UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Testosterone

Program	Prior Authorization
Medication	Preferred product: Testosterone (T gel and pump) Non-preferred products: Androderm (testosterone [T] patch), Androgel (T gel and pump), Axiron (T topical solution), Fortesta (T gel), Natesto (T nasal gel), Striant (T buccal system), Testim (T gel), Vogelxo (T gel and pump), Xyosted (testosterone enanthate), Jatenzo (testosterone undecanoate) capsules
Markets in Scope	California, Hawaii, Maryland, Nevada, New Jersey, New York, New York EPP, Pennsylvania- CHIP, Rhode Island, South Carolina
Issue Date	9/2009
Pharmacy and Therapeutics Approval Date	7/2020
Effective Date	9/2020

1. Background:

Testosterone products are approved by the Food and Drug Administration (FDA) for testosterone replacement therapy in males with primary hypogonadism (congenital or acquired) or hypogonadotropic 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 use has been strongly linked to improvements in muscle mass, bone density, and libido.

The purpose of this program is to provide coverage for androgens and anabolic steroid therapy for the treatment of conditions for which they have shown to be effective and are within the scope of the plan's pharmacy benefit. Coverage for the enhancement of athletic performance or body building will not be provided.

Black boxed warnings may include but may not be limited to secondary exposure to testosterone. Please see full prescribing information for additional details.

2. Coverage Criteria:

A. Initial Authorization for Hypogonadism

1. **One** of the following:

   a. **Two** pre-treatment serum total testosterone levels less than 300 ng/dL (< 10.4 nmol/L) or less than the reference range for the lab, taken at separate times (This may require treatment to be temporarily held. Document lab value and date for both levels)

-OR-

   b. **Both** of the following:

      (1) Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity)
      (2) **One** pre-treatment calculated free or bioavailable testosterone level less than 50 pg/mL (<5 ng/dL or < 0.17 nmol/L) or less than the reference range for the lab (This may require treatment to be temporarily held. Document lab value and date)

-OR-

   c. Patient has a history of **one** of the following:

      (1) Bilateral orchiectomy
      (2) Panhypopituitarism
      (3) A genetic disorder known to cause hypogonadism (e.g., congenital anorchia, Klinefelter's syndrome)

-AND-

2. Patient is **not** taking any of the following:

   a. One of the following growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Nutropin AQ, Omnitrope, Saizen
   b. Aromatase inhibitor (eg, Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

-AND-

3. Patient was male at birth

-AND-

4. Diagnosis of hypogonadism

-AND-

5. **One** of the following:

   a. Significant reduction in weight (less than 90% ideal body weight) (e.g., AIDS wasting syndrome)
   b. Osteopenia
   c. Osteoporosis
   d. Decreased bone density
   e. Decreased libido
   f. Organic cause of testosterone deficiency (eg, injury, tumor, infection, or genetic defects)

-AND-

6. **One** of the following:
   a. If the request is for a non-preferred **topical testosterone** (gel, solution) or **testosterone transdermal systems** (patches), the patient has a history of failure, contraindication, or intolerance to generic testosterone 1% topical gel

-OR-

   b. If the request is for **Xyosted**, **both** of the following:
      i. The patient has a history of failure, contraindication, or intolerance to testosterone cypionate injection (generic Depo-Testosterone)

-AND-

      ii. The patient has a history of failure or rationale for not being able to use intramuscular testosterone enanthate injection (generic Delatestryl)

-OR-

   c. If the request is for Jatenzo, the patient has a history of failure, contraindication, or intolerance to **all** of the following:
      i. testosterone cypionate vials
      ii. testosterone enanthate vials
      iii. testosterone gel- tube, pack or pump bottle

Authorization will be issued for 12 months.

B. Initial Authorization for Gender Dysphoria[+]

1. Using hormones to change physical characteristics

-AND-

2. The covered person must be diagnosed with gender dysphoria, as defined by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM)

-AND-

3. Patient is **not** taking any of the following:

a. One of the following growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Nutropin AQ, Omnitrope, Saizen
b. Aromatase inhibitor (eg, Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

-AND-

4. **One of** the following:
   a. If the request is for a non-preferred **topical testosterone** (gel, solution) or **testosterone transdermal systems** (patches), the patient has a history of failure, contraindication, or intolerance to generic testosterone 1% topical gel

-OR-

   b. If the request is for **Xyosted**, **both** of the following:
      i. The patient has a history of failure, contraindication, or intolerance to testosterone cypionate injection (generic Depo-Testosterone)

-AND-

      ii. The patient has a history of failure or rationale for not being able to use intramuscular testosterone enanthate injection (generic Delatestryl)

-OR-

   c. If the request is for Jatenzo, the patient has a history of failure or rationale for not being able to use **all** of the following:

i. testosterone cypionate
ii. testosterone enanthate vials
iii. testosterone gel- tube, pack or pump bottle

Authorization will be issued for 12 months.

C. <u>Reauthorization for both Non-Gender Dysphoria and Gender Dysphoria</u>

1. Reauthorization will be approved based on **<u>both</u>** of the following:

a. **<u>One</u>** of the following:

(1) Follow-up total serum testosterone level drawn within the past 12 months is within or below the normal male limits of the reporting lab (document value and date)

-OR-

(2) Follow-up total serum testosterone level drawn within the past 12 months is outside of upper male limits of normal for the reporting lab and the dose is adjusted (document value and date)

-OR-

(3) **<u>Both</u>** of the following:

(a) Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity)

-AND-

(b) **<u>One</u>** of the following:

i. Follow-up calculated free or bioavailable testosterone level drawn within the past 12 months is within or below the normal male limits of the reporting lab (document lab value and date)

-OR-

ii. Follow-up calculated free or bioavailable testosterone level drawn within the past 12 months is outside of upper male limits of normal for the reporting lab and the dose is adjusted (document value and date)

-AND-

b. Patient is **not** taking any of the following:

(1) One of the following growth hormones, unless diagnosed with panhypopituitarism: Genotropin, Humatrope, Norditropin FlexPro, Nutropin AQ, Omnitrope, Saizen
(2) Aromatase inhibitor (eg, Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

Authorization will be issued for 12 months.

3. Additional Clinical Rules:

[+]Coverage for patient population may be dependent upon benefit design

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. AACE Hypogonadism Task Force. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 Update. *Endocr Pract*. 2002; 8(No. 6): 439-456.
2. The World Professional Association for Transgender Health (WPATH), Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th Version.
3. Cook, David M, et al. "American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients - 2009 update: executive summary of recommendations." Endocrine practice 15.6 (2009):580-586.
4. Gibney, James, et al. "Growth hormone and testosterone interact positively to enhance protein and energy metabolism in hypopituitary men." American journal of physiology: endocrinology and metabolism 289.2 (2005):E266-E271
5. Bhasin, S, et al. "Testosterone replacement and resistance exercise in HIV-infected men with weight loss and low testosterone levels." *JAMA*. 2000. 283.(6) 763-770.
6. Isidori, Andrea M, et al. Effects of testosterone on sexual function in men: results of a meta-analysis. *Clinical endocrinology*. 2005 63(4):381-394.

7. Kenny, A M, et al. Effects of transdermal testosterone on bone and muscle in older men with low bioavailable testosterone levels. *The journals of gerontology*. 2001. 56(5) M266-M272.
8. Tracz, Michal J, et al. Testosterone use in men and its effects on bone health. A systematic review and meta-analysis of randomized placebo-controlled trials. *The Journal of clinical endocrinology and metabolism.* 2006. 91(6):2011-2016.
9. Bolona, Enrique R, et al. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. *Mayo Clinic proceedings*.2007. 82(1):20-28.
10. Androderm[package insert]. Madison, NJ: Allergan, Inc; May 2020.
11. Androgel [package insert]. North Chicago, IL: AbbVie Inc; May 2020.
12. Fortesta [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; April 2020.
13. Testim [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; May 2019.
14. Striant [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; November 2016.
15. Natesto [package insert]. Englewood, CO: Avtu BioScience Inc; October 2016.
16. Vogelxo [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC; September 2016.
17. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2017; 102:3869.
18. The Endocrine Society. Testosterone therapy in Adult Men with Androgen Deficiency Syndromes. J Clin Endocrinol Metab, May 2018, 103(5):1–30.
19. Mulhall JP, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. American Urological Association Education and Research, Inc 2018.
20. Xyosted [package insert]. Ewing, NJ: Antares Pharma, Inc; November 2019.
21. Jatenzo [package insert]. Northbrook, IL: Clarus Therapeutics, Inc; March 2019.

Program	Prior Authorization
Change Control	
Date	Change
9/2009	Criteria taken from previously approved AmeriChoice policy. Policy was reformatted.
12/2010	Annual Review
3/2011	Annual Review. Added Axiron and Fortesta to non-preferred product list
9/2011	Annual Review. Added Androgel 1.62% to non-preferred product list
12/2011	Changed Androgel 1.62% from non-preferred product list to preferred product list.

	Changed Androgel 1% from preferred product list to non-preferred product list.
12/2012	Annual Review
12/2014	Full updated made to clinical criteria. Serum testosterone requirement changed to two levels less than 280 ng/dL, previously required one level less or equal to 300 ng/dL Added an alternative diagnostic option to serum testosterone testing: conditions that may cause altered sex-hormone binding globulin with one of the following (1) calculated free or bioavailable testosterone level less than 5 ng/dL or bilateral orchiectomy, panhypopituitarism, or (2) a genetic disorder known to cause hypogonadism. Added all of the following new requirements: • Not used in combination with growth hormones or aromatase inhibitors • Patient is male • Diagnosis of hypogonadism • One of the following: significant reduction in weight (less than 90% ideal body weight) (eg, AIDS wasting syndrome), osteopenia, osteoporosis, decreased bone density, decreased libido, organic cause of testosterone deficiency
3/2015	Gender Identity disorder initial criteria created for New Jersey and Washington plans due to plan requirement. Gender Identity disorder added to Male hypogonadism reauthorization criteria for New Jersey and Washington plans due to plan requirement.
6/2015	Changed products that the criteria applies to due to a PDL change.
11/2016	Updated clinical criteria to align with Employer and Individual's policy, added trial/failure of generic testosterone 1% topical gel to section A and B
2/2017	Updated header to define preferred and non-preferred products. Clarified that reauthorization is for non-gender dysphoria indications.
3/2017	Changed authorization durations to 12 months.

4/2017	In the female to male transition section, removed language requiring documented real life experience living as the other gender or a period of psychotherapy as this is not supported by WPATH guidelines.
5/2017	In the female to male transition section, removed language requiring demonstrable knowledge of what hormones medically can and cannot do and their social benefits and risks, and the requirement that if significant medical or mental health concerns are present, they are reasonably well controlled. Changed "transsexual" to "transgender". Updated references. Updated reauthorization header to clarify that it applies to all conditions.
6/2018	Updated required testosterone level to less than 300 ng/dL based on 2018 American Urological Society treatment guidelines.
2/2019	Program name change from Topical Androgens to Testosterone. Xyosted added to program.
6/2019	Added Jatenzo to the program.
7/2020	Annual review, updated references. Minor language update to step therapy language to clarify intent.