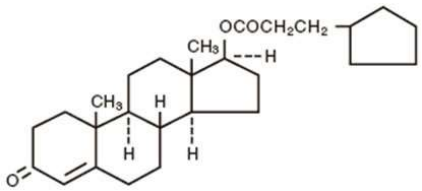
Depo-Testosterone

Testosterone cypionate Injection, USP

DIN: 00096158
200 mg/mL
10 mL Multiple-Dose, Cartons of 1 vial



Systematic name: androst-4-en-3-one,17-(3-cyclopentyl-1-oxopropoxy)-, (17ß)

DESCRIPTION

Depo-Testosterone (Testosterone Cypionate) Injection, USP, for Intramuscular Injection, contains testosterone cypionate which is the oil-soluble 17 (beta) - cyclopentylpropionate ester of the androgenic hormone testosterone. Testosterone cypionate is a white or creamy white crystalline powder, odorless or nearly so and stable in air. It is insoluble in water, freely soluble in alcohol, chloroform, dioxane, ether, and soluble in vegetable oils.

COMPOSITION

Medicinal ingredients and Non-Medicinal ingredients Each mL contains: Testosterone cypionate, 200 mg; benzyl alcohol, 9 mg; In cottonseed oil USP, q.s

CLINICAL PHARMACOLOGY

Endogenous androgens are responsible for the normal growth and development of the male sex organsand for the maintenance of secondary sex characteristics. These effects include growth andmaturation of the prostate, the seminal vesicles, the penis, and the scrotum; development of male hair distribution, such as beard, pubic, chest, and axillary hair; laryngeal enlargement; vocal cord thickening; alterations in body musculature; and fat distribution. Androgens also cause retention of nitrogen, sodium, potassium, and phosphorus, and decrease in the urinary excretion of calcium. Androgens have been reported to increase protein anabolism and to decrease protein catabolism. Nitrogen balance is improved only when there is sufficient intake of calories and protein. Androgens are responsible for the growth spurt of adolescence and for the eventual termination of linear growth which may result in fusion of the epiphyseal growth centers. In children, exogenous androgens accelerate linear growth rates but may cause a disproportionate advancement in bone maturation. Prolonged use may result in fusion of the epiphyseal growth centers and cause the termination of the growth process. Androgens have been reported to stimulate the production of red blood cells by enhancing the production of erythropoieticstimulating factor. During exogenous administration of androgens, the endogenous testosterone release is inhibited through feedback inhibition of

pituitary luteinizing hormone (LH). At large doses of exogenous androgens, spermatogenesis may also be suppressed through feedback inhibition of pituitary follicle stimulating hormone (FSH). There is a lack of substantial evidence that androgens are effective when it comes to fractures, surgery, convalescence, and functional uterine bleeding.

PHARMACOKINETICS

Testosterone esters are less popular than free testosterone. Testosterone esters in oil injected intramuscularly are absorbed slowly from the lipid phase; thus testosterone enanthate can be given at intervals of two to four weeks. Testosterone in plasma is 98 percent bound to a specific testosterone-estradiol binding globulin, and about two percent is free. Generally, theamount of this sex-hormone binding globulin (SHBG) in the plasma will determine the distribution of testosterone between free and bound forms and the free testosterone concentration will determine its half-life. About 90 percent of a dose of testosterone is excreted in the urine as glucuronic and sulfuric acidconjugates of testosterone and its metabolites; about six percent of a dose is excreted in the feces, mostly in the unconjugated form. Inactivation of testosterone occurs primarily in the liver. Testosterone is metabolizedto various 17-keto steroids through two different pathways. There are considerable variations of the half-life of testosterone as reported in the literature, ranging from 10 to 100 minutes. In responsive tissues, the activity of testosterone appears to depend on the reduction of the dihydrotestosterone (DHT), which binds to cytosol receptor proteins. The steroid-receptor complex is transported to the nucleus where it initiates transcription events and cellular changes related to androgen action.

INDICATIONS AND USAGE

Testosterone cypionate injection, USP is indicated for replacement therapy for males in conditions associated with symptoms of deficiency or absence of endogenous testosterone. Primary hypogonadism (congenital or acquired) testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchidectomy. Hypogonadotropic hypogonadism (congenital or acquired) idiopathic gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation.

CONTRAINDICATIONS

Hypersensitivity to the drug affects males with carcinoma of the breast, males with known or suspected carcinoma of the prostate gland, women who are or who may be pregnant, any person with serious cardiac, hepatic or renal disease. WARNINGS Hypercalcemia may occur to immobilized patients. If it occurs, the drug should be discontinued. Prolonged use of high doses of androgens (principally the 17-α alkyl-androgens) has been associated with development of hepatic adenomas, hepatocellular carcinoma, and peliosis hepatis – all potentially life-threatening complications. Geriatric patients treated with androgens may be at an increased risk of developing prostatic hypertrophy and prostatic carcinoma although conclusive evidence to support this concept is lacking. Edema, with or without congestive heart failure, may be a serious complication in patients with pre-existing cardiac, renal or hepatic disease. Gynecomastia may develop and occasionally persist in patients being treated for hypogonadism. This product contains benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal “Gasping Syndrome” in premature infants. An androgen therapy should be used cautiously in healthy males with delayed puberty. The effect on bone maturation should be monitored by assessing bone age of the wrist and hand every 6 months. For children, androgen treatment may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect may result in compromised adult stature. The younger the child, the greater is the risk of compromising final mature height.

GENERAL

Patients with benign prostatic hypertrophy may develop acute urethral obstruction. Priapism or excessive sexual stimulation may develop. Oligospermia may occur after prolonged administration or excessive dosage. If any of these effects appear, the androgen should be stopped and if restarted, a lower dosage should be utilized.

INFORMATION FOR PATIENTS
Patients should be instructed to report any of the following: nausea, vomiting, changes in skin color, ankle swelling, too frequent or persistent erections of the penis. LABORATORY TEST Hemoglobin and hematocrit levels (to detect polycythemia) should be checked periodically in patients receiving long-term androgen administration. The serum cholesterol may increase during androgen therapies. DRUG INTERACTION Androgens may increase sensitivity for oral anticoagulants. Dosage of the anticoagulant may require reduction in order to maintain satisfactory therapeutic hypoprothrombinemia. Concurrent administration of oxyphenbutazone and androgens may result in elevated serum levels of oxyphenbutazone. For diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, insulin requirements.

DRUG/LABORATORY TEST INTERFERENCE
Androgens may decrease levels of thyroxine¬binding globulin, resulting in decreased total T4 serum levels and increased resin uptake of T3 and T4. Free thyroid hormone levels remain unchanged and there is no clinical evidence of thyroid dysfunction. ANIMAL DATA Testosterone has been tested by subcutaneous injection and implantation in mice and rats. The implant induced cervical-uterine tumors in mice, which metastasized in some cases. There is suggestive evidence that injection of testosterone into some strains of female mice increases their susceptibility to hepatoma. Testosterone is also known to increase the number of tumors and decrease the degree of differentiation of chemically induced carcinomas in the rat's liver. HUMAN DATA There are rare reports of hepatocellular carcinoma for patients receiving long-term therapy with androgens in high doses. Withdrawal of the drugs did not lead to regression of the tumors in all cases. Geriatric patients treated with androgens may be at an increased risk of developing prostatic hypertrophy. About prostatic carcinoma, conclusive evidence to support this concept is lacking. TERATOGENIC EFFECTS Pregnancy Category X. (See

CONTRAINDICATIONS.) Nursing Mothers Testosterone cypionate injection, USP is not recommended for use in nursing mothers.

ADVERSE REACTIONS
The following adverse reactions in the male have occurred with some androgens: Endocrine and Urogenital Gynecomastia and excessive frequency and duration of penile erections. Oligospermia may occur at high dosages. Skin and Appendages Hirsutism, male pattern of baldness, seborrhea, and acne. Fluid and Electrolyte Disturbances Retention of sodium, chloride, water, potassium, calcium, andinorganic phosphates. Gastrointestinal Nausea, cholestatic jaundice, alterations in liver function tests, rarely hepatocellular neoplasms and peliosis hepatis (see Hematologic Suppression of clotting factors II, V, VII, and X, bleeding in patients on concomitant anticoagulant therapy, and polycythemia. Nervous System Increase or decrease of libido, headache, anxiety, depression, and generalized paresthesia. Allergic Hypersensitivity, including skin manifestations and anaphylactoid reactions. Miscellaneous Inflammation and pain at the site of intramuscular injection.

DRUG ABUSE AND DEPENDENCE
Controlled Substance Class Testosterone is a controlled substance under the Anabolic Steroid Control Act, and testosterone cypionate injection, USP has been assigned to Schedule III.

OVERDOSAGE
There have been no reports of acute overdosage with the androgens.

DOSAGE AND ADMINISTRATION
Testosterone cypionate injection, USP is for intramuscular use only. It should not be given intravenously. Intramuscular injections should be given deep in the gluteal muscle. The suggested dosage for testosterone cypionate injection, USP varies depending on the age, sex, and diagnosis of the individual patient. Dosage is adjusted according to the patient's response and the appearance of adverse reactions. Various dosage regimens

have been used to induce pubertal changes in hypogonadal males; some experts have advocated lower dosages initially, gradually increasing the dose as puberty progresses, with or without a decrease to maintenance levels. Other experts emphasize that higher dosages are needed to induce pubertal changes and lower dosages can be used for maintenance after puberty. The chronological and skeletal ages must be taken into consideration, both in determining the initial dose and in adjusting the dose. For hypogonadal males, 50 to 400 mg should be administered every two to four weeks.

STORAGE INSTRUCTIONS

Vial should be kept away from light and stored in controlled temperature from 20-25 degree Celsius (68° TO 77°F) Warming and shaking the vial should redissolve any crystals that may have formed during storage. Keep out of reach of children.