Clinical Policy: Testosterone
Reference Number: CP.CPA.291
Effective Date: 11.16.16
Last Review Date: 11.18
Line of Business: Commercial

Coding Implications
Revision Log

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

Description
The following are testosterone agents requiring prior authorization: Jatenzo®, Testim®, Vogelxo™, Natesto™, testosterone, and Testopel®, and Xyosted™.

FDA Approved Indication(s)
Testosterone 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, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals
  - Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropic luteinizing hormone-releasing hormone deficiency, or pituitary - hypothalamic injury from tumors, trauma, or radiation
- Treatment of delayed puberty in carefully selected males (Testopel only)

Limitation(s) of use:

- Safety and efficacy in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) has not been established.
- For all agents other than Testopel, safety and efficacy in males less than 18 years old has not been established.
- Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure.

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 Jatenzo, Testim, Vogelxo, Natesto, testosterone, Testopel, and Xyosted 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. Documentation of serum testosterone level < 300 ng/dL on at least 2 separate days within the last 6 months;
3. Member meets one of the following (a or b):
   a. For Testopel: medical justification supports inability to use topical (e.g., patch, gels) and injectable testosterone;
   b. For all other agents: Both (i and ii):
      i. Age ≥ 18 years;
      ii. Failure of a trial of generic testosterone gel (at up to maximally indicated doses) unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed the FDA approved maximum (see section V).

**Approval duration:**

**Testopel** – 6 months  
**Xyosted** – 6 months or to the member’s renewal date, whichever is longer  
**All other agents** – 12 months

B. **Delayed Puberty** (must meet all):
   1. Request is for Testopel;  
   2. Diagnosis of delayed puberty;  
   3. Prescribed by or in consultation with an endocrinologist;  
   4. Medical justification supports inability to use injectable testosterone;  
   5. Dose does not exceed 450 mg (6 pellets) every 3 months.

**Approval duration:** 6 months

C. **Other diagnoses/indications** (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration:** Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

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 – CP.CPA.09 for commercial or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>testosterone 1% gel</td>
<td>Starting dose: 50 mg applied topically QD. Dose may be titrated to a maximum of 100 mg QD based on serum testosterone level.</td>
<td>100 mg/day</td>
</tr>
<tr>
<td>(AndroGel®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>testosterone 1.62% gel</td>
<td>Starting dose: 40.5 mg applied topically QD. Dose may be titrated to a maximum of 81 mg QD based on serum testosterone level.</td>
<td>81 mg/day</td>
</tr>
<tr>
<td>(AndroGel®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>testosterone 2% gel</td>
<td>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.</td>
<td>70 mg/day</td>
</tr>
<tr>
<td>(Fortesta®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>testosterone cypionate</td>
<td>50 to 400 mg IM once every 2 to 4 weeks</td>
<td>400 mg every 2 to 4 weeks</td>
</tr>
<tr>
<td>testosterone enanthate</td>
<td>50 to 400 mg IM once every 2 to 4 weeks</td>
<td>400 mg every 2 to 4 weeks</td>
</tr>
<tr>
<td>injection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 or breastfeeding women
• Xyosted – men with hypogonadal conditions not associated with structural or genetic etiologies
• Boxed warning(s):  
  o Jatenzo: increases in blood pressure  
  o Testim, Vogelxo: secondary exposure to testosterone  
  o Xyosted – blood pressure increases

Appendix D: General Information
• 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.
• 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).
• 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.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
</table>
| Testopel  | 150-450 mg (2-6 pellets) SC every 3-6 months  
  For every 25 mg/week of testosterone propionate, 150 mg (2 pellets) should be implanted every 3-6 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. | 450 mg (6 pellets) every 3 months |
<p>| Testim    | 50 mg (1 tube) applied topically QD to the shoulders and/or upper arms. Dose may be titrated to a maximum of 100 mg QD based on serum testosterone level. Dose should be titrated to maintain serum testosterone in the range of 300-1000 ng/dL. | 100 mg/day |
| Vogelxo   | 50 mg (1 tube or 1 packet or 4 pump actuations) applied topically QD at approximately the same time each day to the shoulders and/or upper arms. Dose may be titrated to a maximum of 100 mg QD based on serum testosterone level. Dose should be titrated to | 100 mg/day |</p>
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natesto</td>
<td>11 mg (2 pump actuations; 1 actuation per nostril) administered intranasally TID. Discontinue therapy when total testosterone concentration consistently exceeds 1050 ng/dL. Alternative treatment should be considered if total testosterone concentration is consistently below 300 ng/dL.</td>
<td>33 mg/day</td>
</tr>
<tr>
<td>Testosterone</td>
<td>50 mg (4 pump actuations, two 25 mg packets, or one 50 mg packet) applied topically QD in the morning to the shoulders and upper arms and/or abdomen area (preferably at the same time every day). Dose may be titrated to 100 mg as instructed by the physician. Dose should be titrated to maintain normal range of 298-1043 ng/dL.</td>
<td>100 mg/day</td>
</tr>
<tr>
<td>Jatenzo</td>
<td>Starting dose: 237 mg PO BID Adjust the dose based on serum testosterone levels</td>
<td>792 mg/day</td>
</tr>
<tr>
<td>Xyosted</td>
<td>75 mg SC once weekly in the abdominal region. Avoid IM and IV administration.</td>
<td>Varies based on testosterone concentration.</td>
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</tbody>
</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testopel</td>
<td>Pellet for implantation: 75 mg</td>
</tr>
<tr>
<td>Testim</td>
<td>1% gel in tube: 5 gm (50 mg testosterone)</td>
</tr>
<tr>
<td>Vogelxo</td>
<td>Gel in unit-dose tube or packet: 50 mg testosterone in 5 gm of gel Gel in metered-dose pump: 12.5 mg testosterone 1.25 gm of gel per actuation; each 75-gm pump is capable of dispensing 60 metered pump actuations</td>
</tr>
<tr>
<td>Natesto</td>
<td>Intranasal gel in metered dose pump: 11 gm dispensed as 60 metered pump actuations. One pump actuation delivers 5.5 mg of testosterone</td>
</tr>
<tr>
<td>Testosterone</td>
<td>Gel in metered-dose pump: 88 gm capable of dispensing 60 metered pump actuations; each pump actuation delivers 12.5 mg testosterone in 1.25 gm of gel Gel in unit-dose packet: 25 mg testosterone in 2.5 gm of gel, 50 mg testosterone in 5 gm of gel</td>
</tr>
<tr>
<td>Jatenzo</td>
<td>Oral capsules: 158 mg, 198 mg, 237 mg</td>
</tr>
<tr>
<td>Xyosted</td>
<td>Autoinjector: 50 mg/0.5 mL, 75 mg/0.5 mL, 100 mg/0.5 mL</td>
</tr>
</tbody>
</table>

VII. References


**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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
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<tbody>
<tr>
<td>S0189</td>
<td>Testosterone pellet, 75 mg</td>
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<td></td>
</tr>
</tbody>
</table>

**Reviews, Revisions, and Approvals**

- Converted to new template. Minor changes to verbiage and grammar. References updated. 07.25.17 11.17
- 4Q 2018 annual review: incorporated Testopel criteria; clarified requirement for “deficiency of testosterone” to “diagnosis of hypogonadism”; hypogonadism: added requirement for documentation of testosterone levels per PI and guidelines, decreased approval duration from length of benefit to 12 months; delayed puberty: added requirement for specialist involvement in care; Testopel: clarified language from failure of other testosterone formulations to inability to use other testosterone formulations; 08.07.18 11.18
CLINICAL POLICY
Testosterone

Reviews, Revisions, and Approvals | Date | P&T Approval Date
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agents other than Testopel: added age; references reviewed and updated. | | 02.01.19
No clinically significant changes; removed Axiron and Fortesta from criteria as they no longer require PA; modified redirection from trial of AndroGel to generic topical testosterone per SDC. | | 02.01.19
RT4: added Jatenzo and Xyosted to the policy, following previously approved criteria for hypogonadism. References reviewed and updated. | 04.09.19

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.

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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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