Pharmacy Policy Bulletin: J-0197 Testosterone (Androgens) – Commercial and Healthcare Reform	
Number: J-0197	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** 1. Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0197-024	**Original Date:** 06/04/2014
Effective Date: 07/25/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Androderm (testosterone) patch • Androgel (testosterone) packet, gel • Depo-Testosterone (testosterone cypionate) intramuscular oil • Fortesta (testosterone) gel • Jatenzo (testosterone undecanoate) capsule • Kyzatrex (testosterone undecanoate) • Methitest (methyltestosterone) tablet • methyltestosterone capsule • Natesto (testosterone) nasal gel • Testim (testosterone) gel • Testone CIK (testosterone cypionate) kit • Testopel (testosterone) subcutaneous implant pellets • testosterone enanthate intramuscular oil • testosterone subcutaneous implant/pellet • testosterone topical solution • Tlando (testosterone undecanoate) capsule • Undecatrex (testosterone undecanoate) capsule • Vogelxo (testosterone) gel • Xyosted (testosterone enanthate) subcutaneous solution

FDA-Approved Indication(s):	• testosterone (Androderm, Androgel, Fortesta, Natesto, Testim, testosterone topical solution, Vogelxo), testosterone cypionate (Depo-Testosterone, Testone CIK), testosterone undecanoate (Jatenzo, Kyzatrex, Tlando, Undecatrex), testosterone enanthate (Xyosted) ○ Males ▪ Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range. ▪ 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. • testosterone (Testopel) ○ Males ▪ Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome; or orchiectomy. ▪ Hypogonadotropic hypogonadism (congenital or acquired): gonadotropic LHRH deficiency, or pituitary - hypothalamic injury from tumors, trauma or radiation. If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sex characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. ▪ Androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. 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 taken every 6 months to assess the effect of treatment on epiphyseal centers. • methyltestosterone (Methitest), testosterone enanthate intramuscular oil ○ Males ▪ Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsions, orchitis, vanishing testis syndrome; or orchidectomy. ▪ Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary hypothalamic injury from tumors, trauma, or radiation. Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance. If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary

	sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty. Safety and efficacy of methyltestosterone in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established. ▪ Androgens may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. 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. o Females ▪ Androgens may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are 1 to 5 years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or antiestrogen therapy. 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. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

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. • **Gender Dysphoria** o For individuals with a diagnosis of gender dysphoria or gender identity disorder, gender-affirming therapies, including hormone-replacement therapy, have been defined as medically necessary. Improvement in various psychosocial measures has been reported in individuals receiving gender-affirming therapies. o The Gender Dysphoria/Gender Incongruence Guidelines from the Endocrine Society acknowledge it may be appropriate to initiate treatment in adolescents under 16 years old. Adolescents under 16 years old should be treated by clinicians competent in the evaluation and induction of pubertal development. Clinicians with these competencies may include, but are not limited to pediatricians, family medicine physicians, and endocrinologists. o Prescribing gender affirming hormones is within the scope primary care physicians, obstetricians-gynecologists, endocrinologists, advanced practice nurses, and physician assistants. Depending on the practice setting and jurisdiction, other providers with prescriptive rights such as nurse midwives may also be appropriate to prescribe and manage this care. • **Hypogonadism**

- Primary hypogonadism can include Klinefelter's Syndrome, vanishing testis syndrome, orchitis, injury to the testicles, and cancer treatment (chemotherapy or radiation).
- Secondary hypogonadism can include pituitary disorders and treatment of pituitary tumors (surgery or radiation).
- The American Urological Association Clinical Guidelines on the Evaluation and Management of Testosterone Deficiency state that the clinical diagnosis of testosterone deficiency is only made when patients have low total testosterone levels combined with symptoms and/or signs.
- The Endocrine Society Testosterone Therapy in Men with Hypogonadism guidelines state that a diagnosis of hypogonadism should be made only in men with symptoms and signs consistent with testosterone deficiency and unequivocally and consistently low serum testosterone concentrations. Low testosterone concentrations occur frequently without symptoms or signs of testosterone deficiency, and these low levels (alone) do not establish a diagnosis of hypogonadism.
- Symptoms can be classified as specific, suggestive, and non-specific in the diagnosis of testosterone deficiency (TD). These symptoms vary and are modified by age, comorbid illness, severity and duration of testosterone deficiency, variations in androgen sensitivity, and previous testosterone therapy (Table 1).

Table 1: Symptoms and Signs Suggestive of Testosterone Deficiency in Males

Specific Symptoms	• Incomplete or delayed sexual development • Loss of body (axillary and pubic) hair • Very small testes
Suggestive Symptoms and Signs	• Reduced sexual desire (libido) and activity • Breast discomfort, gynecomastia • Eunuchoidal body proportions • Inability to father children, low sperm count • Height loss, low-trauma fracture, low bone mineral density • Hot flushes, sweats

- **Testosterone Levels**
  - Testosterone production occurs in bursts approximately six times per day, with peak levels in the early morning (around 8 am - 10 am) and troughs in the early afternoon to late evening. Two (2) separate measurements are required due to intra-individual variability.
  - Serum total testosterone levels should be used primarily to diagnose hypogonadism in all patients. Serum total testosterone comprises of free testosterone (circulating freely in plasma) and bound testosterone, to either albumin or SHBG.
  - Free testosterone or bioavailable testosterone (BAT) should be reserved for patients in which the serum total testosterone level does not correspond with clinical presentation, the difference between the first two total testosterone levels differ by 20%, or the patient has at least one diagnosed condition that is associated with altering sex-hormone-binding globulin (SHBG) levels.
- There is no evidence demonstrating that any one testosterone replacement therapy (TRT) product is safer or more effective than other TRT products. There are no studies that directly compare the clinical effects of different TRT products.
- Prescribing Considerations:
  - TRT should not be started in men who are at high risk for, or who have, prostate cancer.

	○ Safety and efficacy of TRT in men with age-related hypogonadism have not been established. Safety and efficacy of TRT 1.62% in males less than 18 years old have not been established. • *An initial request is defined as the initial testosterone request (including appeals) when there is no record of a prior approval for the requested product.

Approval Criteria

I. Initial Authorization

A. Hypogonadism in Males

1. Initial request*; New to testosterone therapy

When a benefit, coverage of testosterone products may be approved when all of the following criteria are met **(a. through f.)**:

a. The member is male.

b. The member has a diagnosis of hypogonadism (ICD-10: E29.1).

c. The member meets one (1) of the following criteria **(i. through v.)**:

i. Primary or secondary hypogonadism with testicular failure due to one (1) of the following **(A) through J))**:

A) Bilateral torsions
B) Chemotherapy damage
C) Cryptorchidism
D) Klinefelter's syndrome
E) Orchitis
F) Radiation damage
G) Single orchidectomy
H) Surgery damage
I) Toxic damage
J) Vanishing testis syndrome

ii. Primary or secondary hypogonadism in males with symptoms of low testosterone (see Table 1 for symptoms).

iii. The member has a diagnosis of secondary hypogonadism due to hypopituitarism (pituitary hormone deficiencies).

iv. The member is experiencing weight loss due to HIV-infection.

v. The member is on chronic steroid treatment.

d. The provider submits documentation of low testosterone levels (specifically, laboratory results, chart notes) supported by one (1) of the following criteria **(i., ii., or iii.)**:

i. Two (2) morning total testosterone levels drawn before 11:00 a.m. < 264 ng/dL (9.2 nmol/L) or below the normal range per the laboratory reference range.

ii. The member meets all of the following criteria **(A) and B))**:

A) Two (2) morning total testosterone levels drawn before 11:00 a.m. < 300 ng/dL (10.4 nmol/L) or near the lower limit of the normal range per the laboratory reference range (bottom 20 percent of the reference range).

B) Two (2) morning free testosterone levels drawn before 11:00 am < 65 pg/mL (225 pmol/L) or below the normal range per the laboratory reference range.

iii. The provider submits documentation (specifically, lab results, chart notes) that the member is not producing any testosterone.

e. If the request is for brand Methitest, the member has experienced therapeutic failure or intolerance to plan-preferred, generic methyltestosterone capsules.

f. If the request is for brand Androgel 1%, Androgel 1.62%, Fortesta, Testim, Vogelxo, Natesto, Jatenzo, Kyzatrex, Tlando, Undecatrex, or Xyosted, the member has experienced therapeutic failure or intolerance to one (1) plan-preferred, generic testosterone topical product.

2. **Initial Request*; Established on testosterone therapy**
   When a benefit, coverage of continuation therapy of testosterone products may be approved when all of the following criteria are met **(a. through g.)**:
   - **a.** The member is male.
   - **b.** The member has a diagnosis of hypogonadism (ICD-10: E29.1).
   - **c.** The member meets one (1) of the following criteria **(i. through v.)**:
     - **i.** Primary or secondary hypogonadism with testicular failure due to one (1) of the following **(A) through J))**:
       - **A)** Bilateral torsions
       - **B)** Chemotherapy damage
       - **C)** Cryptorchidism
       - **D)** Klinefelter's syndrome
       - **E)** Orchitis
       - **F)** Radiation damage
       - **G)** Single orchidectomy
       - **H)** Surgery damage
       - **I)** Toxic damage
       - **J)** Vanishing testis syndrome
     - **ii.** Primary or secondary hypogonadism in males with symptoms of low testosterone (see Table 1 for symptoms).
     - **iii.** The member has a diagnosis of secondary hypogonadism due to hypopituitarism (pituitary hormone deficiencies).
     - **iv.** The member is experiencing weight loss due to HIV-infection.
     - **v.** The member is on chronic steroid treatment.
   - **d.** The member meets one (1) of the following criteria **(i. or ii.):**
     - **i.** The provider submits documentation of low pre-treatment testosterone levels (specifically, laboratory results, chart notes) supported by one (1) of the following criteria **(A), B), or C)**:
       - **A)** Two (2) pre-treatment morning total testosterone levels drawn before 11:00 a.m. < 264 ng/dL (9.2 nmol/L) or below the normal range per the laboratory reference range.
       - **B)** The member meets all of the following criteria **(1) and 2)):**
         - **1)** Two (2) morning pre-treatment total testosterone levels drawn before 11:00 a.m. < 300 ng/dL (10.4 nmol/L) or near the lower limit of the normal range per the laboratory reference range (bottom 20 percent of the reference range).
         - **2)** Two (2) morning pre-treatment free testosterone levels drawn before 11:00 am < 65 pg/mL (225 pmol/L) or below the normal range per the laboratory reference range.
       - **C)** The member is not producing any testosterone.
     - **ii.** The provider attests the member's pre-treatment medical records are not available and meets the following criterion **(A)):**
       - **A)** The provider attests the member had at least one (1) low pretreatment serum testosterone level (specifically, < 300 ng/dL).
   - **e.** The provider submits documentation of a testosterone level within the past 12 months (specifically, laboratory results, chart notes) and meets one (1) of the following criteria **(i. or ii.):**
     - **i.** The member's testosterone level is within normal limit (specifically, 300 to 1,000 ng/dL).
     - **ii.** The member's testosterone level is out of normal limit and the provider attests the dosage is being adjusted.
   - **f.** If the request is for brand Methitest, the member has experienced therapeutic failure or intolerance to plan-preferred, generic methyltestosterone capsules.

g. If the request is for brand Androgel 1%, Androgel 1.62%, Fortesta, Testim, Vogelxo, Natesto, Jatenzo, Kyzatrex, Tlando, Undecatrex, or Xyosted, the member has experienced therapeutic failure or intolerance to one (1) plan-preferred, generic testosterone topical product.

B. Double Orchidectomy

When a benefit, coverage of testosterone products may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is male.
2. The member has a diagnosis of primary or secondary hypogonadism with testicular failure (ICD-10: E29.1) due to double orchidectomy.
3. If the request is for brand Methitest, the member has experienced therapeutic failure or intolerance to plan-preferred, generic methyltestosterone capsules.
4. If the request is for brand Androgel 1%, Androgel 1.62%, Fortesta, Testim, Vogelxo, Natesto, Jatenzo, Tlando, Kyzatrex, Undecatrex, or Xyosted, the member has experienced therapeutic failure or intolerance to one (1) plan-preferred, generic testosterone topical product.

C. Gender Dysphoria or Gender Identify Disorder

When a benefit, coverage of testosterone products may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of gender dysphoria or gender identity disorder (ICD-10: F64).
2. If the member is 15 years of age or younger, the member meets the following criterion **(a.)**:
   a. The drug is prescribed by a clinician competent in the evaluation and induction of pubertal development.

D. Palliative Treatment in Metastatic Breast Cancer

When a benefit, coverage of testosterone products may be approved when all of the following criteria are met **(1. through 5.)**:

1. The member is female.
2. The member has a diagnosis of metastatic breast cancer (ICD-10: C50).
3. The drug is used for palliative treatment.
4. The request is for one (1) of the following agents **(a., b., or c.)**:
   a. testosterone cypionate when administered as an intramuscular injection
   b. testosterone enanthate oil for injection
   c. methyltestosterone
5. If the request is for brand Methitest, the member has experienced therapeutic failure or intolerance to plan-preferred, generic methyltestosterone capsules.

II. Reauthorization

A. Subsequent request; Established on testosterone therapy for hypogonadism

When a benefit, reauthorization of testosterone products may be approved when all of the following criteria are met **(1., 2., and 3.)**:

1. The prescriber attests that the member has experienced a positive clinical response to testosterone therapy.
2. The member requires continued therapy with a testosterone product.
3. The provider submits documentation of a testosterone level within the past 12 months (specifically, laboratory results, chart notes) and meets one (1) of the following criteria **(a. or b.):**
   a. The member's testosterone level is within normal limit (specifically, 300 to 1,000 ng/dL).
   b. The member's testosterone level is out of normal limit and the provider attests the dosage is being adjusted.

B. Subsequent request; Established on testosterone therapy for double orchidectomy, gender dysphoria or gender identity disorder, or palliative treatment in metastatic breast cancer

When a benefit, reauthorization of testosterone products may be approved when all of the following criteria are met **(1. and 2.)**:

1. The prescriber attests that the member has experienced a positive clinical response to testosterone therapy.
2. The member requires continued therapy with a testosterone product.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of their FDA-approved indications should be denied based on the lack of clinical data to support their effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

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