Clinical Policy: Testosterone (Androderm)

Reference Number: HIM.PA.87
Effective Date: 12.01.14
Last Review Date: 11.22
Line of Business: HIM

Revision Log

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

Description

Testosterone transdermal system (Androderm®) is a topical androgen.

FDA Approved Indication(s)

Androderm is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testes syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropic lutenizing hormone-releasing hormone deficiency, or pituitary - hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitation(s) of use:

- Safety and efficacy of Androderm in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of Androderm 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 Androderm is **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. Age ≥ 18 years;
3. Documentation of serum testosterone level < 300 ng/dL on at least 2 separate days within the last 6 months;
4. Failure* of testosterone cypionate or testosterone enanthate injection at up to maximally indicated dose unless clinically significant adverse effects are experienced or both are contraindicated;

**Failure is demonstrated by lower than normal total testosterone levels as compared to laboratory reference values*

5. Dose does not exceed 6 mg per day; as a combination of one 2 mg and one 4 mg patch.

Approval duration: 12 months

B. 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 must use testosterone cypionate or testosterone enanthate injection, unless clinically significant adverse effects are experienced or both 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. 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

C. 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; 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; 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.

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 6 mg per day; as a combination of one 2 mg and one 4 mg patch.

Approval duration: 12 months

B. 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 receiving benefit from the referenced states for the applicable product and regulation (*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

C. 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; 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; 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.

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 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

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	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	400 mg every 2 to 4 weeks

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 carcinoma of the breast or known or suspected carcinoma of the prostate
  - Pregnant or breastfeeding women (testosterone may cause fetal harm)
- Boxed warning(s): none reported

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.
- 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

Indication	Dosing Regimen	Maximum Dose
Hypogonadism	1 patch topically nightly for 24 hours	6 mg/day

VI. Product Availability

Transdermal system: 2 mg/day, 4 mg/day

VII. References

1. Androderm Prescribing Information. Irvine, CA: Allergan USA, Inc.; May 2020. Available at https://www.androderm.com. Accessed July 20, 2022.
2. 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.
3. 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.
4. 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).
5. 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.
6. WPATH: World Professional Association for Transgender Health Standards of Care Version 8 Draft. Available at: https://www.wpath.org/soc8. Accessed July 20, 2022.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed July 20, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Reformatted guideline to new format. Added Workflow reference document. Removed exclusion for use in gender reassignment transitioning	12.15	12.15
Removed gender restriction to male. Updated references.	11.16	11.16
Converted to new template. Added testosterone enanthate injection as a trial option.	04.17	08.17
3Q 2018 annual review: no significant changes; added age; references reviewed and updated.	06.17.18	08.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: added requirement for documentation of testosterone levels per PI and guidelines; references reviewed and updated.	07.16.18	11.18
4Q 2019 annual review: added age-related hypogonadism or late-onset hypogonadism to Section III for excluded diagnoses; references reviewed and updated.	08.08.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: modified reference from HIM.PHAR.21 to HIM.PA.154; 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
4Q 2022 annual review: for hypogonadism clarified dosing restriction from 1 patch to "6 mg per day; as a combination of one 2 mg and one 4 mg patch"; clarified redirections are required "unless clinically significant adverse effects are experienced or both are contraindicated"; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.20.22	11.22

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.

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