PRIOR AUTHORIZATION POLICY

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

Oral Testosterone Products
- Jatenzo® (testosterone undecanoate capsules – Clarus Therapeutics, Inc.)
- Striant™ (testosterone buccal system, mucoadhesive – Endo Pharmaceuticals, Inc.) [obsolete]

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

Transdermal Gels
- AndroGel® (testosterone 1% gel, 1.62% gel – AbbVie, Inc., generics)
- Fortesta™ (testosterone 2% gel – Endo Pharmaceuticals, Inc., generics)
- Testim® (testosterone 1% gel – Endo Pharmaceuticals, Inc., generics)
- Vogelxo™ (testosterone 1% gel – Upsher-Smith Laboratories, generics)

Transdermal Solution
- Axiron™ (testosterone 2% solution – Lilly USA, LLC, generics only)

Nasal Gel
- Natesto™ (testosterone nasal gel – Aytu Bioscience, Inc)

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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] The prescribing information for the FDA-approved products define those patients and/or conditions for which use of testosterone replacement products are 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 gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal.
- **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 testosterone serum 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]

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.[13] 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).[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 requires 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 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 signs and symptoms of androgen deficiency and serum testosterone levels prior to the initiation of any testosterone therapy.

   A) Initial Therapy: Patients 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, 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) Patients Continuing 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, 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 patients who have 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® [prescribing information]. Madison, NJ: Allergan USA, Inc.; May 2020.
2. Testim® [prescribing information]. Malvern, PA: Endo Pharmaceuticals, Inc.; April 2018.
3. AndroGel® 1% gel [prescribing information]. North Chicago, IL: AbbVie Inc.;May 2019.
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5. Striant™ buccal system [prescribing information]. Malvern, PA: Endo Pharmaceuticals, Inc.; October 2016.
6. Testosterone solution [prescribing information]. Allegan, MI: Perrigo; April 2020.
7. Fortesta gel for topical use [prescribing information]. Malvern, PA: Endo Pharmaceuticals Inc.; June 2020.
8. Vogelxo™ [prescribing information]. Maple Grove, MN: Upsher-Smith Laboratories, Inc.; April 2020.
9. Natesto™ nasal gel [prescribing information]. Englewood, CO: Aytu BioScience, Inc.; October 2016.
10. Jatenzo® [prescribing information]. Northbrook, IL: Clarus Therapeutics, Inc.; March 2019.
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: http://www.auanet.org/guidelines/testosterone-deficiency-(2018). Accessed on September 1, 2020.
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.