Washington State Health Care Authority

# Androgenic Agents – Testosterone Replacement Therapy (TRT)

## Medical policy no. 23.10.00-2 Effective: July 1, 2018

**Related medical policies:**

- **24.00.00- Hormone Therapy for Gender Dysphoria**

***Note:*** *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

*To see the current publication of the Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx*

## Background:

The Food and Drug Administration (FDA) approved testosterone products for testosterone replacement therapy in males with primary or secondary hypogonadism (congenital or acquired). Primary hypogonadism originates from a deficiency or disorder in the testicles. Secondary hypogonadism indicates a problem in the hypothalamus or the pituitary gland. Testosterone may also be used in the treatment of other conditions, such as delayed puberty, metastatic breast cancer, and gender dysphoria.

## Medical necessity

| Drug | Medical Necessity |
|---|---|
| **Testosterone**<br>• Androderm (Transdermal patch, ER)<br>• AndroGel (Topical gel)<br>• generic (Topical solution)<br>• Fortesta (Topical gel)<br>• generic (Topical gel)<br>• Natesto (Nasal gel)<br>• Striant (Buccal patch, ER)<br>• Testim (Topical gel)<br>• Testopel (Pellets)<br>• Vogelxo (Topical gel)<br><br>**Methyltestosterone**<br>• Methitest (Oral tablet) | Testosterone may be considered medically necessary when used for the following indications:<br><br>• Testosterone Replacement Therapy (TRT) for adult males for the following conditions:<br>○ Primary hypogonadism (congenital or acquired)<br>○ Secondary hypogonadism (congenital or acquired)<br>○ Biologic males with severely low testosterone who are symptomatic.<br>○ HIV-associated weight loss<br>○ Chronic, high-dose glucocorticoid-therapy<br>○ Biologic males with osteoporosis or who are under 50 years old with low trauma fractures |

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| • generic (Oral capsule)<br><br>**Testosterone enanthate**<br>• generic (IM injection)<br>• Xyosted (Auto-injector)<br><br>**Testosterone undecanoate**<br>• Aveed (Injectable solution)<br>• Jatenzo (Oral capsules)<br><br>**Testosterone cypionate**<br>• Depo-Testosterone (IM Injection)<br>• generic (IM injection) | • Delayed puberty<br><br>• Metastatic breast cancer |

## Clinical policy:

| Clinical Criteria | |
|---|---|
| **Testosterone Replacement Therapy for Adult Males**<br>○ Primary hypogonadism<br>○ Secondary hypogonadism<br>○ Biologic males with severely low testosterone who are symptomatic<br>○ HIV-associated weight loss<br>○ Chronic, high-dose glucocorticoid-therapy<br>○ Biologic males with osteoporosis or who are under 50 with low trauma fractures | Testosterone Replacement Therapy (TRT) may be considered medically necessary when patients meet **ALL** of the following criteria:<br><br>1. Patient is biologically male, 18 years of age or older; **AND**<br>2. Patient has had **TWO** morning (between 8 a.m. to 10 a.m.) tests (between at least 1 week but no more than 3 months apart) at baseline demonstrating low testosterone levels. Second morning test should follow ruling out reversible illnesses, drugs, and nutritional deficiencies as causes for low testosterone. Low testosterone is defined by **ONE** following criteria:<br>a. Total serum testosterone level less than 300ng/dL (10.4nmol/L); **OR**<br>b. Total serum testosterone level less than 350ng/dL (12.1nmol/L) **AND** free serum testosterone level less than 50pg/mL (or 0.174nmol/L); **AND**<br>3. Patient has recent LH and FSH labs to guide diagnosis as primary or secondary hypogonadism; **AND**<br>4. Patient has received **ONE** of the following diagnoses:<br>a. **Primary hypogonadism** (congenital or acquired) defined as testicular failure due to conditions such as:<br>i. cryptorchidism,<br>ii. bilateral torsion,<br>iii. orchitis,<br>iv. vanishing testes syndrome,<br>v. orchiectomy,<br>vi. Klinefelter syndrome,<br>vii. chemotherapy,<br>viii. trauma, or<br>ix. toxic damage from alcohol or heavy metals; **OR**<br>b. **Secondary hypogonadism** (congenital or acquired) defined as idiopathic gonadotropin or luteinizing hormone-releasing |

hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma or radiation; **OR**

c. **Biologic males with severely low testosterone who are symptomatic** defined as two tests with total serum testosterone levels less than 100 ng/dL **AND** presence of physical signs of hypogonadism, defined as significant decrease in bone or muscle mass in the last 6 months; **OR**

d. **HIV-associated weight loss** defined as <90% of ideal body weight (IBW) or weight loss of >10% in the last 6 months while diagnosed with HIV
    i. The following documentation is required for approval:
        1) diagnosis of HIV;
        2) most recent weight, ideal body weight, and any documentation of weight loss over the last 6 months;
        3) target body weight goal; **OR**

e. **Chronic, high-dose glucocorticoid-therapy** defined as more than 5 mg/day of prednisone or equivalent daily for greater than two (2) weeks
    i. The following documentation is required for approval:
        1) diagnosis requiring glucocorticoid regimen;
        2) current glucocorticoid regimen;
        3) expected duration of therapy; **OR**

f. **Biologic males with osteoporosis or who are under 50 with low trauma fractures**
    i. The following documentation is required for approval:
        1) diagnosis of osteoporosis or low trauma fracture within the previous 12 months
        2) patient is currently being treated for osteoporosis or low trauma fracture; **AND**

5. Patient meets **ALL** of the following criteria:
    a. Patient does not have **ANY** of the following contraindications to testosterone therapy:
        i. breast cancer or known or suspected prostate cancer
        ii. elevated hematocrit (>50%)
        iii. untreated severe obstructive sleep apnea
        iv. severe lower urinary tract symptoms
        v. uncontrolled or poorly-controlled heart failure
    b. Patient is not using testosterone for late-onset (age-related) hypogonadism.
    c. Patient has not experienced a major cardiovascular event (e.g., myocardial infraction, stroke, acute coronary syndrome, etc.) in the previous 6 months
    d. Patient does not have uncontrolled or poorly-controlled benign prostate hyperplasia or is at a higher risk of prostate cancer (e.g., elevation of PSA after initiating TRT)

If **ALL** criteria are met, then the request can be approved for the appropriate duration for the indicated treatment:

- **Primary hypogonadism:** approve 12 months
- **Secondary hypogonadism:** approve 12 months
- **Biologic males with severely low testosterone who are symptomatic:** approve 12 months
- **HIV-associated weight loss:** approve 6 months
- **Chronic, high-dose glucocorticoid-therapy:** approve up to the duration of the expected regimen of chronic, high-dose glucocorticoid-therapy with a maximum of 12 months.
- **Biologic males with osteoporosis or young men with low trauma fractures:** approve 12 months

**Criteria (Reauthorization)**

Testosterone may be approved for reauthorization when **ALL** of the following are met:

1. Patient continues to meets criteria 4 and 5 of the initial criteria above; **AND**
2. Patient has not experienced any severe adverse events due to testosterone therapy; **AND**
3. Patient's most recent testosterone labs show that serum testosterone concentration is in the normal range since starting therapy; **AND**
4. Patient has documentation of positive clinical response as defined by the criteria below for each indication:
    a. **HIV-associated weight loss:** patient has shown an increase in body weight and **ONE** of the following:
        i. is not yet at target body weight goal; **OR**
        ii. patient is still experiencing an episode (e.g., a secondary infection) that is causing weight loss;
    b. **Chronic, high-dose glucocorticoid-therapy:** high-dose glucocorticoid therapy is continuing
    c. **Biologic males with osteoporosis or who are under 50 years of age and have experienced a low trauma fractures:** osteoporosis or low trauma fracture therapy is continuing

If **ALL** criteria are met, then the request can be approved for the appropriate duration for the indicated treatment:

- **Primary hypogonadism:** approve 12 months
- **Secondary hypogonadism:** approve 12 months
- **Biologic males with severely low testosterone who are symptomatic:** approve 12 months
- **HIV-associated weight loss:** approve 6 months

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| | • **Chronic, high-dose glucocorticoid-therapy:** approve up to the duration of the expected regimen of chronic, high-dose glucocorticoid-therapy with a maximum duration of 12 months.<br>• **Biologic males with osteoporosis or who are under 50 years of age and have experienced a low trauma fractures:** approve 12 months |
| **Clinical Criteria** | |
| **Testosterone for treatment of delayed puberty** | Testosterone may be considered medically necessary when patients meet **ALL** of the following criteria:<br><br>1. Patient is male and 14 years of age or older; **AND**<br>2. Patient has received the diagnosis of delayed puberty that is **NOT** secondary to a pathological cause; **AND**<br>3. Family history of delayed puberty has been evaluated to support differential diagnosis of delayed puberty; **AND**<br>4. Labs of recent serum LH, FSH, and testosterone are provided; **AND**<br>5. Patient must not have responded to "watchful waiting" with reassurance and psychological support in the previous 6 months<br>a. Non-response of "watchful waiting" may be demonstrated by psychological concerns about delayed puberty and that delayed puberty cannot be addressed by reassurance and psychological support alone<br>6. Patient meets **ALL** of the following criteria:<br>a. Patient does not have **ANY** of the following contraindications to testosterone therapy:<br>i. breast cancer or known or suspected prostate cancer<br>ii. elevated hematocrit (>50%)<br>iii. untreated severe obstructive sleep apnea<br>iv. severe lower urinary tract symptoms<br>v. uncontrolled or poorly-controlled heart failure<br>b. Patient has not experienced a major cardiovascular event (e.g., myocardial infraction, stroke, acute coronary syndrome, etc.) in the previous 6 months<br>c. Patient does not have uncontrolled or poorly-controlled benign prostate hyperplasia or is at a higher risk of prostate cancer (e.g., elevation of PSA after initiating TRT)<br><br>If **ALL** criteria are met, then the request can be approved for 6 months |
| | **Criteria (Reauthorization)**<br>Testosterone may be approved for reauthorization when **ALL** of the following are met:<br><br>1. Puberty has not been completed in the patient; **AND**<br>2. Patient is unable to sustain a normal serum testosterone concentration when not receiving testosterone therapy |

| Clinical Criteria | |
|---|---|
| **Testosterone for use in metastatic breast cancer** | Testosterone may be considered medically necessary when patients meet **ALL** of the following criteria:<br><br>1. Patient is biologically female and 18 years of age or older; **AND**<br>2. Patient has received a diagnosis of advancing, inoperable metastatic breast cancer; **AND**<br>3. Patient has been postmenopausal for 1 to 5 years **OR** is premenopausal and has demonstrated benefit from oophorectomy and has a hormone-responsive tumor; **AND**<br>4. Documentation of first-line treatments used for metastatic breast cancer and information on treatment failures with first-line agents; **AND**<br>5. Drug is prescribed by or in consultation with an oncologist or a physician specializing in the treatment of metastatic breast cancer; **AND**<br>6. Patient does not have **ANY** of the following contraindications to testosterone therapy:<br>a. elevated hematocrit (>50%)<br>b. untreated severe obstructive sleep apnea<br>c. severe lower urinary tract symptoms<br>d. uncontrolled or poorly-controlled heart failure<br>e. pregnant or may become pregnant<br>*f.* major cardiovascular event (e.g., myocardial infraction, stroke, acute coronary syndrome, etc.) in the previous 6 months<br><br>If **ALL** criteria are met, then the request can be approved for 12 months |
| | **Criteria (Reauthorization)**<br>Testosterone may be approved for reauthorization when **ALL** of the following are met:<br><br>1. Patient continues to meet criteria 1-6 above; **AND**<br>2. Patient has not experienced any severe adverse events or acceleration in metastatic breast carcinoma related to testosterone therapy |

## Table 1

## Dosage and quantity limits

| Name | Dosage Form | Strength | Quantity Level Limit |
|---|---|---|---|
| Androderm | transdermal patch | 2mg | #30 patches per 30-days |
| | | 4mg | #30 patches per 30-days |
| AndroGel / generic | gel packet (2.5g) | 1% | 300g (4x75g) per 30-days |
| | gel packet (5g) | 1% | 300g (2x150g) per 30-days |

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| | gel pump | 1% | 300g (4x75g) per 30-days |
| AndroGel / generic | gel packet (1.25g) | 1.62% | 37.5g (30 packets) per 30-days |
| | gel packet (2.5g) | 1.62% | 150g (60 packets) per 30-days |
| | gel pump | 1.62% | 150g (2x75g) per 30-days |
| Aveed | injectable solution | 250mg/mL | 750mg per 30-days |
| generic | topical solution | 30mg/1.5mL | 180mL (2x90mL) per 30-days |
| Fortesta / generic | gel | 2% | 120g (2x60g) per 30-days |
| Jatenzo | oral capsules | 158mg | #60 capsules per 30-days |
| | | 198mg | #60 capsules per 30-days |
| | | 237mg | #60 capsules per 30-days |
| Natesto | Nasal gel | 5.5 mg | 21.96g (3 dispensers) per 30-days |
| Striant | buccal system | 30mg | #60 buccal systems per 30-days |
| Testim | gel | 1% | 300g (60x5g) per 30-days |
| Vogelxo / generic | gel packet | 1% | 300g (4x75g) per 30-days |
| | gel pump | 1% | 300g (60x5g) per 30-days |
| Testopel | pellets (implant) | 75mg | 6 pellets every 3 months |
| Depo-Testosterone / generic (cypionate) | injectable solution | 100mg/mL | 400mg per 28-days |
| | | 200mg/mL | 400mg per 28-days |
| Methitest (methyltestosterone) | oral | 10mg | #150 tablets per 30-days |
| methyltestosterone | oral | 10 mg | #150 capsules per 30-days |
| Xyosted (enanthate) | Solution auto-injector | 50mg/0.5mL | 200mg per 28-days |
| | | 75mg/0.5mL | 300mg per 28-days |
| | | 100ng/0.5mL | 400mg per 28-days |

## Coding:

| HCPCS Code | Description |
|---|---|
| J3121 | Injection, testosterone enanthate, 1mg |
| J1071 | Injection, testosterone cypionate, 1 mg |

## References


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14. Axiron® (testosterone) topical solution. Prescribing Information. Indianapolis, IN: Lilly USA, LLC. October 2016.
15. Fortesta® (testosterone) 2% gel. Prescribing Information. Malvern, PA: Endo Pharmaceuticals. October 2016.
16. Testim® (testosterone) 1% gel. Prescribing information. Malvern, PA: Endo Pharmaceuticals, Inc., October 2016.
17. Striant® (testosterone) buccal system. Prescribing information. Endo Pharmaceuticals. Malvern, PA. October 2016.
18. Natesto® (testosterone) nasal gel. Prescribing information. Endo Pharmaceuticals. Malvern, PA. May 2015.
19. Vogelxo® (testosterone) gel. Prescribing information. Maple Grove, MN: Upsher-Smith Laboratories, September 2016.
20. Hembree, Wylie C, et al. "Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline." The Journal of clinical endocrinology and metabolism 94.9 (2009):3132-3154.
21. Product Information: XYOSTED(TM) subcutaneous injection, testosterone enanthate subcutaneous injection. Antares Pharma Inc (per FDA), Ewing, NJ, 2018

## History

| Date | Action and Summary of Changes |
|---|---|
| **05/26/2021** | Added reference to Gender Dysphoria policy in related medical policies section and added Natesto to list of products |
| **11/30/2020** | Added link to AHPDL publication |
| **06/17/2020** | Approved by DUR Board |
| **02/03/2020** | Added Testopel, updated transgender health criteria |
| **10/03/2019** | Edited Note |
| **06/21/2019** | Reformatted clinical criteria sections; updated clinical documentation required for initial authorization and reauthorization |
| **11/02/2018** | Add Xyosted |
| **04/20/2016** | New Policy |