Clinical Policy Title:	testosterone
Policy Number:	RxA.235
Drug(s) Applied:	Jatenzo®, Testim®, Vogelxo®, Natesto®, Testopel®, and Xyosted®
Original Policy Date:	03/06/2020
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

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

- For Natesto®, Testim®, Vogelxo®, Testopel®, 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Testopel®	Hypogonadism (Primary and Hypogonadotropic), delayed puberty in males	150- 450 mg (2-6 pellets) subcutaneously 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
Testim®	Hypogonadism (Primary and Hypogonadotropic)	50 mg (1 tube) applied topically once daily to the shoulders and/or upper arms. Dose may be titrated to a maximum of 100 mg	100 mg/day

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		once daily based on serum testosterone level. Dose should be titrated to maintain serum testosterone in the range of 300-1,000 ng/dL.	
Vogelxo®	Hypogonadism (Primary and Hypogonadotropic)	50 mg (1 tube or 1 packet or 4 pump actuations) applied topically once daily at approximately the same time each day to the shoulders and/or upper arms. Dose may be titrated to a maximum of 100 mg once daily based on serum testosterone level. Dose should be titrated to maintain serum testosterone in the range of 300-1,000 ng/dL.	100 mg/day
Natesto®	Hypogonadism (Primary and Hypogonadotropic)	11 mg (2 pump actuations; 1 actuation per nostril) administered intranasally three times daily. Discontinue therapy when total testosterone concentration consistently exceeds 1,050 ng/dL. Alternative treatment should be considered if total testosterone concentration is consistently below 300 ng/dL.	33 mg/day
Testosterone	Hypogonadism (Primary and Hypogonadotropic)	50 mg (4 pump actuations, two 25 mg packets, or one 50 mg packet) applied topically once daily 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 298-1,043 ng/dL.	100 mg/day
Jatenzo®	Hypogonadism (Primary and Hypogonadotropic)	Starting dose: 237 mg orally twice daily, adjust the dose based on serum testosterone levels	792 mg/day
Xyosted®	Hypogonadism (Primary and Hypogonadotropic)	75 mg administered subcutaneously in the abdominal region once a week.	Varies based on testosterone concentration.

Dosage Forms

- Testopel®: Pellet for implantation: 75 mg
- Testim®: 1% topical gel in unit-dose tube: 5 gm (50 mg testosterone).
- Vogelxo®:
  - Topical gel in unit-dose tube or packet: 50 mg testosterone in 5 gm of gel.
  - Topical 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.

- Natesto®: Intranasal gel in metered dose pump: 11 gm dispensed as 60 metered pump actuations. One pump actuation delivers 5.5 mg of testosterone.
- Testosterone:
  - 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.
- Jatenzo®: Oral capsules: 158 mg, 198 mg, 237 mg.
- Xyosted®: Autoinjector: 50 mg/0.5 mL, 75 mg/0.5 mL, 100 mg/0.5 mL.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of primary hypogonadism or hypogonadotropic hypogonadism;
2. Documentation of serum testosterone level less than the lower end of the normal range of the assay used on at least 2 separate occasions 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 of age or older;
      ii. Failure 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 dosing information).

Approval duration
Testopel®
Commercial: 6 months
Medicaid: 6 months
Xyosted®
Commercial: 6 months
Medicaid: 6 months
All other agents
Commercial: 12 months
Medicaid: 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

Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the FDA-approved maximum (see dosing information).

Approval duration
Xyosted®
Commercial: 6 months
Medicaid: 6 months
All other agents
Commercial: 12 months
Medicaid: 12 months

B. Delayed Puberty

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration
Commercial: Not applicable
Medicaid: Not applicable

III. Appendices

APPENDIX A: **Abbreviation/Acronym Key**
FDA: Food and Drug Administration
BP: Blood Pressure

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
testosterone 1% gel (AndroGel®)	Starting dose: 50 mg applied topically once daily. Dose may be titrated to a maximum of 100 mg once daily based on serum testosterone level.	100 mg/day
testosterone 1.62% gel (AndroGel®)	Starting dose: 40.5 mg applied topically once daily. Dose may be titrated to a maximum of 81 mg once daily based on serum testosterone level.	81 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
testosterone 2% gel (Fortesta®)	40 mg (4 pump actuations) applied topically once daily 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) once daily 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 cypionate	50 to 400 mg intramuscular once every 2 to 4 weeks	400 mg every 2 to 4 weeks
testosterone enanthate injection	50 to 400 mg intramuscular once every 2 to 4 weeks	400 mg every 2 to 4 weeks

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

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.
  - Jatenzo®, Xyosted®: Men with hypogonadal conditions not associated with structural or genetic etiologies.
  - Known hypersensitivity.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed warning(s):
  - Jatenzo®, Xyosted®: Increases in blood pressure (BP).
  - Testim®, Vogelxo®: Secondary exposure to testosterone.

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.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	02/2020	03/06/2020

Policy was reviewed: 1. Policy description table updated. 2. Dosing Regimen QD is replaced with "once daily". 3. Xyosted®- Dosing regimen updated 4. Continuation therapy criteria II.A.1. rephrased to “Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy” 5. Initial therapy and continued therapy approval duration updated. 6. Appendix A, Abbreviation updated to include SC, BP. 7. Appendix C, Boxed warning updated for Testim®, Vogelxo®. 8. References were updated.	07/29/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample, ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Appendix B: Therapeutic Alternatives header verbiage has been changed to “Below are suggested therapeutic alternatives based on...”. 3. APPENDIX C updated to include contraindications for Jatenzo®, Xyosted® and a boxed warning for Testim®. 4. References were reviewed and updated.	03/31/2021	06/10/2021
Policy was reviewed: 1. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 2. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 3. References were reviewed and updated.	01/05/2022	04/18/2022