UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2018 P 2018-10
Program	Prior Authorization/Medical Necessity – Topical Androgens
Medication	Axiron*, Androderm, Androgel*, Fortesta*, Natesto*, Testim or Striant, Vogelxo*
P&T Approval Date	2/2014, 4/2014, 5/2014, 7/2014, 10/2014, 10/2015, 5/2016, 6/2017, 6/2018
Effective Date	9/1/2018; Oxford only: 9/1/2018

1. Background:

Topical 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. When hypogonadism develops before the age of puberty some of the signs and symptoms of hypogonadism may include: small testes, phallus, or prostate; impaired body hair growth, gynecomastia, persistent high pitched voice, and disproportionate growth of arms and legs in comparison to trunk of body. Signs and symptoms associated with later onset hypogonadism include loss of libido, erectile dysfunction**,** sarcopenia, low bone mass, decreases in muscle mass, depressive thoughts**,** fatigue**,** loss of body hair**,** hot flushes**, and** loss of vigor. Testosterone use has been strongly linked to improvements in muscle mass, bone density, and libido. Topical products include Axiron*, Androderm, Androgel*, Fortesta*, Natesto*, Striant, Testim, and Vogelxo*.

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:

A. <u>Initial Authorization for Hypogonadism</u>

1. Topical testosterone (gel, solution) or testosterone transdermal systems (patches) will be approved based on **<u>all</u>** of the following:

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

      1) **<u>Two</u>** 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-

2) **Both** 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)
b) **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-

3) 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-

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

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

-AND-

c. Patient was male at birth

-AND-

d. Diagnosis of hypogonadism

-AND-

e. **One** of the following:

1) Significant reduction in weight (less than 90% ideal body weight) (e.g., AIDS wasting syndrome)
2) Osteopenia
3) Osteoporosis
4) Decreased bone density
5) Decreased libido
6) Organic cause of testosterone deficiency (eg, injury, tumor, infection, or genetic defects)

Patients new to any topical testosterone therapy: Authorization will be issued for 6 months.
Patients continuing testosterone therapy: Authorization will be issued for 12 months.

B. Initial Authorization for Gender Dysphoria[+]

1. Topical testosterone (gel, solution) or testosterone transdermal systems (patches) 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, Norditropin NordiFlex, Nutropin, Nutropin AQ, Omnitrope, Saizen, Tev-Tropin
2) Aromatase inhibitor (eg, Arimidex [anastrozole], Femara [letrozole], Aromasin [exemestane])

Patients new to any topical testosterone therapy: Authorization will be issued for 6 months.

Patients continuing testosterone therapy: 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 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-

      2) 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-

      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 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-

(ii) 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-

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

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

Authorization will be issued for 12 months.

3. Additional Clinical Rules:

- 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® (testosterone) transdermal system. Prescribing information. Parsippany, NJ: Watson Laboratories, Inc., July 2015.
11. Androgel® (testosterone) 1.62% gel. Prescribing information. Abbvie Inc. Chicago, IL. May 2015.
12. Androgel® (testosterone) 1% gel. Prescribing information. Abbvie Inc. Chicago, IL. October 2016.
13. Axiron® (testosterone) topical solution. Prescribing Information. Indianapolis, IN: Lilly USA, LLC. October 2016.
14. Fortesta® (testosterone) 2% gel. Prescribing Information. Malvern, PA: Endo Pharmaceuticals. October 2016.
15. Testim® (testosterone) 1% gel. Prescribing information. Malvern, PA: Endo Pharmaceuticals, Inc., October 2016.
16. Striant® (testosterone) buccal system. Prescribing information. Endo Pharmaceuticals. Malvern, PA. October 2016.

17. Natesto® (testosterone) nasal gel. Prescribing information. Endo Pharmaceuticals. Malvern, PA. May 2015.
18. Vogelxo® (testosterone) gel. Prescribing information. Maple Grove, MN: Upsher-Smith Laboratories, September 2016.
19. 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.
20. The Endocrine Society. Testosterone therapy in Adult Men with Androgen Deficiency Syndromes. J Clin Endocrinol Metab, May 2018, 103(5):1–30.
21. Mulhall JP, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. American Urological Association Education and Research, Inc 2018.

Program	Prior Authorization/Medical Necessity - Topical Androgens
Change Control	
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.