

TESTOSTERONE CYPIONATE- testosterone cypionate injection Proficient Rx LP

Testosterone Cypionate Injection, USP

Rx Only

CIII

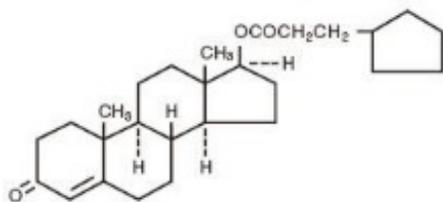
DESCRIPTION

Testosterone Cypionate Injection, USP for intramuscular injection, contains Testosterone Cypionate, USP which is the oil-soluble 17 (beta)- cyclopentylpropionate ester of the androgenic hormone testosterone.

Testosterone Cypionate, USP 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, USP is androst-4-en-3-one,17-(3-cyclopentyl-1-oxopropoxy)-, (17 β). Its molecular formula is C₂₇H₄₀O₃, and the molecular weight 412.61.

The structural formula is represented below:



Testosterone Cypionate Injection, USP is available in one strength, 200 mg/mL Testosterone Cypionate, USP.

Each mL of the 200 mg/mL solution contains:

Testosterone Cypionate, USP	200 mg
Benzyl Benzoate, USP	0.2 mL
Cottonseed Oil, USP	560 mg
Benzyl Alcohol, USP (as preservative)	9.45 mg

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 the prostate, seminal vesicles, penis, and scrotum; development of male hair distribution, such as beard, pubic, chest, and axillary hair; laryngeal enlargement, vocal cord 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, USP 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)*: gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation.

Safety and efficacy of testosterone cypionate in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

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.

There have been postmarketing reports of venous thromboembolic events, including deep vein thrombosis (DVT) and pulmonary embolism (PE), in patients using testosterone products, such as testosterone cypionate. Evaluate patients who report symptoms of pain, edema, warmth and erythema in the lower extremity for DVT and those who present with acute shortness of breath for PE. If a venous thromboembolic event is suspected, discontinue treatment with testosterone cypionate and initiate appropriate workup and management.

Long term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. To date, epidemiologic studies and randomized controlled trials have been inconclusive for determining the risk of major adverse cardiovascular events (MACE), such as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death, with the use of testosterone compared to non-use. Some studies, but not all, have reported an increased risk of MACE in association with use of testosterone replacement therapy in men. Patients should be informed of this possible risk when deciding whether to use or to continue to use testosterone cypionate.

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.

The preservative benzyl alcohol has been associated with serious adverse events, including the "gaspings syndrome", and death in pediatric patients. Although normal therapeutic doses of this product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the "gaspings syndrome", the minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the hepatic capacity to detoxify the chemical. Premature and low-birth weight infants may be more likely to develop toxicity..

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 or 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 T₄ serum levels and increased resin uptake of T₃ and T₄. 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**).

Benzyl alcohol can cross the placenta. See **WARNINGS**.

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.

Cardiovascular Disorders: Myocardial infarction, stroke

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.

Vascular Disorders: Venous thromboembolism.

Miscellaneous: Inflammation and pain at the site of intramuscular injection.

To report SUSPECTED ADVERSE REACTIONS, contact West-Ward Pharmaceuticals Corp. at 1-877-233-2001 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

Prior to initiating testosterone cypionate, confirm the diagnosis of hypogonadism by ensuring that serum testosterone concentrations have been measured in the morning on at least two separate days and that these serum testosterone concentrations are below the normal range.

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 to 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 a clear, pale yellow oleaginous viscous, sterile solution intended for intramuscular administration available as:

10 mL Multiple Dose Vials, Cartons of 1 vial NDC 63187-647-10

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].
Protect from light.

Manufactured by: HIKMA FARMACÊUTICA (PORTUGAL), S.A.
Estrada do Rio da M, nº 8, 8A e 8B - Fervença, - 2705-906 Terrugem SNT, PORTUGAL

Distributed by:
WEST-WARD PHARMACEUTICALS CORP.
Eatontown, NJ 07724 USA

Relabeled by:
Proficient Rx LP
Thousand Oaks, CA 91320

Revised: 05/2015
PIN300-WES/7

PRINCIPAL DISPLAY PANEL

NDC 63187-647-10

Rx ONLY

Testosterone

Cypionate

Injection, USP

CIII

2,000 mg/10 mL

(200 mg/mL)

**Contains Benzyl Alcohol
as a Preservative**

For Intramuscular Use Only

10 mL Multiple Dose Vial

Each mL contains Testosterone Cypionate, USP 200 mg. Also contains Benzyl Benzoate, USP 0.2 mL; Benzyl Alcohol, USP added as preservative, 9.45 mg in Cottonseed Oil, USP 560 mg.

USUAL DOSAGE: See package insert.
 Store at 20° to 25°C (68° to 77°F) [See USP
 Controlled Room Temperature].
 Warming and shaking the vial should
 redissolve any crystals that may have
 formed during storage at temperature lower
 than recommended.

**Store product in the carton to protect
 contents from light.**



NDC 63187-647-10

RX Only

C-III

Lot #:00000
 Exp. 00/00/00
 SN#MASTER

Testosterone Cypionate 200mg/ mL

10ml Injectable

Each mL contains: Testosterone Cypionate,
 USP 200mg

See package insert

Product ID: RT064710

Mfr. By: HIKMA FARMACÊUTICA (PORTUGAL), S.A.
 Store at 20°-25°C (68°-77°F)

Keep medication out of the reach of children

Testosterone Cypionate 200mg/ mL
 10ml Injectable SN#MASTER
 Lot #:00000 Exp:00/00/00
 NDC 63187-647-10

Testosterone Cypionate 200mg/ mL
 10ml Injectable SN#MASTER
 Lot #:00000 Exp:00/00/00
 NDC 63187-647-10

Testosterone Cypionate 200mg/ mL
 10ml Injectable SN#MASTER
 Lot #:00000 Exp:00/00/00
 NDC 63187-647-10

Relabeled By: Proficient Rx LP
 Thousand Oaks, CA 91320

TESTOSTERONE CYPIONATE

testosterone cypionate injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:63187-647(NDC:0143-9726)
Route of Administration	INTRAMUSCULAR	DEA Schedule	CIII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TESTOSTERONE CYPIONATE (UNII: M0XW1UB114) (TESTOSTERONE - UNII:3XMK78S470)	TESTOSTERONE CYPIONATE	200 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BENZYL BENZOATE (UNII: N863NB338G)	0.2 mg in 1 mL
COTTONSEED OIL (UNII: H3E878020N)	560 mg in 1 mL
BENZYL ALCOHOL (UNII: LKG8494WBH)	9.45 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:63187-647-10	10 mL in 1 VIAL; Type 0: Not a Combination Product	12/01/2018	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091244	05/01/2012	

Labeler - Proficient Rx LP (079196022)**Establishment**

Name	Address	ID/FEI	Business Operations
Proficient Rx LP		079196022	RELABEL(63187-647)

Revised: 11/2019

Proficient Rx LP