CYPIONATE®

Testoterone Cypionate, USP 29 grade

Formula: $C_{27}H_{40}O_3$ (CAS-58-20-8, ATC-G03BA03)
Molecular Weight: 412.6 gm/mol
Active life: 15-16 days
Detection time: 3 months
Anabolic/Androgenic ratio: 100:100

DESCRIPTION:

Cypionate® is a steroid compound that is described chemically as 17β-Hydroxyandrost-4-en-3-one cyclopentanepropionate. It is the principal hormone of the testis. The ester, Cypionate, is a white or creamy-white crystalline powder, odourless or has a slight odour that is insoluble in water, freely soluble in alcohol, soluble in vegetable oil. Esterification of the 17 beta-hydroxy group produces compounds which have a longer duration of action

Cypionate® is a sterile solution of Testosterone Cypionate USP29 micronized grade in Miglyol 840, Ethyl oleate, Benzyl benzoate, Benzyl alcohol.

CLINICAL PHARMACOLOGY:

Endogenous androgens are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. These effects include the growth and maturation of the prostate, seminal vesicles, penis, and scrotum; the development of male hair distribution, such as the beard, and pubic, chest, and axillary hair, laryngeal enlargement, vocal-cord thickening; 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 the eventual termination of linear growth which is brought about by fusion of the epiphyseal growth centers. In children, exogenous androgens accelerate linear growth rates but may cause a 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 the production of red blood cells by enhancing the production of erythropoietic stimulating 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 lack of substantial evidence that androgens are effective in fractures, surgery, convalescence, and functional uterine bleeding.
Cypionate® is less polar than free testosterone. Cypionate® in oil injected intramuscularly is absorbed slowly from the lipid phase; thus, it can be given at intervals of 2 to 3 times/week.
Testosterone in plasma is 98% bound to a specific testosterone estradiol binding globulin, and about 2% 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 half-life.
About 90% of a dose of testosterone is excreted in the urine as glucuronic and sulfuric acid conjugates of testosterone and its metabolites; about 6% 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-ketosteroids through two different pathways. The half-life of testosterone as reported in the literature varies considerably; it ranges from 10 to 100 minutes.
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 is initiates transcription events and cellular changes related to androgen action.

INDICATIONS AND USAGE:

Cypionate® 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. Know 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-delta 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 child, the greater 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.

LIVER CELL TUMORS ARE REPORTED. MOST OFTEN THESE TUMORS ARE BENIGN AND ANDROGEN DEPENDENT, BUT FATAL MALIGNANT TUMORS HAVE BEEN REPORTED. WITH DRAWAL OF DRUG OFTEN RESULTS IN REGRESSION OR CESSATION OF PROGRESSION OF THE TUMOR. HOWEVER, HEPATIC TUMORS ASSOCIATED WITH ANDROGENS OR ANABOLIC STEROIDS ARE MUCH MORE VASCULAR THAN OTHER HEPATIC TUMORS AND MAY BE SILENT UNTIL LIFE-THREATENING INTRA-ABDOMINAL HEMORRHAGE DEVELOPS.
PELIOSIS HEPATIS, A CONDITION ARE ALSO REPORTED IN WHICH LIVER AND SOMETIMES SPLENIC TISSUE IS REPLACED WITH BLOOD-FILLED CYSTS, HAS BEEN REPORTED IN PATIENTS RECEVING ANDROGENIC ANABOLIC STEROID THERAPY. THESE CYSTS ARE SOMETIMES PRESENT WITH MINIMAL HEPATIC DYSFUNCTION, BUT AT OTHER TIMES THEY HAVE BEEN ASSOCIATED WITH LIVER FAILURE. THEY ARE OFTEN NOT RECOGNIZED UNTIL LIFE-THREATENING LIVER FAILURE OR INTRA-ABDOMINAL HEMORRHAGE DEVELOPS. WITHDRAWAL OF DRUG USUALLY RESULTS IN COMPLETE DISAPPERRANCE OF LESIONS.
BLOOD LIPID CHANGES THAT ARE KNOWN TO BE ASSOCIATED WITH INCREASED RISK OF ATHEROSCLEROSIS ARE SEEN IN PATIENTS TREATED WITH ANDROGENS AND ANABOLIC STEROIDS. THESE CHANGES INCLUDE DECREASED HIGH-DENSITY LIPOPROTEIN AND SOMETIMES INCREASED LOW-DENSITY LIPOPROTEIN. THE CHANGES MAY BE VERY MARKED AND COULD HAVE A SERIOUS IMPACT ON THE RISK OF ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE.

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.
Cypionate® should not be used interchangeably with testosterone propionate because of differences in duration of action.
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/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 mother: Cypionate® is not recommended for use in nursing mothers.
Pediatric use: Cypionate® is not recommended for use in children.

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.

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 hepatic (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 anaphylactic reactions.
Miscellaneous: Inflammation and pain at the site of intramuscular injection.

OVERDOSAGE:

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

DOSAGE AND ADMINISTRATION:

Cypionate® 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 Cypionate® 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 – Cypionate® injection, solution- Intramuscular-200 mg/ml is supplied in 1 ml vial and 250 mg/ml is supplied in multiple dose 10 ml vial with blue color flip cap.

For shelf-life please refer to the imprint on the pack.

Keep out of reach of children.

Should be at controlled room temperatures 15-30°C (59-86°F)

Do not freeze

This drug 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.

Protect from sun light

This drug has not been shown to be safe and effective for the enhancement of athletic performance!

Manufactured and Distributed by: LA Pharma S.r.l.

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