TESTOSTERONE CYPIONATE- testosterone cypionate injection, solution
Dispensing Solutions, Inc.

TESTOSTERONE CYPIONATE INJECTION USP
FOR INTRAMUSCULAR USE ONLY C-III
Rx only

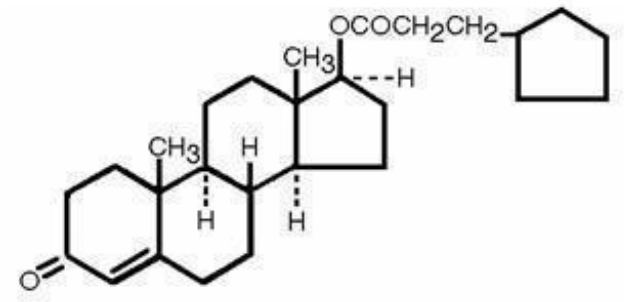
DESCRIPTION

Testosterone Cypionate Injection 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.

The chemical name for testosterone cypionate is androst-4-en-3-one,17-(3-cyclopentyl-1-oxopropoxy)-, (17β)-. Its molecular formula is $C_{27}H_{40}O_3$ and the molecular weight 412.61.

The structural formula is represented below:



Each mL contains: Testosterone Cypionate 200 mg, Benzyl Benzoate 20%, with Benzyl Alcohol 0.9% as preservative in Cottonseed Oil q.s.

CLINICAL PHARMACOLOGY

Endogenous androgens are responsible for normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. These effects include growth and maturation of prostate, seminal vesicles, penis, and scrotum; development of male hair distribution, such as beard, pubic, chest and axillary hair; laryngeal enlargement, vocal chord thickening, and alterations in body musculature and fat distribution. Drugs in this class also cause retention of nitrogen, sodium, potassium, and phosphorus, and decreased urinary excretion of calcium. Androgens have been reported to increase protein anabolism and 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 eventual termination of linear growth, brought about by fusion of the epiphyseal growth centers. In children, exogenous androgens accelerate linear growth rates, but may cause disproportionate advancement in bone maturation. Use over long periods may result in fusion of the epiphyseal growth centers and termination of the growth process. Androgens have been reported to stimulate production of red blood cells by enhancing production of erythropoietic stimulation factor.

During exogenous administration of androgens, 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 in fractures, surgery, convalescence, and functional uterine bleeding.

Pharmacokinetics

Testosterone esters are less polar than free testosterone. Testosterone esters in oil injected intramuscularly are absorbed slowly from the lipid phase; thus, testosterone cypionate 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 2 percent is free. Generally, the amount of this sex-hormone binding globulin 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 acid conjugates of testosterone and its metabolites; about 6 percent of a dose is excreted in the feces, mostly in the unconjugated form. Inactivation of testosterone occurs primarily in the liver. Testosterone is metabolized to various 17-keto steroids through two different pathways.

The half-life of testosterone cypionate when injected intramuscularly is approximately eight days.

In many tissues the activity of testosterone appears to depend on reduction to dihydrotestosterone, 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 is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone.

1. Primary hypogonadism (congenital or acquired)-testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchidectomy.
2. Hypogonadotropic hypogonadism (congenital or acquired)-idiopathic gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation.

CONTRAINDICATIONS

1. Known hypersensitivity to the drug
2. Males with carcinoma of the breast
3. Males with known or suspected carcinoma of the prostate gland
4. Women who are or who may become pregnant
5. Patients with serious cardiac, hepatic or renal disease

WARNINGS

Hypercalcemia may occur in immobilized patients. If this 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 persists 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.

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. In 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 the risk of compromising final mature height.

This drug has not been shown to be safe and effective for the enhancement of athletic performance. Because of the potential risk of serious adverse health effects, this drug should not be used for such purpose.

PRECAUTIONS

General

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

Testosterone cypionate should not be used interchangeably with testosterone propionate because of differences in duration of action.

Testosterone cypionate *is not* for intravenous use.

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 Tests

Hemoglobin and hematocrit levels (to detect polycythemia) should be checked periodically in patients receiving long-term androgen administration.

Serum cholesterol may increase during androgen therapy.

Drug Interactions

Androgens may increase sensitivity to 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.

In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, insulin requirements.

Drug/Laboratory Test Interferences

Androgens may decrease levels of thyroxine-binding globulin, resulting in decreased total T_4 serum levels and increased resin uptake of T_3 and T_4. Free thyroid hormone levels remain unchanged, however, and there is no clinical evidence of thyroid dysfunction.

Carcinogenesis

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 of the liver in rats.

Human Data

There are rare reports of hepatocellular carcinoma in 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 and prostatic carcinoma although conclusive evidence to support this concept is lacking.

Pregnancy

Teratogenic Effects

Pregnancy Category X (See**CONTRAINDICATIONS**).

Nursing Mothers

Testosterone Cypionate Injection is not recommended for use in nursing mothers.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 12 years have not been established.

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, and inorganic phosphates.

Gastrointestinal

Nausea, cholestatic jaundice, alterations in liver function tests, rarely hepatocellular neoplasms and peliosis hepatis (See**WARNINGS**).

Hematologic

Suppression of clotting factors II, V, VII, and X, bleeding in patients on concomitant anticoagulant therapy, and polycythemia.

Nervous System

Increased or decreased 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 Steroids Control Act, and Testosterone Cypionate Injection has been assigned to Schedule III.

OVERDOSAGE

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

DOSAGE AND ADMINISTRATION

Testosterone Cypionate Injection 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 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 replacement in the hypogonadal male, 50-400 mg should be administered every two to four weeks.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Warming and shaking the vial should redissolve any crystals that may have formed during storage at temperatures lower than recommended.

HOW SUPPLIED

Testosterone Cypionate Injection USP, 200 mg/mL is available in:
10 mL multiple dose vials, individually boxed.

Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature].

PROTECT FROM LIGHT.

Literature revised: July 2010
Product No.: 0256-10

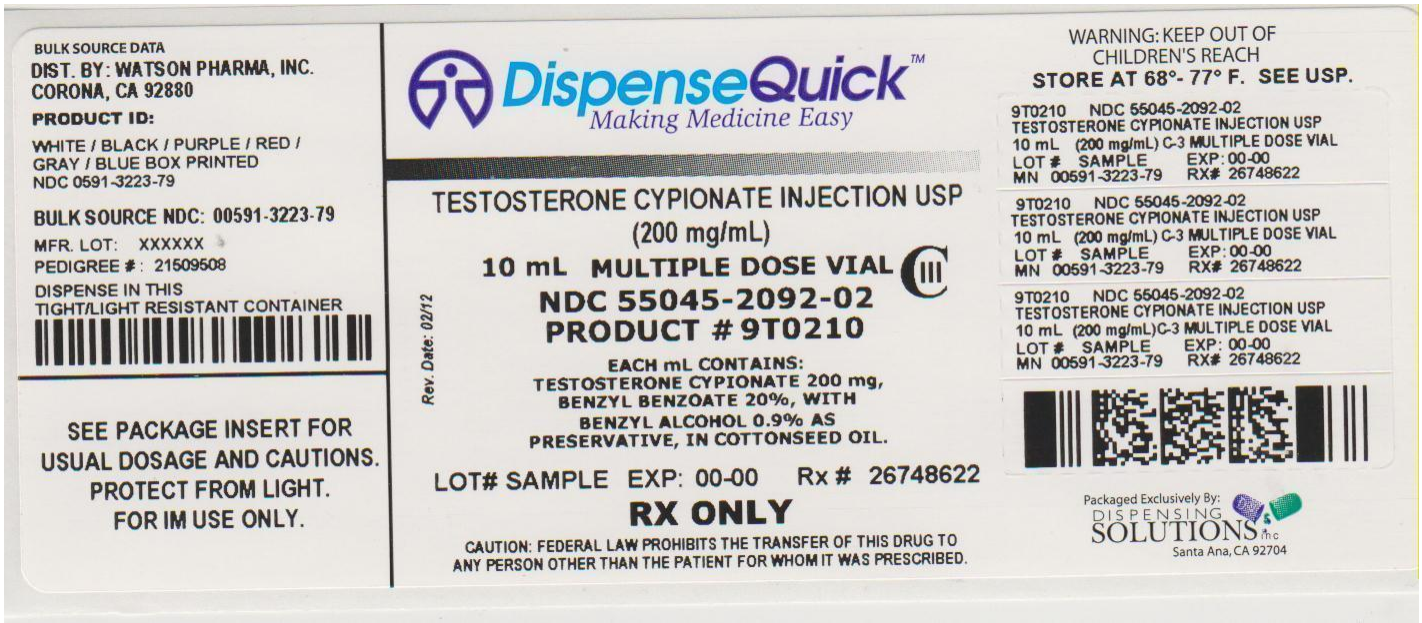
Manufactured by:
Hikma Farmaceutica (Portugal)
S.A. 2705-906 Terrugem SNT, Portugal

Distributed by:
Watson Pharma, Inc.
Corona, CA 92880 USA

PIN230-WAT/1

Package Label

NDC 55045-2092-02
10 mL Multiple Dose Vial
Testosterone Cypionate Injection USP (200 mg/mL)
FOR INTRAMUSCULAR USE ONLY



Rx only

Sterile
Each mL contains: Testosterone Cypionate 200 mg,
Benzyl Benzoate 20%, with
Benzyl Alcohol 0.9% as
preservative, in Cottonseed Oil.

Usual adult dosage: See package insert.

Store at 20°-25°C (68°-77°F)
[See USP Controlled Room Temperature].

PROTECT FROM LIGHT.

Manufactured by:
Hikma Farmaceutica (Portugal)S.A. 2705-906 Terrugem SNT
Portugal

Distributed by:
Watson Pharma, Inc.
Corona, CA 92880 USA

Repackaged by:
Dispensing Solutions, Inc.
Santa Ana, CA 92704 USA

TESTOSTERONE CYPIONATE

testosterone cypionate injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:55045-2092(NDC:0591-3223)
Route of Administration	INTRAMUSCULAR	**DEA Schedule**	CIII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TESTOSTERONE CYPIONATE (TESTOSTERONE)	TESTOSTERONE CYPIONATE	200 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BENZYL BENZOATE	223.6 mg in 1 mL
BENZYL ALCOHOL	9.9 mg in 1 mL
COTTONSEED OIL	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:55045-2092-2	1 in 1 CARTON		
1		10 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA086030	05/04/2011	

Labeler - Dispensing Solutions, Inc. (066070785)

Registrant - PSS World Medical, Inc. (101822682)

Establishment

Name	Address	ID/FEI	Business Operations
Dispensing Solutions, Inc.		066070785	relabel(55045-2092), repack(55045-2092)

Revised: 10/2012 Dispensing Solutions, Inc.