HALOTESTIN®

Fluoxymesterone, USP29 Micronized grade

Molecular Formula: $C_{20}H_{29}FO_3$ (CAS-76-43-7, ATC-G03BA01)
Molecular Weight: 336.4457 gm/mol
Active life: 6-8 hours
Detection Time: 2 months
Anabolic/Androgenic Ratio: 1,900:850

DESCRIPTION:

Halotestin®, brand of Fluoxymesterone tablets, is an anabolic steroid, a synthetic derivative of testosterone. Each tablet contains 10 mg of Fluoxymesterone USP29, micronized grade. It is designated chemically as 9α-Fluoro-11β, 17β-dihydroxy-17α-methylandrost-4-en-3-one.
It occurs as white or practically white, odourless, crystalline powder. Practically insoluble in water; sparingly soluble in alcohol; slightly soluble in chloroform.
Each tablet also contains lactose monohydrate, sodium starch glycolate, polyvidone 25,000, microcrystalline cellulose and magnesium stearate as excipients and also contains yellow ferric oxide (E172) and indigo carmine aluminium lake (E132) as colouring agent.

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). Inactivation of testosterone occurs primarily in the liver.
The half-life of Fluoxymesterone after oral administration is approximately 9.2 hours.

INDICATIONS:

In the male— Halotestin® are indicated for:
1. Replacement therapy in conditions associated with symptoms of deficiency or absence of endogenous testosterone.
   a. Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome or orchidectomy.
   b. Hypogonadotropic hypogonadism (congenital or acquired): idiopathic gonadotropin or LHRH deficiency, pituitary-hypothalamic injury from tumors, trauma, or radiation.
2. Delayed puberty, provided it has been definitely established as such, and is not just a familial trait.

In the female— Halotestin® are indicated for palliation of androgen responsive recurrent mammary cancer in women who are more than one year but less than five years postmenopausal, or who have been proven to have a hormone-dependent tumor as shown by previous beneficial response to castration.

DRUG ABUSE AND DEPENDENCE:

Controlled Substance Class: Fluoxymesterone is a controlled substance under the Anabolic Steroids Control Act, and Halotestin® has been assigned to Schedule III.

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 known or suspected to be pregnant.
5. Patients with serious cardiac, hepatic or renal disease.

WARNINGS:

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.

Hypercalcemia may occur in immobilized patients and in patients with breast cancer. 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.
Cholestatic hepatitis and jaundice may occur with 17-α-alkyl-androgens. Should this occur, the drug should be discontinued. This is reversible with discontinuation of the drug.
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.
Androgen therapy should be used cautiously in males with delayed puberty. Androgens can accelerate bone maturation without producing compensatory gain in linear growth. The effect on bone maturation should be monitored by assessing bone age of the wrist and hand every six months.
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.

ANABOLIC STEROIDS HAVE NOT BEEN SHOWN TO ENHANCE ATHLETIC ABILITY.

PRECAUTIONS:

General
Women should be observed for signs of virilization which is usual following androgen use at high doses. Discontinuation of drug therapy at the time of evidence of mild virilism is necessary to prevent irreversible
virilization. A decision may be made by the patient and the physician that some virilization will be tolerated during treatment for breast carcinoma.
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.
This product contains FD&C which may cause allergic type reactions (including bronchial asthma) in certain susceptible individuals. Although the overall incidence of FD&C sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

Information for patients
Patients should be instructed to report any of the following: nausea, vomiting, changes in skin color, and ankle swelling. Males should be instructed to report too frequent or persistent erections of the penis and females any hoarseness, acne, changes in menstrual periods or increase in facial hair.

Carcinogenesis, mutagenesis, impairment of fertility
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.
This compound has not been tested for mutagenic potential. However, as noted above, carcinogenic effects have been attributed to treatment with androgenic hormones. The potential carcinogenic effects likely occur through a hormonal mechanism rather than by a direct chemical interaction mechanism.
Impairment of fertility was not tested directly in animal species. However, as noted below under Adverse Reactions, oligospermia in males and amenorrhea in females are potential adverse effects of treatment with Halotestin®. Therefore, impairment of fertility is a possible outcome of treatment with Halotestin®.

Pregnancy
Teratogenic effects: Pregnancy Category X. (See CONTRAINDICATIONS.)

Nursing mothers
Halotestin® is not recommended for use in nursing mothers.

Pediatric use
Androgen therapy should be used very cautiously in children and only by specialists aware of the adverse effects on bone maturation. Skeletal maturation must be monitored every six months by an X-ray of the hand and wrist (See WARNINGS).

ADVERSE REACTIONS:

Endocrine and urogenital:
Female: the most common side effects of androgen therapy are amenorrhea and other menstrual irregularities; inhibition of gonadotropin secretion; and virilization, including deepening of the voice and clitoral enlargement. The latter usually is not reversible after androgens are discontinued. When administered to a pregnant woman, androgens can cause virilization of external genitalia of the female fetus.
Male: Gynecomastia, and excessive frequency and duration of penile erections. Oligospermia may occur at high dosage.
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.

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

DRUG INTERACTION:
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.

PATIENT MONITORING:
Laboratory tests
Women with disseminated breast carcinoma should have frequent determination of urine and serum calcium levels during the course of androgen therapy (See WARNINGS).
Because of the hepatotoxicity associated with the use of 17-alpha-alkylated androgens, liver function tests should be obtained periodically. Periodic (every six months) X-ray examinations of bone age should be made during treatment of prepubertal males to determine the rate of bone maturation and the effects of androgen therapy on the epiphyseal centers.
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 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.
Lipid profile: Serum Cholesterol, HDL, LDL, TG.
Hemoglobin and Hematocrit,
Liver function test: Total protein, Albumin, Globulin, Total and direct bilirubin, AST, ALT and alkaline phosphatase, tumor marker for liver: AFP and CA19-9
Prostatic specific antigen: PSA, Testosterone: total, free, and bioavailable.
Dihydrotestosterone & Estradiol
Male patients over 40 should undergo a digital rectal examination and evaluate PSA prior to androgen use. Periodic evaluations of the prostate should continue while on androgen therapy, especially in patients with difficulty in urination or with changes in voiding habits.

DOSAGE AND ADMINISTRATION:
The dosage will vary depending upon the individual, the condition being treated, and its severity. The total daily oral dose may be administered single or in divided (three or four) doses.
Male hypogonadism: For complete replacement in the hypogonadal male, a daily dose of 5 to 20 mg will suffice in the majority of patients. It is usually preferable to begin treatment with full therapeutic doses which are later adjusted to individual requirements. Priapism is indicative of excessive dosage and is indication for temporary withdrawal of the drug.
Delayed puberty: Dosage should be carefully titrated utilizing a low dose, appropriate skeletal monitoring, and by limiting the duration of therapy to four to six months.
Inoperable carcinoma of the breast in the female: The recommended total daily dose for palliative therapy in advanced inoperable carcinoma of the breast is 10 to 40 mg. Because of its short action, fluoxymesterone should be administered to patients in divided, rather than single, daily doses to ensure more stable blood levels. In general, it appears necessary to continue therapy for at least one month for a satisfactory subjective response, and for two to three months for an objective response.
For body building: 10-40 mg per day

HOW SUPPLIED:
Halotestin® 10 mg is supplied in bottle of 30 green tablets.

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)

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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