

## New Drug Bulletin: Testosterone gel (Fortesta™ - Endo Pharmaceuticals)

January 4, 2012

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Fortesta™ is a new topical testosterone gel product approved for replacement therapy in adult males with congenital or acquired conditions related to testosterone deficiency. Specific conditions resulting in testosterone deficiency include primary hypogonadism (defects of the gonads) or hypogonadotropic hypogonadism (failure of the hypothalamus or pituitary to produce gonadotropins). Topical testosterone products provide an exogenous source of testosterone. Fortesta™ produces similar plasma testosterone levels as those seen in healthy men. Fortesta™ is a schedule III controlled substance and has the potential for dependence and abuse.

Fortesta™ is applied topically. The gel delivers testosterone continuously for 24 hours following application. Testosterone plasma levels of > 300 ng/dL are achieved and peak steady state plasma concentrations occur approximately 4 hours after application. Testosterone is primarily bound to sex hormone-binding globulin (SHBG) and albumin in the serum. In plasma, approximately 40% of testosterone is bound to SHBG, 2% is unbound, and the remainder is loosely bound to other proteins, including albumin. Testosterone is metabolized to two major active metabolites, estradiol and dihydrotestosterone (DHT). The elimination half-life of testosterone reported in the literature varies considerably from 10-100 minutes. Testosterone is inactivated primarily in the liver. Following an intramuscular dose of testosterone, approximately 90% is excreted in the urine as conjugates of testosterone and its metabolites. Six percent is excreted in the feces and is primarily unconjugated.

The clinical efficacy of Fortesta™ was evaluated in one multicenter, open-label, non-comparative trial. Males age 18-75 years with total serum testosterone < 250 ng/dL on a single occasion or < 300 ng/dL on two consecutive occasions were treated with a starting dose of 40 mg of testosterone (4 pump actuations of Fortesta™). The dose was titrated (minimum 10 mg, maximum 70 mg) based on serum testosterone levels at 2 hours post application on Days 14, 35, and 60. On Day 90, a majority of patients (77.5%) had average testosterone levels within the normal range (300-1140 ng/dL). On Day 90, 5.4% of patients had maximum testosterone levels > 1500 ng/dL and 1.6% of patients had maximum levels of 1800-2499 ng/dL. No patient had maximum testosterone levels ≥ 2500 ng/dL on Day 90.

The most common adverse reaction experienced by patients in the clinical trial was skin reaction at the application site (16.1%). Other adverse reactions included an increase in prostate specific antigen (1.3%) and abnormal dreams (1.3%). In addition, secondary exposure to testosterone from direct and indirect contact with testosterone gel products can occur in women and children. Fortesta™ is contraindicated in men with breast carcinomas or known or suspected prostate carcinomas and in women who are pregnant, may become pregnant, or breastfeeding. Fortesta™ carries warnings for the potential worsening of benign prostatic hyperplasia, increased risk of prostate cancer, virilization of women and children as a result of secondary exposure to testosterone, polycythemia, suppression of spermatogenesis, life-threatening hepatic complications, edema, gynecomastia, sleep apnea, changes in lipid profile, hypercalcemia, and decreased thyroxine-binding globulin. Monitor patients for these conditions. Testosterone therapy may result in changes in insulin sensitivity

or glycemic control, specifically decreased blood glucose. Diabetic patients may have decreased insulin requirements.

Testosterone therapy may affect anticoagulant activity. Monitor the PT/INR of patients more frequently. Patients on concurrent testosterone and corticosteroids or adrenocorticotrophic hormone (ACTH) may experience increased fluid retention. Monitor fluid status in patients with cardiac, renal, or hepatic disease.

Fortesta™ is applied topically once daily in the morning. The recommended starting dose is 40 mg. Adjust the dose at 14 and 35 days after initiation or a dose adjustment based on serum testosterone concentration 2 hours after application. See the package insert for the specific dose adjustment algorithm. The minimum recommended dose is 10 mg daily. Do not exceed a maximum dose of 70 mg daily. Fortesta™ cannot be interchanged with other topical testosterone products on a mg per mg basis. Fortesta™ has not been studied in patients with renal or hepatic impairment. The safety and efficacy is also unknown in patients < 18 years and > 65 years of age.

Fortesta™ is supplied as a 60 gm metered dose canister that delivers approximately 120 pump actuations. Each pump actuation contains 10 mg of testosterone. Prior to the first dose, prime the canister by pumping the actuator eight times. Apply the gel to clean, dry, intact skin of the front and inner thighs. Avoid the genitals and other body parts. Use one finger to gently rub the gel evenly onto the skin. Fortesta™ is an alcohol based product and is flammable until the gel is dry. Avoid fire, flames, or smoking immediately after application. Once the gel is dry, cover with clothing and wash hands with soap and water. Do not swim, shower, or wash the site for at least 2 hours after application. Avoid contact of women and children with the application site or unwashed clothing. Prior to potential skin-to-skin contact with another individual, wash the application site thoroughly. If another individual is exposed to Fortesta™, wash the exposed area immediately with soap and water. Store at room temperature and do not freeze. Dispose the canister in the trash and prevent accidental exposure to children and pets. Table 1 summarizes the cost of therapy of topical testosterone products labeled for treatment of testosterone deficiency.

**Table 1.** Cost of Therapy of Topical Testosterone Products

Agent	Dosage Regimen (Range)	Cost per Day (Range) AWP
<i>Testosterone topical gel</i>		
Fortesta™ 2%	10 mg to 70 mg once daily	\$2.89 - \$20.22
AndroGel® 1%	50 mg to 100 mg once daily	\$12.40 - \$24.81
AndroGel® 1.62%	20.25 mg to 81 mg once daily	\$2.93 - \$11.70
Testim® 1%	50 mg to 100 mg once daily	\$11.74 – 23.48
<i>Testosterone topical solution</i>		
Axiron® 2%	30 mg to 120 mg once daily	\$5.57 - \$22.29

In summary, Fortesta™ is a new topical testosterone gel product labeled for use in males with conditions associated with testosterone deficiency. Fortesta™ offers an additional option for patients who prefer a topical gel treatment.

## References:

1. Endo Pharmaceuticals Inc. Fortesta (testosterone) Gel for topical use CIII [product information]. Chadds Ford, PA: Endo Pharmaceuticals Inc.; 2010.
2. Abbott Laboratories. Androgel (testosterone gel) 1% for topical use [product information]. North Chicago, IL: Abbott Laboratories; 2011.
3. Abbott Laboratories. Androgel (testosterone gel) 1.62% for topical use [product information]. North Chicago, IL: Abbott Laboratories; 2011.
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5. Eli Lilly and Company. Axiron (testosterone) topical solution [product information]. Indianapolis, IN: Eli Lilly and Company; 2011.
6. Anon, ed. *Red Book Online. Via Drugdex System [internet database]*. Greenwood Village, CO: Thomson Healthcare; 2011.

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