Oxandrolone Tablets USP

DESCRIPTION
Oxandrolone oral tablets contain 2.5 mg or 10 mg of the anabolic steroid oxandrolone. Oxandrolone is 17β-hydroxy-17α-methyl-2-oxa-5α-androstan-3-one with the following structural formula:

Molecular Weight: 306.44

Inactive ingredients include: hypromellose, lactose monohydrate, pregelatinized starch, and magnesium stearate.

CLINICAL PHARMACOLOGY
Anabolic steroids are synthetic derivatives of testosterone. Certain clinical effects and adverse reactions demonstrate the androgenic properties of this class of drugs. Complete dissociation of anabolic and androgenic effects has not been achieved. The actions of anabolic steroids are therefore similar to those of male sex hormones with the possibility of causing serious disturbances of growth and sexual development if given to young children. Anabolic steroids suppress the gonadotropic functions of the pituitary and may exert a direct effect upon the testes.

During exogenous administration of anabolic androgens, endogenous testosterone release is inhibited through inhibition of pituitary luteinizing hormone (LH). At large doses, spermatogenesis may be suppressed through feedback inhibition of pituitary follicle-stimulating hormone (FSH).

Anabolic steroids have been reported to increase low-density lipoproteins and decrease high-density lipoproteins. These levels revert to normal on discontinuation of treatment.

INDICATIONS AND USAGE
Oxandrolone is indicated as adjunctive therapy to offset the protein catabolism and any bleeding.

Edema with or without congestive heart failure may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. Concomitant administration of adrenal cortical steroid or ACTH may increase the edema.

In children, androgen therapy may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect results in compromised bone age of the left wrist and hand every 6 months (see DOSAGE AND ADMINISTRATION).

DRUG ABUSE AND DEPENDENCE
Oxandrolone is classified as a controlled substance under the Anabolic Steroids Control Act of 1990 and has been assigned to Schedule III (non-narcotic).

CONTRAINDICATIONS
1. Known or suspected carcinoma of the prostate or the male breast.
2. Carcinoma of the breast in females with hypercalcemia (androgenic anabolic steroids may stimulate osteolysis).
3. Pregnancy. Because of possible masculinization of the fetus. Oxandrolone has been shown to cause embryotoxicity, fetotoxicity, infertility, and masculinization of female animal offspring when given in doses 9 times the human dose.
4. Nephrosis, the nephrotic phase of nephritis.
5. Hypercalcemia.

WARNINGS
PELODOSIS HEPATIS. A CONDITION IN WHICH LIVER AND SOMETIMES SPLENIC TISSUE IS REPLACED WITH BLOOD-FILLED CYSTS. HAS BEEN REPORTED IN PATIENTS RECEIVING 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 DISAPPEARANCE OF LESIONS. LIVER CELL TUMORS ARE ALSO REPORTED. MOST OFTEN THESE TUMORS ARE BENIGN AND ANDROGEN-DEPENDENT, BUT FATAL MALIGNANT TUMORS HAVE BEEN REPORTED. WITHDRAWAL OF DRUG OFTEN RESULTS IN REGRESSION OR CESSION 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. BLOOD LIPID CHANGES THAT ARE KNOWN TO BE ASSOCIATED WITH INCREASED RISK OF ATHEROSCLEROSIS ARE SEEN IN PATIENTS TREATED WITH ANDROGENS OR ANABOLIC STEROIDS. THESE CHANGES INCLUDE DECREASED HIGH-DENSITY LIPOPROTEINS AND SOMETIMES INCREASED LOW-DENSITY LIPOPROTEINS. THE CHANGES MAY BE VERY MARKED AND COULD HAVE A SERIOUS IMPACT ON THE RISK OF ATHEROSCLEROSIS AND CORONARY ARTERY DISEASE.

Cholestatic hepatitis and jaundice may occur with 17α-alkylated androgens at a relatively low dose. If cholestatic hepatitis with jaundice appears or if liver function tests become abnormal, oxandrolone should be discontinued and the etiology should be determined. Drug-induced jaundice is reversible when the medication is discontinued.

In patients with breast cancer, anabolic steroid therapy may cause hypercalcemia by stimulating osteolysis. Oxandrolone therapy should be discontinued if hypercalcemia occurs.

Edema with or without congestive heart failure may be a serious complication in patients with pre-existing cardiac, renal, or hepatic disease. Concomitant administration of adrenal cortical steroid or ACTH may increase the edema. In children, androgen therapy may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect results in compromised adult height. The younger the child, the greater the risk of compromising final mature height. The effect on bone maturation should be monitored by assessing bone age of the left wrist and hand every 6 months (see PRECAUTIONS, Laboratory Tests).

Geriatric patients treated with androgenic anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

Anabolic Steroids have not been shown to enhance athletic ability.

PRECAUTIONS
Concurrent dosing of oxandrolone and warfarin may result in unexpectedly large increases in the International Normalized Ratio (INR) or prothrombin time (PT). When oxandrolone is prescribed to patients being treated with warfarin, doses of warfarin may need to be decreased significantly to maintain the desirable INR level and diminish the risk of potentially serious bleeding (See PRECAUTIONS, Drug Interactions).

General
Women should be observed for signs of virilization (deepening of the voice, hirsutism, acne, clitoromegaly). Discontinuation of drug therapy at the time of evidence of mild virilism is necessary to prevent irreversible virilization. Some virilizing changes in women are irreversible even after prompt discontinuance of therapy and are not prevented by concomitant use of estrogens. Menstrual irregularities may also occur.

Anabolic steroids may cause suppression of clotting factors II, V, VII, and X, and an increase in prothrombin time.

Information for Patients
The physician should instruct patients to report immediately any use of warfarin and any bleeding. The physician should instruct patients to report any of the following side effects of androgens:

Males: Too frequent or persistent erections of the penis, appearance or aggravation of acne.

Females: Hoarseness, acne, changes in menstrual periods, or more facial hair.

All patients: Nausea, vomiting, changes in skin color, or ankle swelling.

Geriatric Use: Certain geriatric use information is protected by marketing exclusivity.

Laboratory Tests
Women with disseminated breast carcinoma should have frequent determination of urine and serum calcium levels during the course of therapy (see WARNINGS). Because of the hepatotoxicity associated with the use of 17α-alkylated androgens, liver function tests should be obtained periodically.
Anabolic steroids may increase sensitivity to oral anticoagu-
laus. Dosage of the anticoagulant may have to be decreased in order to maintain
desired prothrombin time. Patients receiving oral anticoagulant therapy require
close monitoring, especially when anabolic steroids are started or stopped.

Warfarin: A multidose study of oxandrolone, given as 5 or 10 mg BID in 15
healthy subjects concurrently treated with warfarin, resulted in a mean increase
in S-warfarin half-life from 26 to 48 hours and AUC from 4.55 to 12.09
ng•hr/mL, similar increases in R-warfarin half-life and AUC were also detected.
Microscopic hematuria (9/15) and gingival bleeding (1/15) were also observed. A
5-8-fold decrease in the mean warfarin prothrombin time (PT) should be monitored
closely and the dose of warfarin adjusted as necessary until a stable
target INR or PT has been achieved.

Furthermore, in patients receiving both drugs, careful monitoring of the INR or
PT, and adjustment of the warfarin dosage if indicated are recommended when
the oxandrolone dose is changed or discontinued. Patients should be closely
monitored for signs and symptoms of occult bleeding.

Oral Hypoglycemic Agents: Oxandrolone may inhibit the metabolism of oral
hypoglycemic agents.

Adrenal Steroids or ACTH: In patients with edema, concomitant administration
with adrenal cortical steroids or ACTH may increase the edema.

Drug/Laboratory Test Interactions

Androgenic anabolic steroids 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. In addition, a decrease in PBI and
radioactive iodine uptake may occur.

Hypoglycemic agents: Use of oxandrolone may increase the hypoglycemic effects
of hypoglycemic agents. The oral LD₅₀ of oxandrolone has not been tested in laboratory animals for carcino-
genic or mutagenic effects. In 2-year chronic oral rat studies, a dose-related
reduction of spermatogenesis and decreased organ weights (testes, prostate,
seminal vesicles, uterus, adrenals, and thyroid) were shown.

Human Data: Liver cell tumors have been reported in patients receiving long-
term therapy with androgenic anabolic steroids in high doses (see WARNING).

Withdrawal of the drug did not lead to a reduction of the tumors in all cases.
Geriatric patients treated with anabolic steroids may be at an increased risk for the development of prostatic hypertrophy and prostatic carcinoma.

Pregnancy

Teratogenic effects-Pregnancy Category X (see CONTRAINDICATIONS).

Nursing Mothers

It is not known whether anabolic steroids are excreted in human milk. Because of the
potential of serious adverse reactions in nursing infants from oxandrolone, a
decision should be made whether to discontinue nursing or to discontinue the
drug, taking into account the importance of the drug to the mother.

Pediatric Use

Anabolic steroids may accelerate epiphyseal maturation more rapidly than linear
growth in children and the effect may continue for 6 months after the drug has
been stopped. Therefore, therapy should be monitored by x-ray studies at 6-
month intervals in order to avoid the risk of compromising adult height.

Androgenic anabolic steroid therapy should be used very cautiously in children
and only by specialists who are aware of the effects on bone maturation (see
WARNING).

ADVERSE REACTIONS

In Males

Prepubertal: Phallic enlargement and increased frequency or persistence of erections.

Postpubertal: Inhibition of testicular function, testicular atrophy and oligospermia,
impatience, chronic priapism, epididymitis, and bladder irritability.

In Females

Citrullation, menstrual irregularities.

CNS

Habituation, excitation, insomnia, depression, and changes in libido.

Hepatic

Bleeding in patients on concomitant anticoagulant therapy.

Breast

Gynecomastia.

Larynx

Deepening of the voice in females.

Hair

Hirsutism and male pattern baldness in females.

Skin

Acne (especially in females and prepubertal males).

Skeletal

Premature closure of epiphyses in children (see PRECAUTIONS, Pediatric Use).

Fluid and Electrolytes

Edema, retention of serum electrolytes (sodium chloride, potassium, phosphate, calcium).

Metabolic/Endocrine

Decreased glucose tolerance (see PRECAUTIONS, Laboratory Tests), increased
creatinine excretion, increased serum levels of creatinine phosphokinase (CPK),
Masculinization of the fetus. Inhibition of gonadotropin secretion.

OVERDOSE

No symptoms or signs associated with overdose have been reported. It is
possible that sodium and water retention may occur.

The oral LD₅₀ of oxandrolone in mice and dogs is greater than 5,000 mg/kg. No
specific antidote is known, but gastric lavage may be used.

DONAGE AND ADMINISTRATION

Therapy with anabolic steroids is adjunctive to and not a replacement for con-
ventional therapy. The duration of therapy with oxandrolone will depend on the
response of the patient and the possible appearance of adverse reactions.

Therapy should be intermittent.

Adults

The response of individuals to anabolic steroids varies. The daily adult dose is
2.5 mg to 20 mg given in 2 to 4 divided doses. The desired response may be achieved with as little as 2.5 mg or as much as 20 mg daily. A course of therapy of
2 to 4 weeks is usually adequate. This may be repeated intermittently as indicated.

Children

For children the total daily dosage of oxandrolone is ≤ 0.1 mg per kilogram body
weight or ≤ 0.045 mg per pound of body weight. This may be repeated intermitt-
ently as indicated.

HOW SUPPLIED

Oxandrolone Tablets USP are supplied as follows:

2.5 mg Tablets: white, modified oval-shaped, debossed ‘E 271’ on one side and
bisected on the reverse side.

Bottles of 100

Bottles of 1000

10 mg Tablets: white, capsule-shaped, debossed ‘E 272’ on one side and plain
on the reverse side.

Bottles of 100

Bottles of 1000

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

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