Testosterone – Topical/Buccal/Nasal

Benefit Application

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

Description

FDA Approved Indications

Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, 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) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) 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.

Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Safety and efficacy of topical, buccal, and nasal testosterone products in males less than 18 years old have not been established.

Topical testosterone products may have different doses, strengths or application instructions that may result in different systemic exposure.

Compendial Uses

Gender Dysphoria in Female-to-Male transgender

Policy

Criteria for Approval

I. Testosterone products will be covered with prior authorization when the following criteria are met:
   o The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.]

AND
Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard male lab reference values OR
For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard male lab reference values OR
The requested drug is being prescribed for female-to-male gender reassignment in a patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy

Approval will be for 12 months.

Prior approval is required. Submit a prior approval/treatment request now.

Dosing and Administration
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

CLINICAL RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone: congenital or acquired primary hypogonadism (testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals), congenital or acquired hypogonadotropic hypogonadism (gonadotropin or luteinizing hormone-releasing hormone [LHRH] deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation). Safety and efficacy of topical, buccal, and nasal testosterone products in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

A testosterone determination, in conjunction with a free testosterone or sex hormone-binding globulin level, is the threshold test in the evaluation of suspected male hypogonadism (serum total testosterone levels less than 300 ng/dL). Testosterone levels should be determined in the morning, and studies should be repeated in patients with subnormal levels. The normative ranges for total and free testosterone levels in healthy young men vary among laboratories and assays. In some laboratories, the lower limit of the normal range for total testosterone level in healthy young men is 280-300 ng/dL and for serum free testosterone level is 5–9 pg/mL. The clinicians should use the lower limit of normal range for healthy young men established in their laboratory. For initial therapy, testosterone will be approved for patients with at least two confirmed low testosterone levels according to current practice guidelines or standard lab reference values. For continuation of therapy, one low testosterone level is required before the patient started testosterone therapy.

Transgender persons seeking to develop the physical characteristics of the desired gender require a safe, effective hormone regimen that will suppress endogenous hormone secretion determined by the person’s genetic/biologic sex and maintain sex hormone levels within the normal range for the person’s desired gender. The two major goals of hormonal therapy are to reduce endogenous hormone levels and, thereby, the secondary sex characteristics of the individual’s biological/genetic sex and to replace endogenous sex hormone levels with those of the reassigned sex. The Endocrine Society suggests that pubertal development of the desired opposite sex be initiated at about the age of 16 years, using a gradually increasing dose schedule of cross-sex steroids. However, the Endocrine Society Guidelines also state that identifying an age at which pubertal development is initiated is arbitrary, and the goal is to start the process
at a time when the individual will be able to make informed, mature decisions to engage in the therapy. Therefore, individuals aged 14 years and older who are able to make an informed, mature decision to engage in therapy will be approved.

For female-to-male (FtM) transgender persons, regimens to change secondary sex characteristics follow the general principle of hormone replacement treatment of male hypogonadism. Either parenteral or transdermal preparations can be used to achieve testosterone values in the normal male range (320-1000 ng/dL). The agent primarily used for endocrine treatment of FtM patients is testosterone. When determining the appropriate method of testosterone delivery, many considerations should be taken into account. The most well-described formulation of testosterone therapy used to treat FtM patients is intramuscular injection of testosterone esters (cypionate or enanthate). Because intramuscular testosterone cypionate or enanthate is often administered every 2-4 weeks, some patients may notice a cyclic variation in effects as well as more time outside the normal physiologic levels. Transdermal testosterone has been shown to provide less variation in serum testosterone levels compared with injectable preparations. Testosterone administered transdermally more closely mimics physiologic testosterone levels. However, transdermal preparations achieve low-normal ranges of testosterone levels in hypogonadal men, which may translate to a lessened change in physical appearance and virilization in the FtM patient.

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PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- Code(s), if applicable

REFERENCES

- Axiron [package insert]. Indianapolis, IN: Lilly USA, LLC; October 2016.
- Coleman E, Bockting W, Botzer M, et al. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People. World Professional Association for Transgender Health. Last Updated 2012. Available at:


**POLICY HISTORY**

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