. Parsippany, NJ: Actavis; February 2019.
7. Fortesta topical gel [prescribing information]. Malvern, PA: Endo; January 2022.
8. Vogelxo™ topical gel [prescribing information]. Maple Grove, MN: Upsher-Smith; April 2020.
9. Natesto™ nasal gel [prescribing information]. Englewood, CO: Acerus; December 2021.
10. Jatenzo® capsules [prescribing information]. Fort Collins, CO: Tolmar; August 2023.
11. 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.
12. Lee M. Erectile dysfunction. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, eds. Pharmacotherapy: a pathophysiologic approach. 7th ed. New York, NY: McGraw-Hill; 2008:1369-1385.
13. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and Management of Testosterone Deficiency. American Urological Association. 2018. Available at: Non-Oncology Guidelines - American Urological Association (auanet.org). Accessed on November 1, 2023.
14. 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.
15. Tlando® capsules [prescribing information]. Ewing, NJ: Antares; March 2022.