Testosterone Products

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO067

Description

Testosterone is the primary endogenous androgen responsible for promoting growth and development of male sex organs and the maintenance of secondary sex characteristics.

Length of Authorization

- Initial:
  i. **For delayed puberty in males (e.g. constitutional growth delay)**: six months
  ii. **All other indications**: 12 months
- Renewal:
  i. **For delayed puberty in males (e.g. constitutional growth delay)**: six months; NOT to exceed 18 months of treatment
  ii. **All other indications**: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
testosterone (Androderm)	Primary hypogonadism; hypogonadotropic hypogonadism; metastatic breast cancer; delayed puberty (males) (e.g. constitutional growth delay)	2 mg/24-hour patch	60 patches/30 days
		4 mg/24-hour patch	30 patches/30 days
testosterone (Axiron)		30 mg actuation roll-on solution	110 ml/30 days
testosterone (Natesto)		5.5 mg/actuation nasal gel	22 g/30 days
testosterone (Striant)		30 mg buccal system	60 buccal systems/ 30 days
testosterone 1% (AndroGel, Testim, Vogelxo)		25 mg/2.5gm gel	300 g/30 days
		50 mg/5gm gel	300 g/30 days
		12.5 mg/actuation gel pump	300 g/30 days
testosterone 1.62% (AndroGel, Vogelxo)		20.25 mg/ 1.25 gm gel packet	150 g/30 days
		40.5 mg/2.5gm gel packet	150 g/30 days
		20.25 mg/actuation gel pump	150 g/30 days
testosterone 2% (Fortesta)		10mg/ actuation gel	120 g /30 days
testosterone cypionate (Depo-testosterone)		100mg/ mL intramuscular injection	8 mL/28 days
		200mg/ mL intramuscular injection	4 mL/28 days

Testosterone enanthate	Primary hypogonadism; hypogonadotropic hypogonadism; metastatic breast cancer; delayed puberty (males) (e.g. constitutional growth delay)	200 mg/mL intramuscular injection	4 mL/28 days
testosterone enanthate (Xyosted)	Primary hypogonadism; hypogonadotropic hypogonadism	50 mg/ 0.5 mL subcutaneous solution autoinjector	5 mL/28 days
		75 mg/0.5 mL subcutaneous solution autoinjector	5 mL/28 days
		100 mg/ 0.5 mL subcutaneous solution autoinjector	4 mL/28 days
testosterone undecanoate (Jatenzo, Tlando, Kyzatrex)	Primary hypogonadism; hypogonadotropic hypogonadism	100 mg capsule	60 capsules/30 days
		150 mg capsule	120 capsules/30 days
		158 mg capsule	120 capsules/30 days
		198 mg capsule	120 capsules/30 days
		200 mg capsule	120 capsules/30 days
		237 mg capsules	60 capsules/30 days
		112.5mg capsules	120 capsules/30 days
methyltestosterone (Methitest)	Primary hypogonadism; hypogonadotropic hypogonadism; metastatic breast cancer; delayed puberty (males) (e.g., constitutional growth delay)	10 mg tablets or capsules	Men: 150 tablets /30 days Women: 600 tablets/30 days

Initial Evaluation

I. **Testosterone products** may be considered medically necessary when the following criteria are met:

A. A diagnosis of one of the following:

1. **Gender dysphoria; OR**
2. **Delayed puberty in males (e.g. constitutional growth delay); AND**
   - i. Age is 14 years or older; **AND**
   - ii. Prescribed by, or in consultation with, an endocrinologist; **AND**
   - iii. Request is for generic testosterone enanthate or cypionate; **OR**
     - a. Treatment with one of the following has been ineffective, contraindicated, or not tolerated:

i. generic testosterone enanthate; **OR**
ii. generic testosterone cypionate; **OR**

3. **Metastatic breast cancer; AND**
   i. Age is 18 years or older; **AND**
   ii. Prescribed by, or in consultation with, an oncologist; **AND**
   iii. Request is for generic testosterone enanthate or cypionate; **OR**
      a. Treatment with one of the following has been ineffective, contraindicated, or not tolerated:
         i. Generic injectable testosterone cypionate; **OR**
         ii. Generic injectable testosterone enanthate; **OR**
4. **Primary or Secondary Hypogonadism; AND**
   i. Diagnosis further defined as one of the following:
      a. Primary hypogonadism (testicular failure) due to: Klinefelter syndrome (KS), cryptorchidism, orchiectomy, vanishing testes syndrome, chemotherapy affecting or radiation to the testes, testicular trauma, torsion, infectious orchitis, HIV infection, anorchia syndrome, or myotonic dystrophy; **OR**
      b. Secondary hypogonadism (pituitary-hypothalamic hypogonadism) due to: hypothalamic or pituitary tumor, iron overload syndromes, idiopathic hypogonadotropic hypogonadism, hyperprolactinemia, head trauma, pituitary surgery, or radiation; **AND**
   ii. (For adults only) Two sub-normal testosterone concentration levels taken on two separate mornings while fasting; **AND**
   iii. Request is for generic injectable testosterone or generic topical testosterone (generic AndroGel); **OR**
      a. Treatment with all of the following has been ineffective, contraindicated, or not tolerated**:**
         i. Generic injectable testosterone; **AND**
         ii. Generic topical testosterone (generic AndroGel);

II. Testosterone is considered not medically necessary when used for all other conditions, including
   A. Men with low testosterone concentration and without clinical symptoms and signs consistent with testosterone deficiency. The routine assessment of testosterone level in the absence of hypogonadal symptoms is not advised.
   B. Men with a single, sub-normal testosterone concentration that is not repeatable per the U.S. Endocrine Society.
   C. Men with symptoms of hypogonadism, however, present with testosterone level within normal range upon initial presentation.

III. Testosterone is considered investigational when used for all other conditions, including but not limited to:
   A. Age-related hypogonadism in adults
   B. Men with type 2 diabetes mellitus with low testosterone for the purpose of improving glycemic control
   C. For the healing of fracture
   D. Functional uterine bleed
   E. Treatment of weight loss unrelated to HIV-wasting

Renewal Evaluation

I. Member has received a previous prior authorization approval for a brand testosterone or high cost generic agent through this health plan or has been established on therapy from a previous health plan; **AND**

II. Member has exhibited improvement or stability of disease symptoms from baseline (e.g., improved mood, decreased fatigue, no or diminished signs of gynecomastia, endogenous testosterone levels increasing after stopping therapy, testes enlargement); **AND**

III. (For Adults Only) One testosterone level within mid-normal range taken within the last 12 months that indicates improvement from baseline levels (pre-treatment); **AND**

IV. If diagnosis of **Delayed puberty (e.g. constitutional growth delay):**
   a. Has NOT had more than 18 months of treatment.

Supporting Evidence

I. Per the 2018 AUA guidelines, diagnosis of hypogonadism should be confirmed prior to initiating testosterone replacement therapy. Testosterone levels should be drawn ideally between 8 and 10 AM while fasting due to the diurnal fluctuation of testosterone and its sensitivity to glucose ingestion. A separate, confirmatory measurement is recommended. Thirty percent of men with an initial testosterone concentration in the hypogonadal range can have a measurement within the normal range on repeat measurement.

II. The Endocrine Society strongly advises against “trial periods” of testosterone in men with a single sub-normal testosterone concentration and vague symptoms of deficiency.

III. The benefit of increasing testosterone concentration has only been shown in patients with organic hypogonadism due to disorders of the hypothalamus, pituitary or testes.

IV. In patients within normal range, or have low testosterone concentration due to age, obesity, or otherwise, the benefit of increased testosterone has not been shown. Rather, in this patient population with low testosterone and an intact gonadal system, increasing testosterone is associated with an increase of certain health risks, including cardiovascular disease. Due to this, the FDA has required manufacturers to label testosterone products warning of the increased risk for heart attack and stroke.

V. Lower limit of the normal total testosterone (TT) to the CDC standard in healthy, non-obese young men is 264 ng/dL (9.2 nmol/L).The lower limit of normal range is considered to be <150 ng/dL, with a noted normal range of 200 to 400 ng/dL. For adult patients, it is recommended to confirm low T concentrations as 30% of men will present with a normal T concentration value when measured again.

VI. Testosterone replacement therapy is subject to abuse at doses higher than recommended for approved indications and in combination with other anabolic androgenic steroids. Abuse-related adverse events include cardiac arrest, myocardial infarction, hypertrophic cardiomyopathy, congestive heart failure, hepatotoxicity, and serious psychiatric complaints.

VII. Guidelines advise to monitor testosterone levels 3-6 months after initiation of therapy and then annually. Serum testosterone concentrations should be brought into the mid-normal range. Testosterone levels may vary depending on dosage form.

VIII. Boys undergo puberty development around the age of 14. Bone age is delayed by 2 years or more in bone maturation in patients with delayed puberty, though not a diagnostic approach but characteristic of disease. Delayed puberty can be treated with short term hormonal therapy by administering testosterone enanthate or cypionate (50 mg IM once monthly) for six months and then reassess endogenous gonadal function and size six months later. Pubertal development was indicated by testicular enlargement and increasing testosterone concentrations after the cessation of therapy. It is unusual for a boy with delayed puberty to require more than two three- to six-month courses of testosterone therapy before spontaneous puberty occurs.

IX. Pediatric testosterone levels are to be very low or not present as boys may not have functioning testes or without testes. Guidelines recommend testing for other blood tests including LH, FSH, TSH. It is not reasonable nor recommended to require pediatric patients to check multiple blood tests.

X. Generic injectable testosterone is primarily used in delayed puberty due to amount of reliable data available; other formulations or salts have not been studied in patients under the age of 18 and are otherwise not readily recommended.

XI. Use of bone age is indicated as characteristic of delayed puberty, but not an absolute indication. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

XII. Androgens in metastatic breast cancer (women that are 1-5 years postmenopausal advanced inoperable metastatic breast cancer or in premenopausal women who have benefited from oophorectomy with hormone response tumors) is rare, including testosterone use. Androgens were found inferior to high-dose estrogens, even though response rates are high. Additionally, if androgen therapy is required, the preferred formulation is fluoxymesterone.

Investigational or Not Medically Necessary Uses

I. Testosterone products are considered not medically necessary when used for conditions or settings listed below:
   A. Men with low testosterone concentration and without clinical symptoms and signs consistent with testosterone deficiency. The routine assessment of testosterone level in the absence of hypogonadal symptoms is not advised.
   B. Men with a single, sub-normal testosterone concentration that is not repeatable per the U.S. Endocrine Society.
   C. Men with symptoms of hypogonadism, however, present with testosterone level within normal range upon initial presentation.

II. Testosterone products have not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Age-related hypogonadism
      i. The role of testosterone replacement to treat the natural decline in serum testosterone common in men over the age of 60, without identified pituitary or hypothalamic disease, is uncertain.
   B. Men with type 2 diabetes mellitus with low testosterone for the purpose of improving glycemic control
   C. For the healing of fracture
   D. Functional uterine bleed
   E. Treatment of weight loss unrelated to HIV-wasting

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Appendix:

I. Testosterone lab monitoring assessment based on dosage form

Dosage Form	Recommendation
Injectable enanthate/cypionate	Adjust dose or frequency if >600 or <350 ng/dL
Transdermal gels	Assess 2-8 hours following application
Transdermal patches	Assess 3-12 hours after application
Buccal bioadhesive tablet	Assess immediately before or after fresh application
Oral undecanoate	Assess 3-5 hours after ingestion with fat-containing meal
Injectable undecanoate	Assess at end of the dosing interval prior to next injection

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated Androgel 1% formulation in QL table to read 12.5 mg/actuation	07/2024
Added new medication Tlando capsules. Added methyltestosterone (Methitest) and accompanying indications. Removed Aveed® as it is HCP administered medication. Updated initial criteria to remove including removal of age requirement and pertinent negative cancer assessments in hypogonadism use. Added renewal criteria. Added criteria for delayed puberty in males and metastatic breast cancer. Updated policy name.	09/2022
Change to policy format; added supplementary evidence section; updated references	07/2018
Add methyltestosterone to policy, remove DDID column from QL section	12/2019
Policy created	06/2019