Clinical Policy: Testosterone (Testopel, Jatenzo, Kyzatrex, Tlando)

Reference Number: CP.PHAR.354
Effective Date: 08.01.17
Last Review Date: 11.24
Line of Business: HIM*, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Testosterone pellet (Testopel®) is an implantable androgen. Testosterone undecanoate capsule (Jatenzo®, Kyzatrex®, Tlando™) is an oral androgen.

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***For Health Insurance Marketplace (HIM),** if request is through pharmacy benefit, Testopel is a pharmacy benefit exclusion; refer to evidence of coverage documents.*

FDA Approved Indication(s)

Testopel is indicated for:

- Replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone:
  - Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome, or orchiectomy
  - Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropic lutenizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation
- Treatment of delayed puberty in carefully selected males

Jatenzo, Kyzatrex, and Tlando are indicated for:

- Replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
  - Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome, or orchiectomy, Klinefelter syndrome, chemotherapy, or toxic damage from alcohol or heavy metals.
  - Hypogonadotropic hypogonadism (congenital or acquired) – gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation.

Limitation(s) of use:

- Testopel: Safety and efficacy of Testopel in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Jatenzo, Kyzatrex, and Tlando: Safety and efficacy in males less than 18 years old have not been established.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Testopel, Jatenzo, Kyzatrex, and Tlando are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hypogonadism (must meet all)**:**

1. Diagnosis of primary hypogonadism or hypogonadotropic hypogonadism;
2. If request is for Jatenzo, Kyzatrex, or Tlando, age ≥ 18 years;
3. Documentation of serum testosterone level < 300 ng/dL (or less than the lab reference range) on at least 2 separate days within the last 6 months;
4. Member must use transdermal testosterone (e.g., patch, gel), unless clinically significant adverse effects are experienced or all are contraindicated;
5. Member must use injectable testosterone, unless clinically significant adverse effects are experienced or all are contraindicated;
6. Dose does not exceed one of the following (a, b, c, or d):
   a. For Testopel: 450 mg (6 pellets) every 3 months;
   b. For Jatenzo, both of the following (i and ii):
      i. 792 mg per day;
      ii. 4 capsules per day;
   c. For Kyzatrex, both of the following (i and ii):
      i. 800 mg per day;
      ii. 4 capsules per day;
   d. For Tlando: 450 mg (4 capsules) per day.

Approval duration:
Testopel – 6 months
All other agents – 12 months

B. Delayed Puberty (must meet all)**:**

1. Diagnosis of delayed puberty;
2. Request is for Testopel;
3. Prescribed by or in consultation with an endocrinologist;
4. Member must use injectable testosterone, unless clinically significant adverse effects are experienced or all are contraindicated;
5. Dose does not exceed 450 mg (6 pellets) every 3 months.

Approval duration: 6 months

C. Gender Dysphoria, Female-to-Male Transition (off-label) (must meet all)**:**

1. Diagnosis of gender dysphoria or request is for gender transition;
2. Prescribed by or in consultation with both of the following (a and b):
   a. An endocrinologist;
   b. A provider with expertise in gender dysphoria and transgender medicine based on a certified training program or affiliation with local transgender health services

(e.g., mental health professional such as psychologist, psychiatrist, see *Appendix D*);

3. Member meets one of the following (a or b):
   a. For Testopel, both of the following (i and ii):
      i. Medical justification supports inability to use transdermal (e.g., patch, gel) testosterone;
      ii. Medical justification supports inability to use injectable testosterone;
   b. For Jatenzo and Kyzatrex, both of the following (i and ii):
      i. Age ≥ 18 years;
      ii. Failure of two formulary testosterone products (e.g., transdermal, intramuscular or subcutaneous injection), at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
4. Member demonstrates understanding of expected testosterone treatment outcomes and has given consent for such treatment;
5. If member has a psychiatric comorbidity, member is followed by mental health provider;
6. Psychosocial support will be provided during treatment;
7. Provider attestation of understanding current State regulations regarding transgender-related health care and such care is coverable under the State regulations (see *Appendix D*);
8. Dose is within FDA maximum limit for any FDA-approved indication (see Section V) or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Hypogonadism (must meet all)**:**

1. Member meets one of the following (a or b):

a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);

2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a, b, c, or d):
   a. For Testopel: 450 mg (6 pellets) every 3 months;
   b. For Jatenzo, both of the following (i and ii):
      i. 792 mg per day;
      ii. 4 capsules per day;
   c. For Kyzatrex, both of the following (i and ii):
      i. 800 mg per day;
      ii. 4 capsules per day;
   d. For Tlando: 450 mg (4 capsules) per day.

Approval duration:
Testopel – 6 months
All other agents – 12 months

B. Delayed Puberty:
1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Gender Dysphoria, Female-to-Male Transition (off-label) (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy (e.g., developing a masculinized body while minimizing feminine characteristics, consistent with member's gender goals);
3. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication (see Section V) or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. Age-related hypogonadism or late-onset hypogonadism.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

LHRH: luteinizing hormone-releasing hormone

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
testosterone cypionate injection	Male hypogonadism: 50 to 400 mg IM once every 2 to 4 weeks	400 mg every 2 to 4 weeks
testosterone enanthate injection	Male hypogonadism: 50 to 400 mg IM once every 2 to 4 weeks Males with delayed puberty: 50 to 200 mg every 2 to 4 weeks for a limited duration, for example, 4 to 6 months.	400 mg every 2 to 4 weeks
testosterone 1% gel (AndroGel®)	Male hypogonadism: Starting dose: 50 mg applied topically QD. Dose may be titrated to a maximum of 100 mg QD based on serum testosterone level.	100 mg/day
testosterone 1.62% gel (AndroGel®)	Male hypogonadism: Starting dose: 40.5 mg applied topically QD. Dose may be titrated to a maximum of 81 mg QD based on serum testosterone level.	81 mg/day
testosterone 2% gel (Fortesta®)	Male hypogonadism: 40 mg (4 pump actuations) applied topically QD to the thighs. Dose may be titrated to a maximum	70 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	of 70 mg (4 pump actuations on one thigh and 3 pump actuations on the other thigh) QD based on serum testosterone level. Dose should be titrated to maintain serum testosterone in the range of 500-1250 ng/dL.	
testosterone transdermal patch (Androderm®)	Male hypogonadism: 1 patch topically nightly for 24 hours	1 patch/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Men with known carcinoma of the breast or known or suspected carcinoma of the prostate
  - Pregnant women
  - Jatenzo, Kyzatrex: hypersensitivity to product or ingredients
  - Tlando: hypogonadal conditions not associated with structural or genetic etiologies
- Boxed warning(s):
  - Jatenzo, Kyzatrex: increases in blood pressure

Appendix D: General Information

- Per the Endocrine Society (2018), the diagnosis of hypogonadism requires unequivocally and consistently low testosterone levels on at least 2 separate mornings. Although the lower limit of normal for testosterone can vary depending on the laboratory used, clinical trials for a number of testosterone agents defined it as < 300 ng/dL. Additionally, the American Urological Association suggests < 300 ng/dL as a reasonable cut-off in support of low testosterone diagnosis (2018).
- Patients with primary hypogonadism usually have low serum testosterone concentrations and gonadotropins (follicle stimulating hormone and luteinizing hormone) above the normal range. Patients with hypogonadotropic hypogonadism have low serum testosterone concentrations but have gonadotropins in the normal or low range.
- Androgens may be used cautiously to stimulate puberty in carefully selected patients with clearly delayed puberty. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support.
- Testopel implantation has much less flexibility for dosage adjustment than oral administration or intramuscular injections of oil solutions or aqueous suspensions, requires surgical removal if testosterone should be discontinued, and carries a risk of sloughing out of the skin.
- WPATH offers their Global Education Institute (GEI) Certified Training Courses: Best Practices in Transgender Medical and Mental Health Care. Additionally, the following link provides a search tool to locate WPATH member providers: https://www.wpath.org/provider/search

- Transgender Care Therapy Certification Training is also offered by the International Transgender Certification Association (ITCA). Professionals with expertise in transgender care can be located using the following search tool: https://transgendercertification.com/locate-a-professional/
- The WPATH Standards of Care Version 8 recommend that adolescents are managed by a multidisciplinary care team that involves both medical and mental health professionals. The list of key disciplines includes but is not limited to: adolescent medicine/primary care, endocrinology, psychology, psychiatry, speech/language pathology, fertility, social work, support staff, and the surgical team. The need to include a healthcare professional with some expertise in mental health does not dictate the inclusion of a psychologist, psychiatrist, or social work in every assessment. Instead, a general practitioner, nurse or other qualified clinician could fulfill this requirement as long as they have sufficient expertise to diagnose gender incongruence, recognize mental health concerns, distinguish between these concerns and gender dysphoria, incongruence or diversity, assist a transgender person in care planning and preparing for gender affirmative medical and surgical treatments, and refer to a mental health professional if needed.
- The Movement Advancement Project can be referenced to confirm transgender-related health care is coverable under the State regulations. This can be accessed at: https://www.lgbtmap.org/equality-maps/healthcare/youth_medical_care_bans

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Testopel	150 to 450 mg (2 to 6 pellets) SC every 3 to 6 months For every 25 mg/week of testosterone propionate, 150 mg (2 pellets) should be implanted every 3 to 6 months. If testosterone therapy needs to be discontinued (e.g., for severe adverse reactions), the pellets may need to be removed by a health care professional. Dosages in delayed puberty generally are in the lower range of that listed above and, for a limited duration, for example 4 to 6 months.	450 mg (6 pellets) every 3 months
Jatenzo	Starting dose: 237 mg PO BID Adjust the dose based on serum testosterone levels	792 mg/day
Kyzatrex	Starting dosage: 200 mg PO BID Adjust the dosage to a minimum of 100 mg once in the morning and a maximum of 400 mg BID based on serum testosterone drawn 3 to 5 hours after the morning dose at least 7 days after starting treatment or following dose adjustment and periodically thereafter	800 mg/day

Drug Name	Dosing Regimen	Maximum Dose
Tlando	225 mg (two 112.5 mg capsules) PO BID	450 mg/day

VI. Product Availability

Drug Name	Availability
Testopel	Pellet for implantation: 75 mg
Jatenzo	Oral capsules: 158 mg, 198 mg, 237 mg
Kyzatrex	Oral capsules: 100 mg, 150 mg, 200 mg
Tlando	Capsules: 112.5 mg

VII. References

1. Jatenzo Prescribing Information. Northbrook, IL: Clarus Therapeutics, Inc.; January 2023. Available at: www.jatenzo.com. Accessed July 10,2024.
2. Kyzatrex Prescribing Information. Raleigh, NC: Marius Pharmaceuticals; July 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/213953s000lbl.pdf. Accessed July 10,2024.
3. Testopel Prescribing Information. Malvern, PA: Endo Pharmaceutical Inc.; March 2024. Available at: www.testopel.com. Accessed July 10,2024.
4. Tlando Prescribing Information. Ewing, NJ: Antares Pharma, Inc.; February 2024. Available at: www.tlando.com. Accessed July 10, 2024.
5. Basin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2018; 103(5): 1715-1744. Available at: https://academic.oup.com/jcem/article/103/5/1715/4939465.
6. Jayasena CN, Anderson RA, Llahana S, et al. Society for Endocrinology guidelines for testosterone replacement therapy in male hypogonadism. Clinical Endocrinology. 2022 February; 96(2): 200-219.
7. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and management of testosterone deficiency AUA guideline. American Urological Association. Published 2018. Available at: http://www.auanet.org/guidelines/testosterone-deficiency-(2018).
8. Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender nonconforming people. WPATH: World Professional Association for Transgender Health. 7th version; 2012. Available at https://www.wpath.org/media/cms/Documents/SOC%20v7/SOC%20V7_English2012.pdf?_t=1613669341. Accessed July 18, 2024.
9. WPATH: World Professional Association for Transgender Health Standards of Care Version 8 Draft. Available at: https://www.wpath.org/soc8. Accessed July 18, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
S0189	Testosterone pellet, 75 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: modified HIM-Medical Benefit to HIM line of business; delayed puberty dosing added to appendix B; contraindications added to appendix C; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: modified reference from HIM.PHAR.21 to HIM.PA.154; revised "Medical justification" to "Member must use" language; references reviewed and updated.	07.14.21	11.21
Added criteria set for off-label use in gender dysphoria, female-to-male transition; references reviewed and updated.	12.14.21	02.22
RT4: added newly approved Tlando to the policy.	05.12.22	
4Q 2022 annual review: modified initial approval duration for hypogonadism for products other than Testim from 6 to 12 months, for continued approval duration for Testim modified from 12 to 6 months; in Section II for hypogonadism clarified quantity limits for Jatenzo and Tlando consistent with those included in Section I; clarified redirection is required unless all alternatives are contraindicated; RT4: added newly approved Kyzatrex to the policy; redirection language that stated member must used transdermal and injectable testosterone split into separate requirements for added clarity; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.20.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.07.23	11.23
4Q 2024 annual review: for hypogonadism serum testosterone requirement added allowance for levels less than the lab reference range; references reviewed and updated.	07.11.24	11.24
For gender dysphoria and gender transition, added requirement for provider attestation of understanding current State regulations regarding transgender-related health care and such care is coverable under the State regulations, added to Appendix D link and notation that the Movement Advancement Project can be referenced to confirm transgender-related health care is coverable under the State regulations.	02.12.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in

developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.