

Testosterone Therapies Medical Policy

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Presentation Objectives

- To provide **background information** relevant to testosterone therapies
- To present the proposed **medical policy** for **testosterone therapy**

Background Information

Available Testosterone Therapies

Name	Market Entry	Indications	Restrictions
Delatestryl (enanthate)	12/1953	Primary H; Hypogonadotropic H; Delayed Puberty; Metastatic Breast Cancer	LOH not studied
Depo-Testosterone (cypionate)	07/1979	Primary H; Hypogonadotropic H	LOH not studied; not <18
AndroDerm (patch)	09/1995	Primary H; Hypogonadotropic H	LOH not studied; not <18
AndroGel 1% (gel)	02/2000	Primary H; Hypogonadotropic H	LOH not studied; not <18
Testim (gel)	10/2002	Primary H; Hypogonadotropic H	LOH not studied; not <18
Striant (buccal system)	06/2003	Primary H; Hypogonadotropic H	LOH not studied; not <18
Axiron (topical solution)	11/2010	Primary H; Hypogonadotropic H	LOH not studied; not <18
Fortesta (gel)	12/2010	Primary H; Hypogonadotropic H	LOH not studied; not <18
AndroGel 1.62% (gel)	04/2011	Primary H; Hypogonadotropic H	LOH not studied; not <18
Vogelxo (gel)	06/2014	Primary H; Hypogonadotropic H	LOH not studied; not <18

H: hypogonadism. Hypogonadotropic hypogonadism is sometimes referred to as secondary hypogonadism.

HCA Approved Uses

- Hypogonadism in adult males¹
 - Primary Hypogonadism (congenital or acquired)
 - defined as testicular failure due to such conditions as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, Klinefelter's syndrome, chemotherapy, trauma, or toxic damage from alcohol or heavy metals
 - Hypogonadotropic Hypogonadism (congenital or acquired)
 - defined by idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma or radiation
 - HIV-associated weight loss
 - HIV-associated weight loss is defined as <90% of ideal body weight or weight loss of >10% in the last 6 months
 - Chronic, high-dose glucocorticoid-therapy
 - Defined as more than 5mg/day of prednisone or equivalent daily for greater than two (2) weeks
 - Osteoporosis or low trauma fractures in young men

1.) Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010 Jun;95(6):2536-59.

HCA Approved Uses

- Delayed Puberty
 - For delayed puberty that is **NOT** secondary to a pathological cause
 - Diagnosis should include family history to demonstrate familial delayed puberty
 - Provider should obtain random measurements of serum LH, FSH, and testosterone to support diagnosis
- Metastatic Breast Cancer
 - Available to patients 1 to 5 years postmenopausal or is premenopausal and have demonstrated benefit from oophorectomy and have hormone-responsive tumor
- Hormone Replacement Therapy [Transgender Health]²

2.) Uniform Medical Plan. 2016 Uniform Medical Plan Certificate of Coverage. 2016.

Background: Estimated HCA Population at Risk

Estimates on the epidemiology of hypogonadism and other conditions for which testosterone therapy is appropriate are lacking. Many studies use different criteria for defining hypogonadism, which results in wide variations in the estimation of its prevalence³. For example:

- HIM estimates **38.7%** of men ≥ 45 years of age
 - Inclusion criteria: total testosterone $< 300\text{ng/dL}$
- BLSA estimates **12%** of men in their 50s, **19%** in their 60s, **28%** in their 70s, and **49%** in their 80s
 - Inclusion criteria: total testosterone $< 325\text{ng/dL}$
- BACH estimates **5.6%** of men 30–79 years of age
 - Inclusion criteria: symptomatic androgen deficiency
- MMAS estimates **12.3%** of men 40–70 years of age
 - Inclusion criteria: total testosterone $< 200\text{ng/dL}$ and ≥ 3 clinical features of androgen deficiency
- Studies from 7 European countries estimate **20%** of adult men
 - Inclusion criteria: moderate to severe symptoms using AMS scale

3.) Meryn S. The epidemiology and burden of male hypogonadism. International Society of Men's Health. Presentation.

Medical Policy

Medical Policy: TRT for Adult Males

Testosterone Replacement Therapy (TRT) may be considered medically necessary for the treatment of hypogonadism when the patient meets the following criteria:

INCLUSION CRITERIA

1. Patient is male, 18 years of age or older
2. Patient has had **TWO** morning (between 8 a.m. to 10 a.m.) tests (at least 1 week apart) at baseline demonstrating low testosterone levels as defined by the following criteria:
 - a. Total serum testosterone level <300ng/dL (10.4nmol/L);
 - b. Total serum testosterone level <350ng/dL (12.1nmol/L) **AND** free serum testosterone level <50pg/mL (0.174nmol/L);
 - c. Second morning test should be performed after excluding reversible illnesses, drugs, nutritional deficiencies and other possible causes of low serum testosterone. Providers should also include LH and FSH draws to guide diagnosis as primary or secondary hypogonadism.

1.) Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010 Jun;95(6):2536-59.

4.) Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2006 Jun;91(6):1995-2010

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Medical Policy: TRT for Adult Males

3. Patient has received **ONE** of the following diagnoses as defined by the criteria on slide 5:
 - a. Primary Hypogonadism (congenital or acquired)
 - b. Hypogonadotropic Hypogonadism (congenital or acquired)
 - c. HIV-associated weight loss
 - d. Men receiving chronic, high-dose glucocorticoid-therapy
 - e. Men with osteoporosis or young men with low trauma fractures

EXCLUSION CRITERIA

1. Patient has **ANY** of the following contraindications or other precautions:
 - a. Breast cancer or known or suspected prostate cancer
 - b. Elevated hematocrit (>50%)
 - c. Untreated severe obstructive sleep apnea
 - d. Severe lower urinary tract symptoms
 - e. Uncontrolled or poorly-controlled heart failure
2. Patient has experienced a major cardiovascular event (such as a myocardial infarction, stroke, acute coronary syndrome) in the past six months
3. Patient has uncontrolled or poorly-controlled benign prostate hyperplasia or is at a higher risk of prostate cancer, such as elevation of PSA after initiating TRT

1.) Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010 Jun;95(6):2536-59.

5.) Testosterone enanthate injection [prescribing information]. Eatontown, NJ: West-Ward Pharmaceutical; July 2014.

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Medical Policy: TRT for Adult Males

PRIOR AUTHORIZATION APPROVAL DURATION AND LIMITS

Patients meeting the criteria above may receive TRT. Approved medications are listed in Table 1 on the following slide (slide 13). Quantity level limits are listed along with each product.

Approval is for one (1) year except for patients who meet the diagnosis criteria for (c) HIV-associated weight loss or (d) men receiving chronic, high-dose glucocorticoid therapy.

- For men who meet criterion (c) HIV-associated weight loss, the approval is set for 6 months.
- For men who meet criterion (d) men receiving chronic, high-dose glucocorticoid-therapy, the approval is set for the expected regimen of chronic, high-dose glucocorticoid-therapy with a maximum of one (1) year.

Medical Policy: TRT for Adult Males

Table 1. Quantity Level Limits for Testosterone Replacement Therapy in Adult Males

Name	Dosage Form	Strength	Quantity Level Limit
Androderm	transdermal patch	2mg	60 patches per 30 days
		2.5mg	60 patches per 30 days
		4mg	30 patches per 30 days
		5mg	30 patches per 30 days
AndroGel	gel packet (2.5g)	1%	300g (4x75g) per 30 days
	gel packet (5g)	1%	150g (2x75g) per 30 days
	gel pump	1%	300g (4x75g) per 30 days
AndroGel	gel packet (1.25g)	1.62%	37.5 (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
Axiron	topical solution	30mg	180mL (2x90mL) per 30 days
Fortesta	gel	2%	120g (2x60g) per 30 days
Striant	buccal system	30mg	60 systems per 30 days
Testim	gel	1%	300g (2x5g tubes/day) for 30 days
Vogelxo	gel packet	1%	300g (4x75g) per 30 days
	gel pump	1%	300g (60x5g tubes) per 30 days
Depo-Testosterone (cypionate)	injectable solution	100mg/mL	400mg per 28 days
		200mg/mL	400mg per 28 days
Delatestryl (enantane)	injectable solution	200mg/mL	400mg per 28 days
Methitest	oral	10mg	150 tablets per 30 days
Android	oral	10mg	150 tablets per 30 days
Testred	oral	10mg	150 tablets per 30 days

Note: Testopel (implanted pellets) is excluded from this policy and is covered under medical benefit

Medical Policy:

Testosterone Therapy for Delayed Puberty

Testosterone Therapy may be considered medically necessary for treatment of delayed puberty when the patient meets the following criteria:

INCLUSION CRITERIA

1. Patient is male, 14 years of age or older
 - a. Under very severe and unusual circumstances, the patient may be under 14 years of age with documentation on why the patient cannot wait until 14 years of age for the treatment of delayed puberty
2. Patient has received the diagnosis of delayed puberty, as defined on slide 6
3. Patient must try and fail "watchful waiting" with reassurance and psychological support
 - a. Failure of "watchful waiting" may be demonstrated by psychological concerns about delayed puberty that cannot be addressed by reassurance and psychological support alone

Medical Policy:

Testosterone Therapy for Delayed Puberty

EXCLUSION CRITERIA

1. Patient has **ANY** of the following contraindications:
 - a. Breast cancer or known or suspected prostate cancer
 - b. Elevated hematocrit (>50%)
 - c. Untreated severe obstructive sleep apnea
 - d. Severe lower urinary tract symptoms
 - e. Uncontrolled or poorly-controlled heart failure
2. Patient has experienced a major cardiovascular event (such as a myocardial infarction, stroke, acute coronary syndrome) in the past six months
3. Patient has uncontrolled or poorly-controlled benign prostate hyperplasia or are at higher risk of prostate cancer, such as elevation of PSA after initiating testosterone therapy

Medical Policy:

Testosterone Therapy for Delayed Puberty

RECOMMENDED THERAPY

Patients meeting the criteria above may receive testosterone therapy.

The recommended dosage form is testosterone enanthate injection. The recommended dose is 50–200mg every 2–4 weeks for a limited duration, such as 4 to 6 months. For example, one recommended therapy plan is 50mg every 4 weeks for 6 months.

Methyltestosterone (Methitest, Android, Testred) may also be considered. Treatment with these oral methyltestosterone products is 10–50mg daily.

Medical Policy:

Testosterone Therapy for Metastatic Breast Cancer

Testosterone therapy may be considered medically necessary for treatment of metastatic breast cancer when the patient meets criteria 1–4 of the **INCLUSION CRITERIA** and none of the **EXCLUSION CRITERIA**. The treatment recommendations follow this policy. (Documentation from the patient's chart is **REQUIRED**):

INCLUSION CRITERIA

1. Patient is female, 18 years of age or older
2. Patient has received a diagnosis of advancing, inoperable metastatic breast cancer
3. Patient is 1 to 5 years postmenopausal **OR** is premenopausal and has demonstrated benefit from oophorectomy and has a hormone-responsive tumor
4. Testosterone treatment is considered secondarily to failure of first-line therapies and is being prescribed by an oncologist with expertise in the field

Medical Policy:

Testosterone Therapy for Metastatic Breast Cancer

EXCLUSION CRITERIA

1. Patient has **ANY** of the following contraindications:
 - a. Elevated hematocrit (>50%)
 - b. Untreated severe obstructive sleep apnea
 - c. Severe lower urinary tract symptoms
 - d. Uncontrolled or poorly-controlled heart failure

2. Patient has experienced a major cardiovascular event (such as a myocardial infarction, stroke, acute coronary syndrome) in the past six months

1.) Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010 Jun;95(6):2536-59.

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5.) Testosterone enanthate injection [prescribing information]. Eatontown, NJ: West-Ward Pharmaceutical; July 2014.

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Medical Policy:

Testosterone Therapy for Metastatic Breast Cancer

RECOMMENDED THERAPY

Patients meeting the criteria above may receive testosterone therapy.

The recommended dosage form is testosterone enanthate injection. The recommended dose is 200–400mg every 2–4 weeks.

Methyltestosterone (Methitest, Android, Testred) may also be considered. Treatment with these oral methyltestosterone products is 50–200mg daily.

Medical Policy: HRT for Transgender Health

The intent of this section is to describe an existing medical benefit where testosterone is used as hormone replacement therapy (HRT) as covered under Transgender Health. Pharmacists may process claims for testosterone therapy as an expedited authorization (EA) during the following circumstances when:

1. Patient identifies as a female-to-male (FTM); **AND**
2. Patient has received the diagnosis of gender dysphoria as defined by Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria by a licensed behavioral health practitioner, OR a licensed physician, advanced registered nurse practitioner (ARNP), physician's assistant (PA), or psychologist who is treating the patient for primary care or transgender services who is continuing to treat the patient with a comprehensive patient-centered treatment plan AND demonstrates that gender dysphoria is not due to another mental or physical health conditions

Medical Policy: HRT for Transgender Health

Testosterone for HRT should be prescribed under the following guidelines for providers to follow as part of standard of practice:

1. Provider has documentation that the patient has the capacity to make fully informed decisions and consents for the treatment of gender dysphoria
2. Provider prescribing hormone replacement therapy must meet the following criteria:
 - a. Meet the requirements of professional licensure and practice according to the scope of practice for their license; AND
 - b. Demonstrate specialized competencies in managing hormone therapies for gender dysphoria (including documentation of supervised training or mentoring by a more experienced physician); AND
 - c. Follow the standards of care for the health of transgender, transsexual and gender-nonconforming people outlined by the World Professional Association for Transgender Health (WPATH)

Medical Policy: HRT for Transgender Health

3. Patient does not have any of the following contraindications or other precautions:
- Breast cancer
 - Elevated hematocrit (>50%)
 - Untreated severe obstructive sleep apnea
 - Severe lower urinary tract symptoms
 - Uncontrolled or poorly-controlled heart failure
 - Experienced a major cardiovascular event (such as a myocardial infarction, stroke, acute coronary syndrome) in the past six months

1.) Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010 Jun;95(6):2536-59.

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5.) Testosterone enanthate injection [prescribing information]. Eatontown, NJ: West-Ward Pharmaceutical; July 2014.

Medical Policy: HRT for Transgender Health

RECOMMENDED THERAPY

The recommended dosage route is via injection and the recommended dose is 100–200mg every 2 weeks. Doses may escalate depending on patient response.

Transdermal therapies are also available under the Transgender Health medical policy, but may have lower efficacy and slower response. Transition to transdermal therapies may be appropriate once initial virilization is complete to avoid supraphysiological testosterone concretions for those 18 years of age and older.

Questions?

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Works Cited

1. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2010 Jun;95(6):2536-59.
2. Uniform Medical Plan. 2016 Uniform Medical Plan Certificate of Coverage. 2016.
3. Meryn S. The epidemiology and burden of male hypogonadism. International Society of Men's Health. Presentation.
4. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2006 Jun;91(6):1995-2010
5. Testosterone enanthate injection [prescribing information]. Eatontown,NJ: West-Ward Pharmaceutical; July 2014.
6. UMP Clinical Criteria. 2016.
7. Uniform Medical Plan Transgender Services Clinical Criteria. 2015.

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