

TESTOSTERONE POWDER

Testosterone (cypionate, enanthate, and propionate) powder, Fluoxymesterone powder, Methyltestosterone powder

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).

Testosterone is commercially available in multiple dosage forms including oral, buccal, implant, injectable, nasal, and topical.

Regulatory Status

FDA-approved indications: (3-19)

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.
3. Delayed puberty in males: to induce pubertal changes in hypogonadal males.
4. In women who have been postmenopausal for 1 to 5 years, androgens may be used as secondary treatment for advancing inoperable metastatic (skeletal) mammary cancer. This has also been used to treat hormone-responsive breast cancer in premenopausal women post- oophorectomy.

TESTOSTERONE POWDER

Testosterone (cypionate, enanthate, and propionate) powder, Fluoxymesterone powder, Methyltestosterone powder

Off-Label Use:

Testosterone can be used in the treatment of Gender Dysphoria (GD) and should only be started once a diagnosis of GID or transsexualism has been made per the DSM V or ICD-10 criteria (24).

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 (3-9).

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. Check prostate-specific antigen (PSA) levels in men over age 50 years, or in those over age 40 having a family history of prostate cancer or if African-American; to ensure proper dosing. Patients should be re-evaluated 12 months after initiation of treatment, and then in accordance with prostate cancer screening practices (3-19).

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 (23).

Hematocrit levels must be less than 54% prior to initiation of testosterone therapy and reevaluated annually thereafter (3-19).

Androgen use for delayed puberty in males should be prescribed only by specialists who are aware of the adverse effects on bone maturation. An X-ray of the hand and wrist every 6 months will be required to determine bone age and to assess the effect of treatment on the epiphyseal centers (12-19).

TESTOSTERONE POWDER

Testosterone (cypionate, enanthate, and propionate) powder, Fluoxymesterone powder, Methyltestosterone powder

Androgen therapy in treatment for women with breast cancer should be made by an oncologist with expertise in this field. Hypercalcemia may occur in immobilized patients and in patients with breast cancer. If this occurs, the drug should be discontinued (16).

Extreme caution should be used in patients with a history of cardiovascular disease (6).

Due to lack of controlled studies in women and potential virilizing effects, the nasal formulation is not indicated for use in women. Safety and efficacy of the nasal formulation has not been established in pediatric patients less than 18 years of age. Improper use may result in acceleration of bone age and premature closure of epiphyses (11).

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).

Hormone replacement therapy is prescribed to post-menopausal women for their effects in preventing postmenopausal osteoporosis (20). Among the progestogens available to the prescriber and recommended to be added to estrogen replacement therapy (ERT) are the molecules derived from testosterone. Low doses of any type of progestogen could be both protective of the target organs and devoid of harmful effects. The use of ERT affords protection against osteoporosis and cardiovascular disease (21). The addition of testosterone to HRT has shown a significant increase in hip bone mineral density (22).

Safety and efficacy of testosterone transdermal in patients younger than 18 years have not been established (3-19).

Summary

Testosterone is approved for testosterone replacement therapy in men for conditions associated with a deficiency of testosterone such as: hypogonadotropic hypogonadism (congenital or acquired), primary hypogonadism (congenital or acquired), and delayed puberty. In women, testosterone therapy is approved to treat metastatic breast carcinoma. Liver function and hematocrit should be monitored in all patients. In adult men, the following is recommended to be



TESTOSTERONE POWDER

Testosterone (cypionate, enanthate, and propionate) powder, Fluoxymesterone powder, Methyltestosterone powder

monitored: prostate-specific antigen (PSA) levels, serum testosterone concentrations, prostate specific antigen (PSA), presence of prostate cancer, and worsening effects of *benign prostatic hypertrophy* (BPH), if present, and assessment of their cardiovascular risk is recommended. Calcium levels in women should be monitored. For pubescent males, radiographic evidence to determine bone maturation needs to be obtained (1-6).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of testosterone powders while maintaining optimal therapeutic outcomes.

References

1. Male Hypogonadism. Mayo Foundation for Medical Education and Research 1998-2014: <http://www.mayoclinic.org/diseases-conditions/male-hypogonadism/basics/causes/con-20014235>. Accessed on September 24, 2021.
2. Bhasin S, Cunningham GR, Hayes FJ et al. Testosterone therapy in men with androgen deficiency syndromes: an endocrine society clinical practice guideline. [J Clin Endocrinol Metab](#). 2010;95 (6):2536-59.
3. Androderm [package insert]. Madison, NJ: Allergan USA Inc.; May 2020.
4. AndroGel 1% [package insert]. North Chicago, IL: AbbVie Inc.; May 2019.
5. Axiron [package insert]. Indianapolis, IN: [Eli Lilly](#); July 2017.
6. Fortesta [package insert]. Malvern, PA: [Endo Pharmaceuticals Inc.](#); June 2020.
7. AndroGel 1.62% [package insert]. North Chicago, IL: AbbVie Inc.; November 2020.
8. Testim [package insert]. Malvern, PA: [Endo Pharmaceuticals](#); August 2021.
9. Vogelxo [package insert]. Maple Grove, MN: [Upsher-Smith](#) Laboratories, Inc.; April 2020.
10. Aveed [package insert]. Malvern, PA: [Endo Pharmaceuticals Inc.](#); August 2021.
11. Natesto Nasal gel [package insert]. Christ Church, Barbados: Acerus Pharmaceutical; October 2016.
12. Striant [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; October 2016.
13. Testopel [package insert]. Malvern, PA: Endo Pharmaceuticals, Inc.; August 2018.
14. Depo-Testosterone [package insert]. New York, NY: Pfizer Pharmacia and Upjohn Co; August 2020.
15. Android [package insert]. Aliso Viejo, CA: Valeant Pharmaceuticals; November 2016.
16. Delatestryl [package insert]. Malvern, PA: Endo Pharmaceuticals; October 2016.



TESTOSTERONE POWDER

Testosterone (cypionate, enanthate, and propionate) powder, Fluoxymesterone powder, Methyltestosterone powder

17. Androxy [package insert]. Maple Grove, MN: [Upsher-Smith](#) Laboratories, Inc; September 2017.
18. Dailymed Methitest resources page National Institutes of Health Web site
<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=77bb4ef4-c10e-4acc-8225-651d003f4561>. Accessed on September 6, 2018.
19. Testred [package insert]. Bridgewater, NJ; Valeant Pharmaceuticals; June 2014.
20. Savvas M. et al. Skeletal effects of oral estrogen compared with subcutaneous estrogen and testosterone in postmenopausal women. *BMJ* 1988 Jul 30;297 (6644):331-3.
21. Sitruk-Ware R. Estrogen therapy during menopause. Practical treatment recommendations. *Drugs* 1990 Feb;39(2):203-17.
22. Miller BE, et al. Sublingual administration of micronized estradiol and progesterone, with and without micronized testosterone: effect on biochemical markers of bone metabolism and bone mineral density. *Menopause* 2000 Sep-Oct; 7(5):318-26.
23. Carnegie C. Diagnosis of Hypogonadism: Clinical Assessments and Laboratory Tests. *Rev Urol.* 2004; 6(Suppl 6): S3-S8. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1472884>
24. Hembree, WC, Cohen-Kettenis, P, et al. Endocrine Treatment of Transsexual Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2009; 94(9):3132-3154.