Clinical Policy: Testosterone (Testopel)

Reference Number: LA.PHAR.354
Effective Date:
Last Review Date: 05.09.23
Line of Business: Medicaid

Coding Implications
Revision Log

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

*Please note: This policy is for medical benefit**

Description
Testosterone pellet (Testopel®) is an implantable androgen.

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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

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.

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 Louisiana Healthcare Connections® 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 on at least 2 separate days within the last 6 months;
4. Member must use transdermal (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 450 mg (6 pellets) every 3 months;

Approval duration: 6 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 an endocrinologist and 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 following:
    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;
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. 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 LA.PMN.255
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: LA.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 450 mg (6 pellets) every 3 months;

Approval duration: 6 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. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
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 LA.PMN.255
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: LA.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 – LA.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 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.	70 mg/day
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

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 draft of WPATH Standards of Care Version 8 are available and open for public comment. These standards of care 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.

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

VI. Product Availability

Drug Name	Availability
Testopel	Pellet for implantation: 75 mg

VII. References

1. Jatenzo Prescribing Information. Northbrook, IL: Clarus Therapeutics, Inc.; March 2019. Available at: www.jatenzo.com. Accessed July 20, 2022.
2. Kyzatrex Prescribing Information. Raleigh, NC: Marius Pharmaceuticals; July 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/213953s000lbl.pdf. Accessed August 22, 2022.
3. Testopel Prescribing Information. Malvern, PA: Endo Pharmaceutical Inc.; August 2018. Available at: www.testopel.com. Accessed July 20, 2022.
4. Tlando Prescribing Information. Ewing, NJ: Antares Pharma, Inc.; March 2022. Available at: www.accessdata.fda.gov. Accessed 20, 2022
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 20, 2022.
9. WPATH: World Professional Association for Transgender Health Standards of Care Version 8 Draft. Available at: https://www.wpath.org/soc8. Accessed July 20, 2022.

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	LDH Approval Date
Policy created	05.09.23	

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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.

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