

Topical, Nasal, and Oral Testosterone Products

Policy # 00335

Original Effective Date: 01/09/2013

Current Effective Date: 03/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on a review of the available data, branded AND generic topical, nasal, and oral testosterone products, including, but not limited to AndroGel^{®‡} (testosterone gel), Natesto^{™‡} (testosterone nasal gel), branded topical Testosterone, Vogelxo^{®‡} (testosterone gel), Jatenzo^{®‡} (testosterone undecanoate capsules), Tlando^{®‡} (testosterone undecanoate capsules), Kyzatrex^{®‡} (testosterone undecanoate capsules), Undecatrex^{™‡} (testosterone undecanoate capsules) and Testim^{®‡} (testosterone gel) may be considered **eligible for coverage**** when the below patient selection criteria are met:

Patient Selection Criteria:

Coverage eligibility will be considered for branded or generic topical, nasal, and oral testosterone products when the following criteria are met for the requested drug:

- For Jatenzo, Tlando, Kyzatrex, and Undecatrex requests:
 - Patient is a male with hypogonadism (primary or secondary) as confirmed by serum testosterone measurements taken in the MORNING on TWO separate days BOTH showing levels BELOW the normal laboratory reference value; AND
 - Patient is 18 years of age or older; AND
 - Patient has tried and failed (e.g., intolerance or inadequate response) BOTH of the following prescription GENERIC products: testosterone enanthate vials for injection AND testosterone cypionate vials for injection unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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- Patient has tried and failed (e.g., intolerance or inadequate response) a generic topical testosterone product unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient;
OR
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- For all other requests (topical and nasal):
 - Patient is a male with hypogonadism (primary or secondary) as confirmed by a low for age serum testosterone level defined by the normal laboratory reference value;
AND
*(Note: The portion of this criterion regarding the testosterone level is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
 - For brand requests ONLY: There is clinical evidence or patient history that suggests the use of generic topical testosterone products will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of branded or generic topical and nasal testosterone products in male patients when the patient does NOT have a low for age serum testosterone level (based on normal laboratory reference levels) when treating hypogonadism (primary or secondary) to be **not medically necessary**.**

Based on review of available data, the Company considers the use of branded topical and nasal testosterone products, unless there is clinical evidence or patient history that suggests the use of generic topical testosterone products will be ineffective or cause an adverse reaction to the patient, to be **not medically necessary**.**

Based on review of available data, the Company considers the use of Jatenzo (testosterone undecanoate capsules), Tlando (testosterone undecanoate capsules) Kyzatrex (testosterone undecanoate capsules), and Undecatrex (testosterone undecanoate capsules) when the patient has not tried and failed the prerequisite testosterone products to be **not medically necessary**.**



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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of branded or generic topical, nasal, and oral testosterone products for 1.) indications such as athletic enhancement, 2.) contraindicated situations (e.g. male with carcinoma of the breast OR known or suspected carcinoma of the prostate (excluding males with treated and cured prostate cancer), or 3.) for usage not included in the above patient selection criteria to be **investigational**.*

Based on review of available data, the Company considers the use of Jatenzo (testosterone undecanoate capsules), Tlando (testosterone undecanoate capsules) Kyzatrex (testosterone undecanoate capsules), and Undecatrex (testosterone undecanoate capsules) when the patient selection criteria are not met (with the exception of those considered to be **not medically necessary****) to be **investigational**.*

Background/Overview

Transdermal, nasal, and buccal testosterone replacement products are indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone. The prescribing information for these drugs defines those patients and/or conditions for which they are indicated:

- Primary hypogonadism (congenital or acquired) – testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter’s syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations accompanied by gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Secondary hypogonadism (i.e., hypogonadotropic hypogonadism) (congenital or acquired) – idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low serum testosterone concentrations without associated elevations in gonadotropins. Appropriate adrenal cortical and thyroid hormone replacement therapy may be necessary in patients with multiple pituitary or hypothalamic abnormalities.

Jatenzo, Tlando, Kyzatrex, and Undecatrex are oral testosterone replacement therapies used in adult males for conditions associated with a deficiency or absence of endogenous testosterone. The package inserts note that the prescriber should confirm the diagnosis of hypogonadism by ensuring that serum testosterone concentrations have been measured in the morning on at least two separate days and that these concentrations are below the normal range. Jatenzo, Tlando, Kyzatrex, and Undecatrex were not studied in comparison to the other testosterone formulations. All four medications were studied in an open label fashion.



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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Multiple topical testosterone products, a nasal testosterone product, and three oral testosterone products are U.S. Food and Drug Administration (FDA)-approved for the treatment of primary or secondary hypogonadism in males. These products are contraindicated in women. They are also contraindicated in men with carcinoma of the breast or known or suspected carcinoma of the prostate (excluding males with treated and cured prostate cancer).

For topical and nasal testosterone products, the patient selection criteria presented in this policy take into consideration the FDA approved indications as well as clinical evidence or patient history that suggests generic topical testosterone products will be ineffective or cause an adverse reaction to the patient. Based on a review of the data, in the absence of the above-mentioned caveats, there is no advantage of using branded topical or nasal testosterone products over generic topical testosterone products for testosterone replacement.

For Jatenzo, Tlando, Kyzatrex, and Undecatrex the patient selection criteria presented in this policy take into consideration the FDA approved indications as well as whether or not the patient has tried and failed other generic alternative formulations of testosterone. Based on a review of the data, in the absence of the above-mentioned caveats, there is no advantage of using Jatenzo, Tlando, Kyzatrex, or Undecatrex over generic topical and injectable testosterone products for testosterone replacement.

References

1. Express Scripts Prior Authorization Policy. topical testosterone products. August 2012.
2. Testim [package insert]. Norristown, PA: Auxilium Pharmaceuticals, Inc.; September 2009.
3. AndroGel 1% gel [package insert]. North Chicago, IL: Abbott Laboratories; March 2011.
4. AndroGel 1.62% gel [package insert]. North Chicago, IL: Abbott Laboratories; April 2011
5. Delemarre EM, Feliuss B, Delemarre-van de Wall HA. Inducing puberty. Eur J Endocrinol. 2008;159:S9-S15.



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6. Ambler GR. Androgen therapy for delayed male puberty. *Curr Opin Endocrinol Diabetes Obes.* 2009;16(3):232-239.
7. Richmond EJ, Rogol AD. Male pubertal development and the role of androgen therapy. *Nat Clin Pract Endocrinol Metab.* 2007;3(4):338-344.
8. Natesto [package insert]. Malvern, PA. Endo Pharmaceuticals Inc. October 2016.
9. Jatenzo [package insert]. Northbrook, Illinois. Clarus Therapeutics, Inc. March 2019.
10. Tlando [package insert]. Antares Pharma, Inc. March 2022.
11. Kyzatrex [package insert]. Raleigh, North Carolina. Marius Pharmaceuticals. July 2022.
12. Undecatrex [package insert]. San Antonio, Texas. Trifluent Pharma, LLC. September 2022.

Policy History

Original Effective Date: 01/09/2013

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01/03/2013	Medical Policy Committee review
01/09/2013	Medical Policy Implementation Committee approval. New Policy
02/19/2013	Format revision. Coding section removed.
01/09/2014	Medical Policy Committee review
01/15/2014	Medical Policy Implementation Committee approval. No change to coverage.
10/02/2014	Medical Policy Committee review
10/15/2014	Medical Policy Implementation Committee approval. Added the statement that Axiron or Androgel should be used unless there is clinical evidence or patient history that suggests the use of Axiron or Androgel will be/was ineffective or will/did cause an adverse reaction to the patient.
10/08/2015	Medical Policy Committee review
10/21/2015	Medical Policy Implementation Committee approval. Added Nasal products to the policy. Title change.
10/06/2016	Medical Policy Committee review
10/19/2016	Medical Policy Implementation Committee approval. No change to coverage.
10/05/2017	Medical Policy Committee review
10/18/2017	Medical Policy Implementation Committee approval. Criteria changed to prefer Androgel 1.62% or generic products. Removed the indication of delayed puberty.
10/04/2018	Medical Policy Committee review
10/17/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. Removed the requirement to use Androgel 1.62% as this is now generic. Generic usage is still required. Updated language throughout to reflect this change.
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.



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12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. Title changed from “Topical and Nasal Testosterone Products” to “Topical, Nasal, and Oral Testosterone Products”. Added a new product, Jatenzo, to the policy. Updated relevant background information. Updated title to reflect the addition of an oral product to the policy.
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/02/2022	Medical Policy Committee review
06/08/2022	Medical Policy Implementation Committee approval. Added a new product, Tlando, to the medical policy and updated relevant sections.
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. Added new drug, Kyzatrex, to the medical policy and updated relevant sections.
02/01/2024	Medical Policy Committee approval
02/14/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2025	Medical Policy Committee review
02/12/2025	Medical Policy Implementation Committee approval. Added new drug, Undecatrex, to the medical policy and updated relevant sections. Removed discontinued products, Androderm, Axiron, Fortesta, and Striant, from medical policy.

Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.



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****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

