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Section:	Prescription Drugs	**Effective Date:**	January 1, 2026
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	May 30, 2014
Subject:	Testosterone Oral Buccal Nasal	**Page:**	1 of 11

Last Review Date: December 12, 2025

Testosterone Oral Buccal Nasal

Description

Methitest* (methyltestosterone tablet)
methyltestosterone capsule*
Natesto* (testosterone nasal gel)
Striant (testosterone buccal system)
Jatenzo, Kyzatrex*, Tlando* (testosterone undecanoate capsule)

*Non-covered medications must go through prior authorization and the formulary exception process

Background
Endogenous androgens, including testosterone and dihydrotestosterone (DHT), are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. These effects include the growth and maturation of prostate, seminal vesicles, penis and scrotum; the development of male hair distribution, such as facial, pubic, chest and axillary hair; laryngeal enlargement, vocal cord thickening, alterations in body musculature and fat distribution (1-7).

Androgens stimulate growth in adolescence and cause the eventual closure of the femoral epiphysis. In children, exogenous androgens accelerate linear growth rates but may cause a disproportionate advancement in bone maturation. Chronic use may result in fusion of the epiphyseal growth centers and termination of growth process (1-2).

Regulatory Status
FDA-approved indications: Androgens are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone. Jatenzo, Kyzatrex,

Methitest, methyltestosterone capsule, Natesto, Striant and Tlando are indicated for the treatment of: (1-7)

- 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 range.
- Hypogonadotropic hypogonadism (congenital or acquired): idiopathic 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.

Methitest and methyltestosterone capsule are also indicated for the treatment of: (1-2)

- Delayed puberty in males*:* to induce pubertal changes in hypogonadal males. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every 6 months to assess the effect of treatment on the epiphyseal centers.
- In women as secondary treatment with advancing inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal. This treatment has also been used in premenopausal women with breast cancer who have benefitted from oophorectomy and are considered to have a hormone-responsive tumor.

Off-Label Use: (10)
Testosterone can be used as part of a treatment plan for sex trait modification.

The drugs addressed by this policy have warnings regarding polycythemia, worsening of benign prostatic hyperplasia (BPH) and potential risk of prostate cancer, venous thromboembolism (VTE), abuse of testosterone and monitoring of serum testosterone concentration, potential for adverse effects on spermatogenesis, edema, sleep apnea, lipid changes and increases in prolactin. Prolonged use of high doses of androgens has been associated with the development of peliosis hepatitis and hepatic neoplasms including hepatocellular carcinoma (1-7).

Hematocrit levels and liver function tests must be monitored while on testosterone therapy (1-7).

Male patients, with benign prostatic hyperplasia (BPH), must be monitored for worsening of signs and symptoms of BPH. Physicians should evaluate male patients for the presence of prostate cancer prior to the initiation of therapy. A normal prostate cancer risk is a PSA level

that is less than 4 ng/ml. High prostate cancer risk patients, such as African American men and men whose father or brother had prostate cancer, should have a PSA less than 3 ng/ml. Check prostate-specific antigen (PSA) levels in men over 50 years of age, or in those over 40 having a family history of prostate cancer or if African-American; to ensure proper dosing. Patients should be re-evaluated 12 months after initiation of treatment, and then in accordance with prostate cancer screening practices (1-9).

Two total testosterone levels are required to determine medical necessity of testosterone replacement. Two morning samples drawn between 8:00 a.m. and 10:00 a.m. obtained on different days are required. Total testosterone levels need to be below 300ng/dL on both days in order to be considered for therapy (9).

Androgen therapy in the treatment of women with breast cancer should be made by an oncologist with expertise in this field. Hypercalcemia may occur in immobilized patients and in patients with breast cancer. If this occurs, the drug should be discontinued (1-2).

Jatenzo and Tlando have a boxed warning regarding blood pressure (BP) increases that can increase the risk of major adverse cardiovascular events (MACE), including non-fatal myocardial infarction, non-fatal stroke and cardiovascular death (5-6). Patients should be assessed for cardiovascular risk prior to initiating treatment with androgens (1-7).

Due to lack of clinical data on the safety or efficacy, Natesto is not recommended for use in patients with the following: (3)

- History of nasal disorders
- History of nasal or sinus surgery
- History of nasal fracture within the previous 6 months or nasal fracture that caused a deviated anterior nasal septum
- Mucosal inflammatory disorders (e.g., Sjogren’s syndrome), and
- Sinus disease

The safety and effectiveness of Jatenzo, Kyzatrex, Natesto, Striant and Tlando in pediatric patients less than 18 years of age have not been established (3-7).

Methitest and methyltestosterone capsule therapy should be used very cautiously in pediatric patients and only by specialists who are aware of the adverse effects on bone maturation (1-2).

Related policies
Testosterone Implant Injectable, Testosterone Powder, Testosterone Topical

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Jatenzo, Kyzatrex, Methitest, methyltestosterone capsule, Natesto, Striant, and Tlando may be considered **medically necessary** if the conditions indicated below are met.

Jatenzo, Kyzatrex, Methitest, methyltestosterone capsule, Natesto, Striant, and Tlando may be considered **investigational** for all other indications.

Prior-Approval Requirements

Methitest and methyltestosterone capsule ONLY

Age 12 years of age or older
Gender Male

Diagnosis

Patient must have the following:

Delay in sexual development and/or puberty

a. **NO** dual therapy with another testosterone product

AND confirmation that the following will be monitored every 6 months:

1. Assessment of bone age of the hand and wrist (as determined by radiographic evidence)
2. Liver function tests
3. Hematocrit levels

Methitest and methyltestosterone capsule ONLY

Age 18 years of age or older
Gender Female only

Diagnosis

Patient must have the following:

1. Inoperable metastatic breast or mammary cancer
2. The patient has received at least one prior therapy
3. **NOT** being used for sex trait modification
4. **NO** dual therapy with another testosterone product

AND confirmation that the following will be monitored every 6 months:

a. Hypercalcemia and agreement to discontinue the drug if present
b. Liver function tests
c. Hematocrit level

Age 18 years of age or older
Gender Male

Diagnosis

Patient must have the following:

Deficiency of testosterone (hypogonadism)

AND ALL of the following:

1. Two morning total testosterone levels less than 300 ng/dL on different days
2. Patients over 40 years of age must have baseline PSA less than 4 ng/ml
    a. Prostatectomy patients excluded from the requirement
3. Absence of current prostate cancer / palpable prostate nodules
4. Hematocrit less than 54%
5. Patients with concurrent diagnosis of benign prostatic hypertrophy (BPH) **ONLY**: patient will be monitored for worsening of BPH symptoms
6. Evaluation of cardiovascular risk for myocardial infarction (MI), angina, stroke
7. Absence of untreated sleep apnea
8. **NO** dual therapy with another testosterone product

AND NONE of the following (Natesto **ONLY**):

1. Chronic nasal conditions or alterations in nasal anatomy

Prior – Approval *Renewal* Requirements

Methitest and methyltestosterone capsule ONLY

Age 12 years of age or older
Gender Male

Diagnosis

Patient must have the following:

Delay in sexual development and/or puberty

a. **NO** dual therapy with another testosterone product

AND confirmation that the following will be monitored every 6 months:

1. Assess bone age of the hand and wrist (as determined by radiographic evidence)
2. Liver function tests
3. Hematocrit levels

Methitest and methyltestosterone capsule ONLY

Age 18 years of age or older
Gender Female only

Diagnosis

Patient must have the following:

1. Inoperable metastatic breast or mammary cancer
2. The patient has received at least one prior therapy
3. **NO** dual therapy with another testosterone product

AND confirmation that the following will be monitored every 6 months:

a. Hypercalcemia and agreement to discontinue the drug if present
b. Liver function tests
c. Hematocrit level

Age 18 years of age or older

Gender Male

Diagnosis

Patient must have the following:

Deficiency of testosterone (hypogonadism)

AND ALL of the following:

1. Total testosterone levels of 800 ng/dL or less
2. Patients with concurrent diagnosis of benign prostatic hypertrophy (BPH) **ONLY**: absence of worsening of BPH symptoms
3. Re-evaluation of cardiovascular risk for MI, angina, stroke
4. **NO** dual therapy with another testosterone product

AND confirmation that the following are being monitored every 12 months:

1. Serum testosterone concentrations
2. Prostate specific antigen (PSA) for patients over 40 years of age
   a. Prostatectomy patients excluded from the requirement
3. Hematocrit levels

Age 19 years of age or older

Diagnosis

Patient must have the following:

Sex trait modification

1. Patient has initiated therapy prior to 1/1/2026 under the Blue Cross and Blue Shield Service Benefit Plan (FEP)
2. **NO** dual therapy with another testosterone product

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Oral Testosterone	Gender	Quantity	Days Supply
Jatenzo	Male (adult only)	158 mg = 360 capsules	90
		198 mg = 360 capsules	90
		237 mg = 180 capsules	90
Striant buccal system	Male (adult only)	180 buccal systems (3 boxes)	90

Oral Testosterone with approved FE only	Gender	Quantity	Days Supply
Kyzatrex	Male (adult only)	360 capsules	90
Methitest	Male	450 tablets	90
	Female	1800 tablets	
Methyltestosterone capsule	Male	450 capsules	90
	Female	1800 capsules	
Natesto nasal gel	Male (adult only)	66 grams (9 bottles)	90
Tlando	Male (adult only)	360 capsules	90

Duration 6 months for all diagnoses

Prior Approval *Renewal* Limits

Oral Testosterone	Gender	Quantity	Days Supply
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Methyltestosterone capsule	Male	450 capsules	90
	Female	1800 capsules	
Natesto nasal gel	Male (adult only)	66 grams (9 bottles)	90
Tlando	Male (adult only)	360 capsules	90

Duration 12 months for all diagnoses except sex trait modification
2 years for sex trait modification

Rationale

Summary

Testosterone is approved for replacement therapy in men for conditions associated with testosterone deficiency such as: hypogonadotropic hypogonadism, primary hypogonadism, and delayed puberty. In women, methyltestosterone is approved to treat metastatic breast cancer. Liver function and hematocrit levels should be monitored in all patients taking testosterone. In adult men, the following should also be monitored: prostate-specific antigen (PSA) levels, serum testosterone concentrations, presence of prostate cancer, worsening of benign prostatic hypertrophy (BPH), and cardiovascular risk. For pubescent males, radiographic evidence to determine bone maturation needs to be obtained (1-9).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of the testosterone products while maintaining optimal therapeutic outcomes.

References

1. Methyltestosterone capsule [package insert]. East Windsor, NJ: Novitium Pharma LLC; June 2021.
2. Methitest tablet [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; February 2022.
3. Natesto nasal gel [package insert]. Regensburg, Germany: Acerus Pharmaceuticals Corporation; December 2021.
4. Striant buccal system [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; November 2016.
5. Jatenzo [package insert]. Northbrook, IL: Clarus Therapeutics, Inc.; March 2019.
6. Tlando [package insert]. Ewing, NJ: Antares Pharma, Inc.; March 2022.

7. Kyzatrex [package insert]. Raleigh, NC: Marius Pharmaceuticals; July 2022.
8. Bh*asin S, Cunningham GR, H*ayes FJ et al. Testosterone therapy in men with androgen deficiency syndromes: an endocrine society clinical practice guideline*. J Clin Endocrinol Metab*. 2010;95(6):2536-59.
9. Carnegie C. Diagnosis of Hypogonadism: Clinical Assessments and Laboratory Tests. Rev Urol. 2004; 6(Suppl 6): S3-S8. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1472884. Accessed on August 30, 2018.
10. Hembree, WC, Cohen-Kettenis, P, et al. Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2009; 94(9):3132-3154.

Policy History

Date	Action
April 2014	Addition to PA
May 2014	Addition of nasal dosage form, Natesto, to PA
September 2014	Removal of absence of severe sleep apnea, severe lower urinary tract symptoms and addition of hematocrit level of 54% Revision of testosterone levels for continuation
August 2014	Revision of diagnosis for male patients 18 years or older to deficiency of testosterone/hypogonadism. Revision of renewal duration to 12 months.
October 2014	Change of age from 9 to 12 years of age for delayed puberty.
December 2014	Annual review and reference update. Change for patients over 40 years of age must have baseline PSA less than 4 ng/ml and prostatectomy patients excluded from the requirement
March 2015	Annual review and reference update.
April 2015	Addition of assessment of cardiovascular risk to criteria
June 2015	Annual review Addition of the evaluation of cardiovascular risk for MI, angina, stroke and absence of untreated sleep apnea and no dual therapy with another testosterone product.
December 2015	Annual review Addition of Gender Dysphoria (GD) use and duration
May 2016	Addition of transgender specialist to GD prescriber requirement Policy number change from 5.08.32 to 5.30.32
June 2016	Annual review

September 2016	Annual editorial review and reference update
January 2017	Removal of GD age requirements
March 2017	Annual Review
December 2017	Annual editorial review and reference update
November 2018	Annual review and reference update
March 2019	Annual review
April 2019	Addition of Jatenzo and revised quantity limits
June 2019	Annual review
July 2019	Changed approval duration for Gender Dysphoria from lifetime to 2 years
September 2019	Annual review
January 2020	Revised chart for Jatenzo so that the strengths are separate
March 2020	Annual review and reference update
October 2021	Annual review
April 2022	Addition of Tlando to policy. Removed Androxy from policy due to being discontinued. Removed methyltestosterone capsule brand names (Android and Testred) from policy due to being discontinued
June 2022	Annual review
September 2022	Annual review
October 2022	Addition of Kyzatrex to policy
December 2022	Annual review. Removed GD requirements of meeting DSM criteria and being prescribed by an endocrinologist or transgender specialist. Moved Tlando to FE + PA only
September 2023	Annual review
September 2024	Annual review
March 2025	Per FEP, changed duration for GD in patients less than 19 years of age to the end of plan year
June 2025	Annual review
December 2025	Annual review. Changed GD diagnosis to “sex trait modification” and added requirements that patient has initiated therapy prior to 2026. For initiation requests, “no sex trait modification” added for female patients. Moved Methitest tablets, methyltestoterone capsules, Natesto gel and Kyzatrex to require FE

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.