Clinical Policy: Testosterone

Reference Number: AZ.CP.PHAR.02
Effective Date: 11.16.16
Last Review Date: 09.12.18
Line of Business: Arizona Medicaid

Revision Log

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

Description
The following are testosterone replacement agents requiring prior authorization: testosterone gel (Androgel®, Testim®), testosterone transdermal patch (Androderm®), testosterone solution (Axiron®), testosterone cypionate (Depo-Testosterone®), testosterone enanthate (Delatestryl®).

FDA approved indication
- Androgel, Androderm, Axiron, Testim, testosterone cypionate and testosterone enanthate are indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone
- Testosterone enanthate is indicated for palliation of inoperable metastatic (skeletal) mammary cancer in women who are 1 to 5 years postmenopausal

Limitation of use:
- The safety and efficacy of (testosterone therapy) has not been established in men with late-onset (age-related) hypogonadism.
- Safety and efficacy of (testosterone therapy) in males less than 18 years old have not been established.
- Topical testosterone products may have different strengths or application instructions that may result in different systemic exposure.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Androderm, Androgel, Axiron, Testim, testosterone cypionate, and testosterone enanthate are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Testosterone Replacement Therapy (must meet all)**:**

1. Diagnosis of primary hypogonadism or hypogonadotropic hypogonadism, congenital or acquired, as evidenced with recent (within past 90 days) lab values below therapeutic range;
2. For Testim requests: failure or clinically significant adverse effects to Androgel, Androderm and Axiron;

3. Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 12 months

B. Advanced Inoperable Carcinoma of the Breast: (must meet all)**:**
1. Diagnosis of metastatic skeletal mammary cancer;
2. Prescribed by or in consultation with an oncologist;
3. Member is 1-5 years post-menopausal;
4. Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 12 months

C. Other diagnoses/indications
1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. Testosterone Replacement Therapy (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. Documentation of response to therapy and appropriate monitoring of lab values within appropriate therapeutic range for the patient;
3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 12 months

B. Advanced Inoperable Carcinoma of the Breast: (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. Member is 1-5 years post-menopausal;
3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Centene Corporation and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
BPH: benign prostatic hypertrophy
DVT: deep vein thrombosis
MRI: magnetic resonance imaging
PE: pulmonary embolism

Appendix B: General Information

- In females, testosterone has been used for the palliative treatment of androgen-responsive, advanced, inoperable metastatic (skeletal) carcinoma of the breast in women who are 1-5 years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity include adrenalectomy, hypophysectomy, and/or antiestrogen therapy (e.g. tamoxifen). Androgen therapy also has been used in premenopausal women with carcinoma of the breast who have benefited from oophorectomy and are considered to have a hormone-responsive tumor. The decision to use androgen therapy in women with carcinoma of the breast should be made by an oncologist with expertise in the treatment of this carcinoma.
- Monitor patients with BPH receiving testosterone supplementation for worsening of signs and symptoms of BPH. Venous thromboembolism, including DVT and PE, have been reported in patients using testosterone products. Some postmarketing studies have shown an increased risk of myocardial infarction and stroke associated with the use of testosterone replacement therapy. Monitor serum testosterone, prostate specific antigen, liver function, lipid concentrations, hematocrit and hemoglobin periodically.
- Skin burns have been reported at the application site in patients wearing an aluminized transdermal system during a MRI scan. Because Androderm contains aluminum, it is recommended to remove the system before undergoing an MRI.
- Androgens may decrease blood glucose and insulin requirement in diabetic patients.
- Testosterone is contraindicated in men with carcinoma of the breast or known or suspected prostate cancer. Testosterone may cause fetal harm and should be avoided in pregnant or breastfeeding women.
- Secondary exposure to testosterone can produce signs of virilization. Children should avoid contact with unwashed or unclothed application sites in men using testosterone gel.

Appendix C: Therapeutic Alternatives
N/A

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Testosterone Gel (Testim)	Testosterone Replacement Therapy	5 gm of gel (50 mg testosterone) applied topically QD, titrate based on serum testosterone levels. Dose may be titrated to a maximum of 100 mg QD based on	100mg once daily

		serum testosterone level. Dose should be titrated to maintain serum testosterone within therapeutic range.	
Testosterone Gel (Androgel)	Testosterone Replacement Therapy	1% starting dose: 50 mg testosterone (two 25 mg packets, or one 50 mg packet) applied topically QD Dose may be titrated to 75mg daily followed by 100mg daily based on serum testosterone level. Dose should be titrated to maintain serum testosterone within therapeutic range. 1.62% starting dose: 40.5 mg (2 pump actuations or a single packet) applied topically QD. Dose may be titrated to a maximum of 81 mg QD based on serum testosterone level. Dose should be titrated to maintain serum testosterone level within the therapeutic range.	N/A
Androderm (testosterone transdermal patch)	Testosterone Replacement Therapy	Starting dose 4mg patch applied topically QD at night for 24 hours. Dose should be titrated up/down to maintain serum testosterone level within the therapeutic range.	6mg per day
Axiron	Testosterone	Starting dose is 60mg	120mg per day (4

(testosterone topical solution)	Replacement Therapy	of testosterone (1 pump actuation of 30mg testosterone to each axilla) applied once daily at the same time each morning. May increase or decrease by 30mg at a time based on serum levels up to 120mg per day.	actuations)
Injectable Testosterone Various	Testosterone Replacement Therapy	50-400mg IM every 2-4 weeks	N/A

VI. Product Availability

Drug	Availability
Testosterone (Androderm)	Transdermal Patch, Extended Release: 2mg/24 HR, 4mg/24 HR
Testosterone (Androgel)	Gel: 2.5-gm unit-dose packet (containing 25 mg testosterone), 5-gm unit dose packet (containing 50 mg testosterone); Gel: 1.62%: 88-gm metered-dose pump (dispenses 60 metered actuations with 20.25 mg testosterone in 1.25 gm gel per actuation), 1.25-gm unit-dose packet (containing 20.25 mg testosterone)2.5-gm unit-dose packet (containing 40.5 mg testosterone)
Testosterone (Axiron)	Solution: Metered Dose Pump 30mg per actuation
Testosterone (Testim)	Topical Gel: 1%, 50mg per 5 grams
Testosterone Cypionate injection (various)	100mg/ml in 10 ml vials, 200mg/ml in 1ml and 10ml vials
Testosterone Enanthate injection (various)	200mg/ml in 5 ml vials

VII. References

1. Testim [Prescribing Information] Malvern, PA: Auxilium Pharmaceuticals, Inc; October 2016.
2. Androderm [Prescribing Information] Parsipanny, NJ: Actavis Pharma, Inc.; October 2016.
3. Androgel 1% [Prescribing Information] North Chicago, IL: AbbVie Inc.; October 2016.
4. Androgel 1.62% [Prescribing Information] North Chicago, IL: AbbVie Inc.; October 2016.
5. Testosterone Cypionate Injection [Prescribing Information] New York, NY: Pharmacia & Upjohn Pharmaceutical Corp; May 2015.

6. Testosterone Enanthate Injection [Prescribing Information] Malvern, PA: Endo Pharmaceutical Solutions Inc.; October 2016.
7. Testosterone, Testosterone Cypionate, Testosterone Enanthate, American Hospital Formulary Service Drug Information. Available at: http://www.medicinescomplete.com/mc/ahfs/current/. Accessed June 14, 2017.
8. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colorado: Thomson Healthcare. Updated periodically. Accessed June 14, 2017.
9. Clinical Pharmacology Web site, Available at http://clinicalpharmacology-ip.com/default.aspx. Accessed June 14, 2017.
10. Axiron [Prescribing Information] Indianapolis, IN: Lilly USA; February 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template Annual Review: - Addition of Axiron to criteria - Addition of requirement of lab values confirming diagnosis and proper management for initial and continued therapy approval	06.17	11.17
Annual Review: Addition of additional Limitations of Use from Prescribing Information Modified preferred products to include Adroderm and Axiron per AHCCCS Drug List	09.12.18	

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.