

UnitedHealthcare Pharmacy  
Clinical Pharmacy Programs

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| Program Number    | 2021 P 2018-14   |
| Program           | Prior Authorization/Medical Necessity – Testosterone   |
| Medication        | Axiron*, Androderm, Androgel*, Fortesta*, Jatenzo*, Natesto*, Testim, Vogelxo*, Xyosted*                 |
| P&T Approval Date | 2/2014, 4/2014, 5/2014, 7/2014, 10/2014, 10/2015, 5/2016, 6/2017, 6/2018, 2/2019, 6/2019, 7/2020, 8/2021 |
| Effective Date    | 11/1/2021;<br>Oxford only: 11/1/2021   |

**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.

**2. Coverage Criteria<sup>a</sup>:**

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| <p><b>A. <u>Initial Authorization for Hypogonadism</u></b></p> <p>1. <b>Topical testosterone</b> (gel, solution), <b>testosterone transdermal systems</b> (patches), and <b>oral testosterone</b> (capsules) will be approved based on <b><u>one</u></b> of the following:</p> <p>a. Patient has a history of <b><u>one</u></b> of the following:</p> <p style="margin-left: 40px;">1) Bilateral orchiectomy</p> <p style="margin-left: 40px;">2) Panhypopituitarism</p> <p style="margin-left: 40px;">3) A genetic disorder known to cause hypogonadism (eg, congenital anorchia, Klinefelter's syndrome)</p> <p style="text-align: center;"><b>-OR-</b></p> <p>b. <b><u>All</u></b> of the following:</p> <p style="margin-left: 40px;">1) <b><u>One</u></b> of the following:</p> |
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- 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:
- i. Patient has a condition that may cause altered sex-hormone binding globulin (SHBG) (e.g., thyroid disorder, HIV disease, liver disorder, diabetes, obesity)
  - ii. 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)

**-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)

**Authorization will be issued for 6 months.**

2. **Xyosted\*** will be approved based on **one** of the following:

a. **Both** of the following:

1) Patient has a history of **one** of the following:

- a) Bilateral orchiectomy
- b) Panhypopituitarism
- c) A genetic disorder known to cause hypogonadism (eg, congenital anorchia, Klinefelter's syndrome)

**-AND-**

2) History of failure, contraindication, or intolerance to **both** of the following:

- a) testosterone cypionate injection (generic Depo-Testosterone)
- b) testosterone enanthate injection

**-OR-**

b. **All** of the following:

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)

**-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) History of failure, contraindication, or intolerance to **both** of the following:
- a) testosterone cypionate injection (generic Depo-Testosterone)
  - b) testosterone enanthate injection

**Authorization will be issued for 6 months.**

**B. Initial Authorization for Gender Dysphoria<sup>+</sup>**

1. **Topical testosterone** (gel, solution), **testosterone transdermal systems** (patches), and **oral testosterone** (capsules) will be approved based on **all** of the following:

a. Using hormones to change physical characteristics

**-AND-**

b. 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-**

c. 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 6 months.**

2. **Xyosted\*** (testosterone enanthate) will be approved based on **all** of the following:

a. Using hormones to change physical characteristics

**-AND-**

b. 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-**

c. 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])

**-AND-**

- d. History of failure, contraindication, or intolerance to **both** of the following:
  - 1) testosterone cypionate injection (generic Depo-Testosterone)
  - 2) testosterone enanthate injection

**Authorization will be issued for 6 months.**

**C. Reauthorization for both Non-Gender Dysphoria (includes hypogonadism) and Gender Dysphoria**

1. Reauthorization will be approved based on **one** of the following:

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

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

**-OR-**

- b. Reauthorization will be approved based on **both** of the following:

- 1) **One** of the following:

- a) Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e. on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e. on therapy for one year or longer), is within or below the normal male limits of the reporting lab (document value and date)

**-OR-**

- b) Follow-up total serum testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e. on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e. on therapy for one year or longer), is outside of upper male limits of normal for the reporting lab and the dose is adjusted (document value and date)

-OR-

c) **Both** of the following:

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

-AND-

ii. **One** of the following:

- (a) Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e. on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e. on therapy for one year or longer), is within or below the normal male limits of the reporting lab (document lab value and date)

-OR-

- (b) Follow-up calculated free or bioavailable testosterone level drawn within the past 6 months for patients new to testosterone therapy (i.e. on therapy for less than one year), or 12 months for patients continuing testosterone therapy (i.e. on therapy for one year or longer), is outside of upper male limits of normal for the reporting lab and the dose is adjusted (document value and date)

-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])

**Authorization will be issued for 12 months.**

<sup>a</sup> State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

### 3. Additional Clinical Rules:

- 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.
- \* May be excluded from coverage
- + Coverage for patient population may be dependent upon benefit design

### 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; June 2020.
13. Testim [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; November 2020.
14. Natesto [package insert]. Englewood, CO: Aytu BioScience, Inc; October 2016.
15. Vogelxo [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC; April 2020.



16. 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.
17. The Endocrine Society. Testosterone therapy in Adult Men with Androgen Deficiency Syndromes. *J Clin Endocrinol Metab*, May 2018, 103(5):1–30.
18. Mulhall JP, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. American Urological Association Education and Research, Inc 2018.
19. Xyosted [package insert]. Ewing, NJ: Antares Pharma, Inc; November 2019.
20. Jatenzo [package insert]. Northbrook, IL: Clarus Therapeutics, Inc; March 2019.

| Program               | Prior Authorization/Medical Necessity - Testosterone   |
|-----------------------|--|
| <b>Change Control</b> |  |
| Date                  | Change   |
| 2/2014                | Create Prior Authorization Criteria  |
| 4/2014                | Revised Reauthorization Criteria; formatting corrections, references updated.  |
| 5/2014                | Revised the initial authorization criteria to include subsections for the male population and the female to male transsexual population, updated to include language from the gender identity disorder/ gender dysphoria treatment medical coverage determination guideline, references updated        |
| 7/2014                | Added Natesto and Vogelxo to criteria. Changed coverage criteria from specific product names to topical testosterone products.   |
| 10/2014               | Modified criteria for total testosterone to consider reference range of the laboratory. Added criteria for when Free Testosterone level may be utilized. Added criteria for conditions that do not require testosterone levels. Extended initial authorization period for patients already on therapy. |
| 12/2014               | Testosterone free level units corrected.   |
| 10/2015               | Clarified initial authorization periods. Clarified that levels for reauthorization should be within the past 6 months for patients new to testosterone and within the past 12 months for continuing users. Updated references.   |
| 5/2016                | Removed age requirement from female to male transsexual coverage requirements. Updated gender identity disorder to gender dysphoria.   |
| 6/2017                | Updated criteria for Gender Dysphoria. Updated reauthorization criteria to clarify that new to therapy refers to use of less than one year and continuing therapy refers to use of one year or longer.   |
| 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                | Jatenzo added to program.  |

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| 7/2020 | Updated initial authorization to 6 months for both new and existing users. Added state mandate language. Updated references. |
| 8/2021 | Annual review. Updated references. Removed Striant as it is no longer on the market.   |