BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.30.037

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	July 2, 2014
Subject:	Testosterone Powder	**Page:**	1 of 13

Last Review Date: December 13, 2024

Testosterone powder

Description

Testosterone (cypionate, enanthate, and propionate) powder, Fluoxymesterone powder, Methyltestosterone powder

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).

Testosterone is commercially available in multiple dosage forms including oral, buccal, implant, injectable, nasal, and topical.

Regulatory Status
FDA-approved indications: (3-19)

1. 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.

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 who have been postmenopausal for 1 to 5 years, androgens may be used as secondary treatment for advancing inoperable metastatic (skeletal) mammary cancer. This has also been used to treat hormone-responsive breast cancer in premenopausal women post- oophorectomy.

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 (24).

Topical testosterone includes a boxed warning of secondary exposure: Virilization has been reported in children who were secondarily exposed to transdermal testosterone. Children should avoid contact with unwashed or unclothed application sites in men using transdermal testosterone (3-9).

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 (3-19).

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 below 300 ng/dL on both days in order to be considered for therapy (23).

Hematocrit levels must be less than 54% prior to initiation of testosterone therapy and reevaluated annually thereafter (3-19).

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 (12-19).

Androgen therapy in treatment for 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 (16).

Extreme caution should be used in patients with a history of cardiovascular disease (6).

Due to lack of controlled studies in women and potential virilizing effects, the nasal formulation is not indicated for use in women. Safety and efficacy of the nasal formulation has not been established in pediatric patients less than 18 years of age. Improper use may result in acceleration of bone age and premature closure of epiphyses (11).

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).

Hormone replacement therapy is prescribed to post-menopausal women for their effects in preventing postmenopausal osteoporosis (20). Among the progestogens available to the prescriber and recommended to be added to estrogen replacement therapy (ERT) are the molecules derived from testosterone. Low doses of any type of progestogen could be both protective of the target organs and devoid of harmful effects. The use of ERT affords protection against osteoporosis and cardiovascular disease (21). The addition of testosterone to HRT has shown a significant increase in hip bone mineral density (22).

Safety and efficacy of testosterone transdermal in patients younger than 18 years have not been established (3-19).

Related policies
Testosterone Injectable/Implant, Testosterone Oral, 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.

Testosterone powder may be considered **medically necessary** if the conditions indicated below are met.

Testosterone powder may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 12 years of age or older
Gender Male only

Diagnosis

Patient must have the following:

Delay in sexual development and/or puberty
a. **NO** dual therapy with another testosterone product

AND ALL of the following:
1. The requested dosage form is commercially available
2. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength of the requested dosage form

AND ONE of the following:
1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available products' inactive ingredient(s) of preferred dosage form

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 only

Diagnosis

Patient must have the following:

Deficiency of testosterone (hypogonadism)

AND ALL of the following:

1. The requested dosage form is commercially available
2. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength for the requested dosage form
3. Two morning total testosterone levels less than 300 ng/dL on different days
4. Patients over 40 years of age must have baseline PSA less than 4 ng/ml
    a. Prostatectomy patients excluded from the requirement
5. Absence of prostate cancer / palpable prostate nodules
6. Hematocrit level less than 54%
7. If concurrent diagnosis of benign prostatic hypertrophy (BPH), then patient will be monitored for worsening symptoms
8. Evaluation of cardiovascular risk for MI, angina, stroke
9. Absence of un-treated sleep apnea
10. **NO** dual therapy with another testosterone product

AND ONE of the following:

1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available equivalent products' inactive ingredient(s) of preferred dosage form

Age	18 years of age or older
Gender	Female only

Diagnosis

Patient must have **ALL** of the following:

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

AND ALL of the following:

1. The requested dosage form is commercially available
2. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength for the requested dosage form

AND ONE of the following:

1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available equivalent products' inactive ingredient(s) of preferred dosage form

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

Patient must have the following:

Gender Dysphoria (GD)

AND ALL of the following:

1. Female to male transition
2. **NO** dual therapy with another testosterone product
3. The requested dosage form is commercially available
4. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength of the requested dosage form

AND ONE of the following:

1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available products' inactive ingredient(s) of preferred dosage form

Prior – Approval *Renewal* Requirements

Age 12 years of age or older
Gender Male only

Diagnosis

Patient must have the following:

Delay in sexual development and/or puberty
a. **NO** dual therapy with another testosterone product

AND ALL of the following:
1. The requested dosage form is commercially available
2. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength of the requested dosage form

AND ONE of the following:
1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available products' inactive ingredient(s) of preferred dosage form

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. Total testosterone levels of 800 ng/dL or less
2. Absence of worsening effects of benign prostatic hypertrophy (BPH), if present
3. The requested dosage form is commercially available
4. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength for the requested dosage form
5. Re-evaluation of cardiovascular risk for MI, angina, stroke
6. **NO** dual therapy with another testosterone product

AND ONE of the following:

1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available products' inactive ingredient(s) of preferred dosage form

AND confirmation that the following will be 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

Diagnosis

Patient must have **ALL** of the following:

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

AND ALL of the following:

1. The requested dosage form is commercially available
2. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength for the requested dosage form

AND ONE of the following:

1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available products' inactive ingredient(s) of preferred dosage form

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

Patient must have the following:

Gender Dysphoria (GD)

AND ALL of the following:

1. Female to male transition
2. **NO** dual therapy with another testosterone product
3. The requested dosage form is commercially available
4. The requested dose/ strength is **NOT** equal to or exceeding the FDA-approved dose/strength of the requested dosage form

AND ONE of the following:

1. The patient has tried and failed at least one other commercially available product other than the requested dosage form and the requested dosage form
2. The patient has an intolerance to the commercially available products' inactive ingredient(s) of preferred dosage form

Policy Guidelines

Pre - PA Allowance

This drug is a covered benefit for female members greater than 50 years of age

Prior - Approval Limits

Duration 6 months for all diagnoses except GD
2 years for GD

Prior – Approval *Renewal* Limits

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

Rationale

Summary

Testosterone is approved for testosterone 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 is recommended to be monitored: prostate-specific antigen (PSA) levels, serum testosterone concentrations, prostate specific antigen (PSA), presence of prostate cancer, and worsening effects of benign prostatic hypertrophy (BPH), if present, and assessment of their cardiovascular risk is recommended. Calcium levels in women should be monitored. For pubescent males, radiographic evidence to determine bone maturation needs to be obtained (1-6).

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

References

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Policy History

Date	Action
June 2014	Addition to PA 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 diagnoses, standard allowance for women over 50, commercially available product and renewal duration
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
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 un-treated sleep apnea and no dual therapy with another testosterone product and intolerance or contraindication to the equivalent commercially available product and one other commercially available product. Clarified the requested dose/ strength is not equal to or exceeding the FDA- approved dose/strength for the requested dosage form
September 2015	Annual review
December 2015	Annual review Addition of Gender Dysphoria (GD) use and duration
March 2016	Annual review Policy number change from 5.08.37 to 5.30.37
May 2016	Addition of transgender specialist to GD prescriber requirement
June 2016	Annual review
September 2016	Annual 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 editorial review and reference update
March 2019	Annual review
July 2019	Changed approval duration for gender dysphoria from lifetime to 2 years
September 2019	Annual review
December 2020	Annual review and reference update
December 2021	Annual review and reference update
September 2022	Annual review
December 2022	Annual review. Removed GD requirements of meeting DSM criteria and being prescribed by an endocrinologist or transgender specialist
September 2023	Annual review
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.