



TESTOSTERONE TOPICAL AGENTS

(Androderm patch, AndroGel packets and pump, Axiron solution, Fortesta gel, Testim gel, Vogelxo)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Endogenous androgens, including testosterone and dihydrotestosterone (DHT), are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics (1).

Male hypogonadism results from insufficient secretion of testosterone and is characterized by low serum testosterone concentrations. Symptoms associated with male hypogonadism include the following: impotence and decreased sexual desire, fatigue and loss of energy, mood depression, regression of secondary sexual characteristics, and osteoporosis (1).

Regulatory Status

FDA-approved indications: For testosterone replacement therapy in men for conditions associated with a deficiency or absence of endogenous testosterone for the following (2-9):

1. Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
2. Hypogonadotropic hypogonadism (congenital or acquired): idiopathic 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.

Off-Label Use:

Testosterone can be used in the treatment of Gender Dysphoria (GD) and should only be started once a diagnosis of GD or transsexualism has been made per the DSM V or ICD-10 criteria (11).

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Topical testosterone includes a boxed warning of **secondary exposure**. Virilization has been reported in children who were secondarily exposed to transdermal testosterone. Children should avoid contact with unwashed or unclothed application sites in men using transdermal testosterone. Patients should be advised to strictly adhere to recommended instructions for use (2-9).

Male patients, with benign prostatic hyperplasia (BPH), must be monitored for worsening of signs and symptoms of BPH. Physicians should evaluate male patients for the presence of prostate cancer prior to the initiation of therapy. A normal prostate cancer risk is a PSA level that is less than 4 ng/ml. High prostate cancer risk patients, such as African American men and men whose father or brother had prostate cancer, should have a PSA less than 3 ng/ml. Patients should be re-evaluated 12 months after initiation of treatment, and then in accordance with prostate cancer screening practices (2-9).

Two total testosterone levels are required to determine medical necessity of testosterone replacement. Two morning samples drawn between 8:00 a.m. and 10:00 a.m. obtained on different days are required. Total testosterone levels need to be below 300 ng/dL on both days in order to be considered for therapy (12).

Hematocrit levels must be less than 54% prior to initiation of testosterone therapy and reevaluated annually thereafter (2-9).

Patients with severe obstructive sleep apnea and severe lower urinary tract symptoms are recommended not to use androgen therapy due to possible worsening of symptoms and/or even death (2).

Extreme caution should be used in patients with history of cardiovascular disease (2).

Safety and efficacy of transdermal testosterone in patients younger than 18 years have not been established. Improper use may result in acceleration of bone age and premature closure



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of epiphyses (2-9).

Summary

Topical testosterone is approved for testosterone replacement therapy in men for conditions associated with a deficiency of testosterone such as: hypogonadotropic hypogonadism (congenital or acquired), and primary hypogonadism (congenital or acquired). The following should be monitored: prostate-specific antigen (PSA) levels, serum testosterone concentrations, hematocrit, presence of prostate cancer, and worsening effects of benign prostatic hypertrophy (BPH), if present and been assessed for their cardiovascular risk. Safety and efficacy of testosterone transdermal in patients younger than 18 years have not been established (2-12).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of the topical testosterone products Androderm patch, AndroGel packets and pump, Axiron solution, Fortesta gel, Testim gel, and Vogelxo gel while maintaining optimal therapeutic outcomes.

References

1. Male Hypogonadism. Mayo Foundation for Medical Education and Research; 1998-2014.
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