Testosterone Oral Buccal Nasal

Description

Android, Androxy, Jatenzo*, Methitest, Natesto, Striant, Testred

*This medication is included in this policy but is not available in the market as of yet

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 (1).

Male hypogonadism results from insufficient secretion of testosterone and is characterized by low serum testosterone concentrations. Symptoms associated with male hypogonadism include the following: impotence and decreased sexual desire, fatigue and loss of energy, mood depression, regression of secondary sexual characteristics, and osteoporosis (1).

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. Androgens have been shown to stimulate the red blood cell production by the increased production of erythropoietic stimulating factor (2).

Regulatory Status

FDA-approved indications: (2-8)
1. Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchietomy, 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.

2. 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.

3. Delayed puberty in males: to induce pubertal changes in hypogonadal males.

4. In women as secondary treatment with advancing inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal (2). 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:
Testosterone can be used in the treatment of Gender Dysphoria (GD) and should only be started once a diagnosis of GID or transsexualism has been made per the DSM V or ICD-10 criteria (11).

Chronic high dose therapy of androgens has shown development of peliosis hepatitis and hepatic neoplasms including hepatocellular carcinoma. Peliosis hepatitis can be a life-threatening or fatal complication. Low doses of 17-alpha-alkylandrogens have been associated with cholestatic hepatitis and jaundice. The medication should be discontinued and the cause should be determined if these conditions occur. Drug-induced jaundice is reversible upon withdrawal of medication therapy (2-5).

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 age 50 years, or in those over age 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 (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 (10).

Hematocrit levels must be less than 54% prior to initiation of testosterone therapy and reevaluated annually thereafter (7-9).

Androgen use for delayed puberty in males should be prescribed only by specialists who are aware of the adverse effects on bone maturation. An X-ray of the hand and wrist every 6 months will be required to determine bone age and to assess the effect of treatment on the epiphyseal centers (2-4,7).

Androgen therapy in the treatment in 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 (2-4,7).

Patients with severe obstructive sleep apnea and severe lower urinary tract symptoms are recommended not to use androgen therapy due to possible worsening of symptoms and/or even death (2).

Extreme caution should be used in patients with a history of cardiovascular disease (9).

Due to lack of clinical data on the safety or efficacy, Natesto is not recommended for use in the following patients: (6)

- 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

Women and children should not use Natesto (6). Striant is not indicated for use in women (7).

Related policies
Testosterone injection/implant, 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.*

Android, Androxy, Methitest, and Testred may be considered *medically necessary* in males who are 12 years of age or older with a delay in sexual development and/or puberty and if the conditions indicated below are met.

Android, Androxy, Jatenzo, Methitest, Natesto, Striant, Testred may be considered *medically necessary* in males who are 18 years of age and older with a deficiency of testosterone (hypogonadism) and if the conditions indicated below are met.

Android, Androxy, Methitest, Testred may be considered *medically necessary* in females with previously treated inoperable metastatic breast or mammary cancer and if the conditions indicated below are met.

Android, Androxy, Jatenzo, Methitest, Natesto, Striant, Testred may be considered *medically necessary* in patients that are 16 years of age and older with Gender Dysphoria (GD) that transitioning from female to male and if the conditions indicated below are met.

Android, Androxy, Jatenzo, Methitest, Natesto, Striant, Testred may be considered *investigational* for all other indications.

**Prior-Approval Requirements**

<table>
<thead>
<tr>
<th>Age</th>
<th>12 years of age or older</th>
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</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
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</tbody>
</table>

*For all testosterones included in this policy EXCEPT Jatenzo, Natesto, and Striant*

**Diagnosis**

Patient must have the following:

- Delay in sexual development and/or puberty
  - 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

**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. If concurrent diagnosis of benign prostatic hypertrophy (BPH), then patient will be monitored for worsening symptoms
6. Evaluation of cardiovascular risk for MI, angina, stroke
7. Absence of un-treated sleep apnea
8. **NO** dual therapy with another testosterone product

**AND NONE** of the following (for Natesto nasal product only):

- Chronic nasal conditions or alterations in nasal anatomy

**Age**
- 18 years of age or older

**Gender**
- Female only

*For all testosterones included in this policy EXCEPT Jatenzo, Natesto, and Striant*

**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

**Diagnosis**

The patient must have the following:

Gender Dysphoria (GD)
   1. Female to male transition
   2. Prescribed by an endocrinologist or transgender specialist
   3. Patient has met the DSM V criteria for GD
   4. **NO** dual therapy with another testosterone product

**Prior – Approval **\textit{Renewal Requirements}\

<table>
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<td>Diagnosis</td>
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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. Absence of worsening effects of benign prostatic hypertrophy (BPH), if present
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
18 years of age or older

Gender
Female only

Same as above

Diagnosis
The patient must have the following:

Gender Dysphoria (GD)
1. Female to male transition
2. Prescribed by an endocrinologist or transgender specialist
3. NO dual therapy with another testosterone product

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits

<table>
<thead>
<tr>
<th>Oral Testosterone</th>
<th>Gender</th>
<th>Quantity</th>
<th>Days Supply</th>
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<tbody>
<tr>
<td>Android, Methitest,</td>
<td>Male</td>
<td>450 capsules</td>
<td>90</td>
</tr>
<tr>
<td>Testred</td>
<td>Female</td>
<td>1800 capsules</td>
<td>90</td>
</tr>
<tr>
<td>Androxy</td>
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<td>180 capsules</td>
<td>90</td>
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<td>---------</td>
<td>------</td>
<td>--------------</td>
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<tr>
<td>Female</td>
<td>360 capsules</td>
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<tr>
<td>Jatenzo</td>
<td>Male (adult only)</td>
<td>158 mg, 237 mg: 180 capsules 198 mg: 360 capsules</td>
<td>90</td>
</tr>
<tr>
<td>Female (for GD only)</td>
<td>158 mg, 237 mg: 180 capsules 198 mg: 360 capsules</td>
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<tr>
<td>Natesto Nasal</td>
<td>Male (adult only)</td>
<td>66 grams (9 bottles)</td>
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</tr>
<tr>
<td>Striant buccals</td>
<td>Male (adult only)</td>
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**Duration**
6 months for all diagnoses except GD
2 years for GD

**Prior Approval Renewal Limits**

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Section: Prescription Drugs  Effective Date: October 1, 2019
Subsection: Endocrine and Metabolic Drugs  Original Policy Date: May 30, 2014
Subject: Testosterone Oral Buccal Nasal  Page: 9 of 11

Duration  
- 12 months for all diagnoses except GD
- 2 years for GD

Rationale

Summary
Testosterone is approved for replacement therapy in men for conditions associated with a deficiency of testosterone such as: hypogonadotropic hypogonadism (congenital or acquired), primary hypogonadism (congenital or acquired), and delayed puberty. In women, testosterone therapy is approved to treat metastatic breast carcinoma. Liver function and hematocrit should be monitored in all patients. In adult men, the following should be monitored: prostate-specific antigen (PSA) levels, serum testosterone concentrations, presence of prostate cancer, and worsening effects of benign prostatic hypertrophy (BPH), if present and has been evaluated for their cardiovascular risk. Calcium levels in women should be monitored. For pubescent males radiographic evidence to determine bone maturation needs to be obtained (1-8).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of the testosterone products Android, Androxy, Methitest, Natesto, Striant, and Testred while maintaining optimal therapeutic outcomes.

References
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Policy History

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<tr>
<th>Date</th>
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<tr>
<td>April 2014</td>
<td>Addition to PA</td>
</tr>
<tr>
<td>May 2014</td>
<td>Addition of nasal dosage form, Natesto, to PA</td>
</tr>
<tr>
<td>September 2014</td>
<td>Removal of absence of severe sleep apnea, severe lower urinary tract symptoms and addition of hematocrit level of 54%</td>
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<tr>
<td>August 2014</td>
<td>Revision of diagnosis for male patients 18 years or older to deficiency of testosterone/hypogonadism. Revision of renewal duration to 12 months.</td>
</tr>
<tr>
<td>October 2014</td>
<td>Change of age from 9 to 12 years of age for delayed puberty.</td>
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<tr>
<td>December 2014</td>
<td>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</td>
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<tr>
<td>March 2015</td>
<td>Annual review and reference update.</td>
</tr>
<tr>
<td>April 2015</td>
<td>Addition of assessment of cardiovascular risk to criteria</td>
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<tr>
<td>June 2015</td>
<td>Annual review</td>
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<tr>
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<td>Addition of the evaluation of cardiovascular risk for MI, angina, stroke and absence of un-treated sleep apnea and no dual therapy with another testosterone product.</td>
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<td>December 2015</td>
<td>Annual review</td>
</tr>
<tr>
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<td>Addition of Gender Dysphoria (GD) use and duration</td>
</tr>
<tr>
<td>May 2016</td>
<td>Addition of transgender specialist to GD prescriber requirement</td>
</tr>
<tr>
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<td>Policy number change from 5.08.32 to 5.30.32</td>
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<td>June 2016</td>
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### Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.