Androgenic Agents – Testosterone Replacement Therapy (TRT)

WA.PHAR.28 Effective: July 1, 2018

Related medical policies:

- **WA.PHAR.104- 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 Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit: *https://pharmacy.envolvehealth.com/content/dam/centene/envolve-pharmacy-solutions/pdfs/PDL/FORMULARY-CoordinatedCare_Washington.pdf*

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

Testosterone enanthate • generic (IM injection) • Xyosted (Auto-injector) **Testosterone undecanoate** • Aveed (Injectable solution) • Jatenzo, Kyzatrex, Tlando (Oral capsules) **Testosterone cypionate** • Depo-Testosterone (IM Injection) • generic (IM injection)	• Metastatic breast cancer ****For requests relating to Hormone Therapy for Gender Dysphoria, please refer to policy 24.00.00.** If all criteria are not met, but there are documented medically necessary or situational circumstances, based on the professional judgement of the clinical reviewer, requests may be approved on a case-by-case basis up to the initial or reauthorization duration. Clients new to Apple Health or new to an MCO, who are requesting regimens for continuation of therapy should be reviewed following the reauthorization criteria listed below.

Clinical policy:

Clinical Criteria	
Testosterone Replacement Therapy for Adult Males ○ Primary hypogonadism ○ Secondary hypogonadism ○ Biologic males with severely low testosterone who are symptomatic ○ HIV-associated weight loss ○ Chronic, high-dose glucocorticoid-therapy ○ 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: 1. Patient is biologically male, 18 years of age or older; **AND** 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: a. Total serum testosterone level less than 300ng/dL (10.4nmol/L); **OR** 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** 3. Patient has recent LH and FSH labs to guide diagnosis as primary or secondary hypogonadism; **AND** 4. Patient has received **ONE** of the following diagnoses: a. **Primary hypogonadism** (congenital or acquired) defined as testicular failure due to conditions such as: i. cryptorchidism, ii. bilateral torsion, iii. orchitis, iv. vanishing testes syndrome, v. orchiectomy, vi. Klinefelter syndrome, vii. chemotherapy, viii. trauma, or ix. toxic damage from alcohol or heavy metals; **OR** 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

	• **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. • **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: 1. Patient is male and 14 years of age or older; **AND** 2. Patient has received the diagnosis of delayed puberty that is **NOT** secondary to a pathological cause; **AND** 3. Family history of delayed puberty has been evaluated to support differential diagnosis of delayed puberty; **AND** 4. Labs of recent serum LH, FSH, and testosterone are provided; **AND** 5. Patient must not have responded to "watchful waiting" with reassurance and psychological support in the previous 6 months 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 6. 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 has not experienced a major cardiovascular event (e.g., myocardial infraction, stroke, acute coronary syndrome, etc.) in the previous 6 months 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) If **ALL** criteria are met, then the request can be approved for 6 months
	Criteria (Reauthorization) Testosterone may be approved for reauthorization when **ALL** of the following are met: 1. Puberty has not been completed in the patient; **AND** 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: 1. Patient is biologically female and 18 years of age or older; **AND** 2. Patient has received a diagnosis of advancing, inoperable metastatic breast cancer; **AND** 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** 4. Documentation of first-line treatments used for metastatic breast cancer and information on treatment failures with first-line agents; **AND** 5. Drug is prescribed by or in consultation with an oncologist or a physician specializing in the treatment of metastatic breast cancer; **AND** 6. Patient does not have **ANY** of the following contraindications to testosterone therapy: a. elevated hematocrit (>50%) b. untreated severe obstructive sleep apnea c. severe lower urinary tract symptoms d. uncontrolled or poorly-controlled heart failure e. pregnant or may become pregnant *f.* major cardiovascular event (e.g., myocardial infraction, stroke, acute coronary syndrome, etc.) in the previous 6 months If **ALL** criteria are met, then the request can be approved for 12 months
	Criteria (Reauthorization)
	Testosterone may be approved for reauthorization when **ALL** of the following are met: 1. Patient continues to meet criteria 1-6 above; **AND** 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
	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	750 mg/3mL (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
Kyzatrex	oral capsules	100 mg	#60 capsules per 30 days
		150 mg	#120 capsules per 30 days
		200 mg	#120 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
Tlando	oral capsules	112.5 mg	#120 capsules 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	10 mL vial: 8 mL per 28-days (1 vial/28 days)
		200mg/mL	1 mL vial: 2 mL per 28-days (2 vials/28 days) 10 mL vial: 4 mL per 28-days (2 vials/56 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
		100mg/0.5mL	400mg per 28-days

Coding:

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

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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
10/02/2023	Version 2 Updates:

	Updated dosage and quantity limits for Aveed, Depo-Testosterone, and Xyosted
10/12/2022	Version 2 Updates: Added reference to Gender dysphoria policy in medical necessity list. -Added Kyzatrex and Tlando to policy and dosage/qty limits.
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