# Clinical Policy: Testosterone

Reference Number: IL.ERX.NPA.52
Effective Date: 06.01.21
Last Review Date: 11.21
Line of Business: Illinois Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
Testosterone is an androgen.

**FDA Approved Indication(s)**
Testosterone is indicated for:

- Replacement therapy in 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, luteinizing hormone) above the normal range
  - Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone 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
- Treatment of delayed puberty in carefully selected males
- Treatment of women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal

Limitation(s) of use:

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

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that testosterone is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Hypogonadism** (must meet all)**:**

1. Diagnosis of primary hypogonadism or hypogonadotropic hypogonadism;
2. Age ≥ 18 years, unless request is for testosterone cypionate or testosterone enanthate;
3. Documentation of subnormal serum testosterone level on at least 2 separate days;
4. If request is agent other than testosterone enanthate or testosterone cypionate: Failure of either testosterone enanthate or testosterone cypionate, unless clinically significant adverse effects are experienced or all are contraindicated;

5. If request is for a non-preferred agent, failure of ≥ 2 preferred with PA agents, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix E*);
6. Dose does not exceed the FDA approved maximum (see section V).

**Approval duration: 3 months**

**B. Delayed Puberty** (must meet all)**:**
1. Request is for testosterone cypionate or testosterone enanthate;
2. Diagnosis of delayed puberty;
3. Dose does not exceed the FDA approved maximum (see section V).

**Approval duration: 6 months**

**C. Breast Cancer** (must meet all)**:**
1. Request is for testosterone enanthate;
2. Diagnosis of breast cancer;
3. Disease is metastatic;
4. Dose does not exceed the FDA approved maximum (see section V).

**Approval duration: 3 months**

**D. Gender Dysphoria, Female-to-Male Transition (off-label)** (must meet all)**:**
1. Documentation of gender dysphoria/gender incongruence or request is for gender transition;
2. Member meets both of the following (a and b):
   a. Capacity to make a well-informed decision;
   b. Documentation that medical and mental health issues are well-controlled;
3. If request is agent other than testosterone enanthate or testosterone cypionate: Failure of either testosterone enanthate or testosterone cypionate, unless clinically significant adverse effects are experienced or all are contraindicated;
4. If request is for a non-preferred agent, failure of ≥ 2 preferred with PA agents, unless contraindicated or clinically significant adverse effects are experienced (see Appendix E);
5. Request meets one of the following (a, b, or c):
   a. For testosterone cypionate and testosterone enanthate: Does not exceed total dose of 200 mg per week;
   b. For testosterone undecanoate, dosing meets one of the following (i or ii):
      i. Initial two doses: Doses do not exceed 1 gram every 6 weeks;
      ii. Subsequent doses (after the initial two doses): Dose do not exceed 1 g every 12 weeks;
   c. Dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Approval duration: 3 months**

**E. Other diagnoses/indications**
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## II. Continued Therapy

**A. Delayed Puberty**
1. Re-authorization is not permitted. Members must meet the initial approval criteria.

**Approval duration: Not applicable**

**B. All Other Indications in Section I** (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving testosterone for breast cancer and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. Member meets one of the following (a or b):

a. For gender dysphoria, request meets one of the following (i, ii, or iii):
   i. For testosterone cypionate and testosterone enanthate: Does not exceed total dose of 100 mg per week;
   ii. For testosterone undecanoate: Dose does not exceed 1 g every 12 weeks;
   iii. Dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence);
b. For all other indications: If request is for a dose increase, new dose does not exceed the FDA approved maximum (see section V).

**Approval duration: 6 months**

**C. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;
**B.** Age-related hypogonadism or late-onset hypogonadism;
**C.** Erectile dysfunction;
**D.** Infertility.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*
FDA: Food and Drug Administration
PA: prior authorization

*Appendix B: Therapeutic Alternatives*
*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| testosterone cypionate injection (Depo®-Testosterone), testosterone enanthate injection | Male hypogonadism: 50 to 400 mg IM once every 2 to 4 weeks or 50-100 mg/week SC<br>Males with delayed puberty: 50 to 200 mg every 2 to 4 weeks for a limited duration, for example, 4 to 6 months | 400 mg every 2 to 4 weeks |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Men with known carcinoma of the breast or known or suspected carcinoma of the prostate
  - Pregnant or breastfeeding women
  - Aveed, depo-testosterone, Jatenzo, testosterone cypionate, testosterone enanthate, Xyosted: hypersensitivity to product or ingredients
  - Depo-testosterone, testosterone cypionate: patients with serious cardiac, hepatic or renal disease
  - Jatenzo, Xyosted: men with hypogonadal conditions not associated with structural or genetic etiologies
- Boxed warning(s):
  - Aveed: serious pulmonary oil microembolism reactions and anaphylaxis

- Axiron, Fortesta, Testim, Voxelgo: secondary exposure to testosterone
- Jatenzo, Xyosted: increases in blood pressure

*Appendix D: General Information*

- Per the Endocrine Society (2018), the diagnosis of hypogonadism requires unequivocally and consistently low testosterone levels on at least 2 separate mornings. Although the lower limit of normal for testosterone can vary depending on the laboratory used, clinical trials for a number of testosterone agents defined it as < 300 ng/dL. Additionally, the American Urological Association suggests < 300 ng/dL as a reasonable cut-off in support of low testosterone diagnosis (2018).
- Patients with primary hypogonadism usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone, luteinizing hormone) above the normal range. Patients with hypogonadotropic hypogonadism have low testosterone serum concentrations but have gonadotropins in the normal or low range.
- Androgens may be used cautiously to stimulate puberty in carefully selected patients with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.

*Appendix E: Preferred and Non-Preferred Agents*

| Drug Name | Strength |
|---|---|
| ***Preferred Agents:*** *One of the following agents must be adequately tried and failed before moving on to preferred with PA agents* | |
| testosterone enanthate | 200 mg/mL |
| Depot-Testosterone (testosterone cypionate) | 100 mg/mL, 200 mg/mL |
| ***Preferred with PA Agents*** *Two or more of the following agents must be adequately tried and failed before moving on to non-preferred agents* | |
| Testim, Vogelxo | 50 mg/5 g (1%) |
| Androgel Packet (testosterone gel packet) | 25 mg/2.5 g (1%), 50 mg/5 g (1%)<br>20.25 mg/1.25 g (1.62%), 40.5 mg/2.5 g (1.62%) |
| Androgel Pump (Testosterone Gel) | 20.25 mg/actuation |
| Fortesta (Testosterone Gel) | 10 mg/actuation (2%) |
| Vogelxo Pump | 12.5 mg/actuation (1%) |
| ***Non-preferred Agents*** | |
| Androderm | 2mg/24hr, 4mg/24hr |
| Aveed | 750 mg/3 mL |
| Jatenzo | 158 mg, 198 mg, 237 mg |
| Xyosted Auto-Injector | 50 mg/0/5mL, 75 mg/0.5 mL, 100 mg/0.5 mL |
| Striant | 30 mg |
| Axiron (testosterone solution) | 30 mg/actuation |
| Methyltestosterone (Methitest, Android) | 10 mg |

## V. Dosage and Administration

Refer to the individual prescribing information for each agent.

## VI. Product Availability

Refer to the individual prescribing information for each agent.

## VII. References

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| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created (adopted from MRX P.228) | 04.21.21 | 05.21 |
| 4Q 2021 annual review: no significant changes; added gender transition to gender dysphoria criteria set; removed coverage of testosterone cypionate for breast cancer; references reviewed and updated. | 07.07.21 | 11.21 |

**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status;

evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.