Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for testosterone products under the patient's prescription drug benefit.

Description:

FDA-approved Indications

AndroGel, Fortesta, Natesto, Testim, testosterone topical gel, testosterone topical solution, Vogelxo

Topical and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

- 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): 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.

Limitations of Use:

- Safety and efficacy of topical and nasal testosterone products in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of topical and nasal testosterone products in males less than 18 years old have not been established.
- Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure.

Azmiro

Azmiro is indicated for testosterone replacement therapy in males in conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchiectomy, Klinefelter's syndrome, or toxic damage from alcohol

or heavy metals, 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): 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.

Limitations of Use
- Safety and efficacy of Azmiro in men with "age- related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of Azmiro in pediatric patients below the age of 12 years have not been established.

Depo-Testosterone
Depo-Testosterone Injection is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone.
- Primary hypogonadism (congenital or acquired)-testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchiectomy.
- Hypogonadotropic hypogonadism (congenital or acquired)-gonadotropic or LHRH deficiency or pituitary- hypothalamic injury from tumors, trauma or radiation.

Safety and efficacy of Depo-Testosterone (testosterone cypionate) in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Jatenzo, Kyzatrex, Tlando, Undecatrex
Testosterone undecanoate is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
- 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 (follicle stimulating hormone (FSH), luteinizing hormone (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.

Limitations of Use
Safety and efficacy of testosterone undecanoate in males less than 18 years old have not been established.

Testopel
MALES
Androgens are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

- 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.
Safety and efficacy of Testopel (testosterone pellets) 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 taken every 6 months to assess the effect of treatment on epiphyseal centers.

Testosterone Enanthate Injection
Males
Testosterone Enanthate Injection (generic Delatestryl), USP is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.
Primary hypogonadism (congenital or acquired) - Testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

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 Testosterone Enanthate Injection (generic Delatestryl), USP in men with age-related hypogonadism have not been established.
Delayed puberty - Testosterone Enanthate Injection (generic Delatestryl), USP 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 six months to assess the effect of treatment on the epiphyseal centers.

Females
Metastatic mammary cancer - Testosterone Enanthate Injection (generic Delatestryl), USP may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five 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 anti-estrogen therapy. This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to a have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

Xyosted
Xyosted (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

- Primary hypogonadism (congenital or acquired): testicular failure due to 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): 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 low or normal range.

Limitations of Use:
- Safety and efficacy of Xyosted in males less than 18 years old have not been established.

Compendial Uses
Gender dysphoria (also known as transgender and gender diverse (TGD) persons)

Applicable Drug List:

Preferred:
TESTOSTERONE CYPIONATE IM SOLUTION 100 mg/ml
TESTOSTERONE CYPIONATE IM SOLUTION 200 mg/ml
TESTOSTERONE ENANTHATE IM SOLUTION 200 mg/ml
TESTOSTERONE TRANSDERMAL GEL 20.25 mg/act (1.62%)

Nonpreferred:
ANDRODERM
ANDROGEL
AZMIRO
DELATESTRYL
DEPO-TESTOSTERONE
FORTESTA
JATENZO

KYZATREX
NATESTO
TESTIM
TESTOPEL
TESTOSTERONE TRANSDERMAL GEL 10 mg/act (2%)
TESTOSTERONE TRANSDERMAL GEL 12.5 mg/act (1%)
TESTOSTERONE TRANSDERMAL GEL 25 mg/2.5gm (1%)
TESTOSTERONE TRANSDERMAL GEL 50 mg/5gm (1%)
TESTOSTERONE TRANSDERMAL SOLUTION 30MG/ACT
TLANDO
UNDECATREX
VOGELXO
XYOSTED

Policy/Guideline:

Note: Requests for non-preferred agents require that the patient is unable to take the required number of preferred formulary alternatives for the given diagnosis, due to a trial and inadequate treatment response, or intolerance, or a contraindication

Coverage Criteria

Breast Cancer (Hormone-Responsive Tumor)
Authorization may be granted when the requested drug is being prescribed for a premenopausal patient with breast cancer who has benefited from oophorectomy AND is considered to have a hormone-responsive tumor when ALL of the following criteria are met:

- The requested drug is NOT being prescribed for age-related hypogonadism (also referred to as late-onset hypogonadism).
- The request is for intramuscular testosterone enanthate injection (generic Delatestryl).

Delayed Puberty
Authorization may be granted when the requested drug is being prescribed for delayed puberty when ALL of the following criteria are met:

- The requested drug is NOT being prescribed for age-related hypogonadism (also referred to as late-onset hypogonadism).
- The request is for intramuscular testosterone enanthate injection (generic Delatestryl) OR testosterone propionate implant pellet (Testopel).

Gender Dysphoria

Authorization may be granted when the requested drug is being prescribed for gender dysphoria in a patient who is able to make an informed decision to engage in hormone therapy when ALL of the following criteria are met:

- The requested drug is NOT being prescribed for age-related hypogonadism (also referred to as late-onset hypogonadism).
- The patient's comorbid conditions are reasonably controlled.
- The patient has been educated on ANY contraindications AND side effects to therapy.
- Before the start of therapy, the patient has been informed of fertility preservation options.
- If the patient is less than 18 years of age, then ALL of the following criteria are met:
    - The requested drug is prescribed by, or in consultation with, a provider specialized in the care of transgender youth (e.g., pediatric endocrinologist, family or internal medicine physician, obstetrician-gynecologist), that has collaborated care with a mental health provider.
    - The patient has reached, or has previously reached, Tanner stage 2 of puberty or greater.

Inoperable Metastatic Breast Cancer

Authorization may be granted when the requested drug is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND had an incomplete response to other therapy for metastatic breast cancer when ALL of the following criteria are met:

- The requested drug is NOT being prescribed for age-related hypogonadism (also referred to as late-onset hypogonadism).
- The request is for intramuscular testosterone enanthate injection (generic Delatestryl).

Primary or Hypogonadotropic Hypogonadism

Authorization may be granted when the requested drug is being prescribed for primary or hypogonadotropic hypogonadism and ALL of the following criteria are met:

- The requested drug is NOT being prescribed for age-related hypogonadism (also referred to as late-onset hypogonadism).
- Before the start of testosterone therapy, the patient has at least TWO confirmed low morning testosterone levels according to current practice guidelines or your standard lab reference values.

Continuation of Therapy

Breast Cancer (Hormone-Responsive Tumor), Delayed Puberty, Gender Dysphoria, Inoperable Metastatic Breast Cancer
All patients (including new patients) requesting authorization for continuation of therapy must meet all requirements in the coverage criteria section.

Primary or Hypogonadotropic Hypogonadism
Authorization may be granted when the requested drug is being prescribed for primary or hypogonadotropic hypogonadism and ALL of the following criteria are met:

- The requested drug is NOT being prescribed for age-related hypogonadism (also referred to as late-onset hypogonadism).
- Before the patient started testosterone therapy, the patient had a confirmed low morning testosterone level according to current practice guidelines or your standard lab reference values.

Approval Duration and Quantity Restrictions:

Approval: 12 months

Quantity Level Limit: Reference Formulary for drug specific quantity level limits

Testosterone cypionate IM solution 100mg/mL – 10mL per 90 days
Testosterone cypionate IM solution 200mg/mL – 10mL per 90 days
Testosterone transdermal gel 10mg/act (2%) - 2 canisters per 30 days
Testosterone transdermal gel 12.5mg/act (1%) - 4 canisters per 30 days
Testosterone transdermal gel 20.25mg/act (1.62%) – 5gm per 1 day
Testosterone transdermal gel solution 30mg/act – 6mL

References:

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3. Depo-Testosterone [package insert]. New York, NY: Pharmacia & Upjohn Co; August 2018.
4. Fortesta [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; January 2022.
5. Jatenzo [package insert]. Fort Collins, CO: Tolmar Inc.; August 2023.
6. Kyzatrex [package insert]. Raleigh NC: Marius Pharmaceuticals LLC; September 2022.
7. Natesto Nasal Gel [package insert]. Mississauga, ON: Acerus Pharmaceutical Corporation; December 2021.

8. Testim [package insert]. Malvern, PA: Endo USA; August 2021.
9. Testopel (testosterone pellets) [package insert]. Malvern, PA: Endo USA; March 2024.
10. Testosterone Enanthate [package insert]. E. Windsor, NJ: Eugia US LLC; February 2024.
11. Testosterone Gel 1% [package insert]. Durham, NC: Encube Ethicals, Inc.; July 2024.
12. Testosterone Topical Gel [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; June 2020.
13. Testosterone Topical Solution [package insert]. Bedminster, NJ: Alembic Pharmaceuticals, Inc.; December 2023.
14. Tlando [package insert]. Ewing, NJ: Verity Pharmaceuticals, Inc.; February 2024.
15. Undecatrex [package insert]. San Antonio, TX: Trifluent Pharma LLC; September 2022.
16. Vogelxo [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC; April 2020.
17. Xyosted [package insert]. Ewing, NJ: Antares Pharma, Inc.; August 2023.
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24. Health Care for Transgender and Gender Diverse Individuals. ACOG Committee Opinion No. 823. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2021;137:e75-88.