Testosterone Cypionate Injection, USP
Rx Only

DESCRIPTION
Testosterone cypionate injection, for intramuscular injection, contains testosterone cypionate which is the oil-soluble (beta-cyclopentylpropionate ester) form of the testosterone.

Testosterone cypionate is a white or cream-colored 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 17-(3-cyclopentyl-1-oxopropoxy)-, (17β). Its molecular formula is C27H40O3, and the molecular weight is 412.61.

The structural formula is represented below:

![Structural Formula](https://source.unsplash.com/random/300x200)

CLINICAL PHARMACOLOGY
Endogenous androgens are responsible for normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. Testosterone is secreted in the male at a constant rate from puberty to about age 50 years and thereafter the rate of secretion gradually declines, as do the levels of the total testosterone in serum, 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, about 5 percent is excreted in the bile as glucuronides 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.

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.

Testosterone cypionate injection is available in one strength, 200 mg/mL testosterone cypionate.

Each mL of the solution contains Testosterone Cypionate, 200 mg; Benzyl Benzoate, 0.2 mL; Cottonseed Oil, 560 mg; Benzyl Alcohol (as preservative), 9.45 mg.

The preservative benzyl alcohol has been associated with serious adverse events, including the occurrence of “gasping 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 “gasping syndrome”, the maximum amount of benzyl alcohol at which toxicity occurs is not known.

Gynecomastia may develop and occasionally persists in patients being treated for hypogonadism. Androgens have been reported to increase protein anabolism and decrease protein catabolism. Nitrogen balance is improved only when sufficient intake of calories and protein is assured.

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 cause premature closure of the epiphyseal plates, resulting in retardation of linear growth and 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 erythropoietin, a hematopoietic factor.

During exogenous administration of androgens, endogenous testosterone release is inhibited through feedback inhibition of pituitary secretion of the hormone (LH). After long doses of exogenous androgens, spermatogenesis may also be suppressed through feedforward inhibition of pituitary follicle stimulating hormone (FSH).

There is no lack of substantial evidence that androgens are effective in fractures, surgical convalescence, and functional uterine bleeding.

Pharmacokinetics
Testosterone cypionate is 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 four to six weeks.

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About 90 percent of a dose of testosterone is excreted in the urine as glucuronic and sulfuric acid conjugates, about 5 percent is excreted in the bile as glucuronides 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.

Testosterone cypionate injection is indicated for replacement therapy in the male 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).

2. Males with carcinoma of the breast

3. Males with breast carcinoma of the breast

4. Males who are or have been suspected of carcinoma of the prostate gland

5. Patients with serious cardiac, hepatic or renal disease

INDICATIONS AND USAGE
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1. Primary hypogonadism (congenital or acquired-testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchidectomy). This condition is usually diagnosed in the prepubertal male, but may be recognized at any age. It may be diagnosed in young men by demonstrating the following features:

- Basal plasma testosterone level below 50 ng/mL
- Inability to respond to human chorionic gonadotropin stimulation test
- Absence of secondary sexual characteristics
- Failure of the penis to grow

2. Males with carcinoma of the breast

3. Males with breast carcinoma of the breast

4. Males who are or have been suspected of carcinoma of the prostate gland

5. Patients with serious cardiac, hepatic or renal disease

CONTRAINDICATIONS
1. Known hypersensitivity to the drug

2. Males with carcinoma of the breast

3. Males who have or have been suspected of carcinoma of the prostate gland

4. Women who are or may become pregnant

5. Patients with serious cardiac, hepatic or renal disease

WARNINGS
Hydrocarbon and/or benzyl alcohol may occur in immunized patients. If this occurs, the drug should be discontinued.

Long-term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy. 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 in the use of testosterone compared to placebo. Studies, both new and old, have not reported an increased risk of MACE in association with use of testosterone replacement therapy in men. Patients should be informed of the possible risk when deciding whether to use or to continue to use testosterone cypionate.

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.

Gynecomastia may develop and occasionally persists in patients being treated for hypogonadism. Androgens have been reported to increase protein anabolism and decrease protein catabolism. Nitrogen balance is improved only when sufficient intake of calories and protein is assured.

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 cause premature closure of the epiphyseal plates, resulting in retardation of linear growth and 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 erythropoietin, a hematopoietic factor.

During exogenous administration of androgens, endogenous testosterone release is inhibited through feedback inhibition of pituitary secretion of the hormone (LH). After long doses of exogenous androgens, spermatogenesis may also be suppressed through feedforward inhibition of pituitary follicle stimulating hormone (FSH).
Drug/Laboratory test interferences:
Androgens may decrease levels of thyroxine-binding globulin, resulting in decreased free T4 and increased resin uptake of T3 and T4. Free thyroid hormone levels remain unchanged, however, and there is no clinical evidence of thyroid dysfunction.

Concurrent administration of exogenous androgens and anticoagulants may result in elevated serum levels of antithrombin.

In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, hence, insulin requirements. The anticoagulant may require reduction in order to maintain satisfactory therapeutic levels.

Drug interactions:
Androgens may increase sensitivity to oral anticoagulants. Dosage of the anticoagulant may require reduction in order to maintain satisfactory therapeutic levels.

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

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

Testosterone cypionate injection should be for intramuscular 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
- Priapism or excessive sexual stimulation
- 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.
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- Venous thromboembolism.
- Hematologic:
- Suppression of clotting factors II, V, VII, and X, bleeding in patients on anticoagulation therapy, and prolongation of the bleeding time.
- Moderate to severe neutropenia, agranulocytosis, and thrombocytopenia.
- Decreased fibrinogen, resulting in decreased total T4 serum levels and increased resin uptake of 1, T3, and T4.
- Free thyroid hormone levels remain unchanged, however, and there is no clinical evidence of thyroid dysfunction.

Testosterone cypionate injection is for intramuscular use only. It should not be given intravenously.

ADVERSE REACTIONS
The following adverse reactions in the male have occurred with some androgens:
- Edema and anguloantral gynecomastia and excessive frequency and duration of penile erections. Oligospermia may occur at high dosages.
- Skin and muscle changes: 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).
- Nervous system: Increased or decreased libido, headache, anxiety, depression, and generalized paresthesia.
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- Vascular Disorders: Venous thromboembolism.
- Miscellaneous:
- Inflammation and pain at the site of intramuscular injection.

To report SUSPECTED ADVERSE REACTIONS, contact Perrigo at 1-866-634-9310 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 the first injection, 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.

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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.

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