PRODUCT MONOGRAPH

DECA-DURABOLIN®

(nandrolone decanoate injection)

U.S.P.

ANDROGEN - ANABOLIC

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Androgen-Anabolic

ACTIONS AND CLINICAL PHARMACOLOGY

Anabolic steroids are synthetic derivatives of testosterone.

DECA-DURABOLIN® (nandrolone decanoate injection) is primarily used for its protein anabolic effect and its catabolic inhibiting effect on tissue. Nitrogen balance is improved with anabolic agents but only when there is sufficient intake of calories and protein. Whether this positive nitrogen balance is of primary benefit in the utilization of protein-building dietary substances has not been established.

Increases in hemoglobin levels have occurred in some cases of aplastic anemia receiving anabolic steroids.

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. They suppress the gonadotropic functions of the pituitary and may exert a direct effect upon the testes. Human growth hormone is preferred treatment of pituitary dwarfism.

If human growth hormone is not available, anabolic agents may be used to treat this condition.

Pharmacokinetics

DECA-DURABOLIN® (nandrolone decanoate injection) is slowly released from the injection site into the blood with a half-life of 6 days. In the blood, the ester is rapidly hydrolysed to nandrolone with a half-life of one hour or less. The half-life for the combined process nandrolone decanoate and of the distribution and elimination of nandrolone is 4.3 hours. Nandrolone is metabolised by the liver. 19-Norandrosterone, 19-noretiocholanolone and 19-norepiandrosterone have been identified as metabolites in the urine. It is not known whether these metabolites display a pharmacological action.

INDICATIONS

As adjunctive therapy in senile and postmenopausal osteoporosis. Anabolic steroids are without value as primary therapy but may be of value in adjunctive therapy. Equal or greater consideration should be given to diet, calcium balance, physiotherapy and good general health-promoting measures. In pituitary dwarfism anabolic agents may be used with care until growth hormone is more available.

The product is also useful in the treatment of those conditions in which a potent tissue-building or protein-sparing action is desired. Its principal uses are to induce weight gain and well-being by virtue its anabolic action. Such therapy is most effective when combined with a good dietary regimen. Anabolic effects have been demonstrated in chronic disease and convalescence, debility states, inoperable mammary carcinoma, corticoid-induced catabolic states, myopathies, decubitus ulcers, burns and as adjuvant therapy of certain types of anemia (aplastic, sickle cell). It should be used only after diagnosis is established.

CONTRAINDICATIONS

1. Male patients with carcinoma of the prostate or breast.
2. Pregnancy, because of masculinization of the fetus.
3. Nephrosis or the nephrotic phase of nephritis.
4. Cardio-renal failure.
5. Liver disease with impaired bilirubin excretion.

WARNINGS

Caution is required in administering these agents to patients with cardiac, renal or hepatic disease.

Anabolic steroids do not enhance athletic ability.

PRECAUTIONS

1. If amenorrhea or menstrual irregularities develop the drug should be discontinued until the etiology is determined.
2. Anabolic steroids may increase sensitivity to oral anti-coagulants. Dosage of the anticoagulant may have to be decreased in order to maintain the prothrombin time at the desired therapeutic level.
3. Anabolic steroids have shown to alter glucose tolerance tests. Diabetics should be followed carefully and the insulin or oral hypoglycemic dosage adjusted accordingly.
4. Anabolic steroids should be used with caution in patients with benign prostatic hypertrophy.
5. Serum cholesterol may increase or decrease during therapy. Therefore, caution is required in administering these agents to patients with a history of myocardial infarction or coronary artery disease. Serial determinations of serum cholesterol should be made and therapy adjusted accordingly.

6. Hypercalcemia may develop both spontaneously and as a result of hormonal therapy in women with disseminated breast carcinoma. If it develops while on this agent, the drug should be stopped.

Signs of masculinization which have been produced by testosterone therapy in women have ranged from mild acne, hoarsening of the voice and an increase in or darkening of the hair of the face. Women and children under seven years of age are more sensitive to androgen therapy. DECA-DURABOLIN® (nandrolone decanoate injection), which is far less androgenic than testosterone, has not produced these signs when given in the recommended doses, save for a few of the milder of these effects which disappeared when treatment was discontinued. As is common with other steroids of this class, it may be possible with large doses or intensive treatment during the first half of the menstrual cycle to inhibit menses; however, with recommended doses, menses are not apt to be disturbed. If signs of masculinization develop, discontinuation of the treatment should be considered, preferably in consultation with the patient.

Pregnancy: DECA-DURABOLIN® should not be used in pregnant women.

Lactation: There are insufficient data on the use of DECA-DURABOLIN® during breast-feeding to assess potential harm to the infant or possible influence on milk production.

ADVERSE REACTIONS

1. In Males
    a. Prepubertal
        1) Phallic enlargement
        2) Increased frequency of erections
    b. Post-pubertal
        1) Inhibition of testicular function, testicular atrophy and oligospermia
        2) Impotence, chronic priapism, gynecomastia
        3) Epididymitis and bladder irritability

2. In Females
    a. Hirsutism, male pattern baldness, deepening of the voice, increase of pubic hair and clitoral enlargement. These changes are usually irreversible even after prompt discontinuance of therapy and are not prevented by concomitant use of estrogens.
    b. Menstrual irregularities

3. In Both Sexes
    a. Nausea
    b. Increased or decreased libido
    c. Acne (especially in females and Prepubertal males)
    d. Habituation
    e. Excitation and sleeplessness
    f. Chills
    g. Bleeding in patients on concomitant anticoagulant therapy
    h. Premature closure of epiphyses in children
    i. Fluid retention

4. Intramuscular preparations have been associated with:
    a. Urticaria at the site of injection
    b. Post-injection induration
    c. Furunculosis

5. Alterations in these clinical laboratory tests:
    a The metyrapone test
    b. The FBS and glucose tolerance test
    c. The thyroid function tests: a decrease in the PBI, in thyroxine-binding capacity and radioactive iodine uptake and an increase in T_3 uptake by the rbc's or resin may occur. Free thyroxine is normal. Altered tests usually persist for 2-3 weeks after stopping anabolic therapy.
    d. The electrolytes: retention of sodium, chlorides, water, potassium, phosphates and calcium.
    e. Liver function tests:
        1) Increased or decreased serum cholesterol
    f. Increase in clotting factors II, V, VII, and X
    g. Miscellaneous Laboratory Tests:
        1) Decreased creatine and creatinine excretion lasting up to two weeks after discontinuing therapy.
        2) Increased 17-ketosteroid excretion.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

To date, no cases of overdosage (acute) with DECA-DURABOLIN® (nandrolone decanoate injection) have been reported. Very large single doses do not give rise to serious side effects. The parenteral form of administration practically precludes the possibility of overdosage.

DOSAGE AND ADMINISTRATION

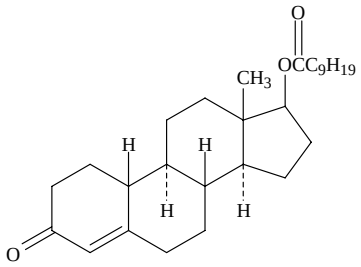
DECA-DURABOLIN® (nandrolone decanoate injection) is intended for intramuscular injection. For general anabolic effects in adults, the average dosage recommended is 50 to 100 mg every 3 to 4 weeks. For children from two to thirteen years of age, the average dose is 25 to 50 mg every 3 to 4 weeks. Since signs of anabolic properties (especially weight gain) are believed best brought out by periodic treatment, it is recommended that DECA-DURABOLIN® be given for continuous periods of up to 12 weeks. If at the end of a four week rest period the indications for it continue, this treatment may then be resumed.

PHARMACEUTICAL INFORMATION

Drug Substance:

Common Name:	nandrolone decanoate
Chemical Name:	17 Beta-Hydroxyestr-4-en-3-one Decanoate
Molecular Formula:	$C_{28}H_{44}O_3$
Molecular Mass:	428.63
Physical Form:	white to yellow crystals
Melting Point:	32-35^{o}C

Structural Formula:



Composition:

Each mL contains : nandrolone decanoate USP 100 mg. Nonmedicinal ingredients: benzyl alcohol and sesame oil.

Stability and Storage Recommendations:

Store at 15°C - 30°C.

Route of Administration:

DECA-DURABOLIN® (nandrolone decanoate injection) is intended for intramuscular injection.

AVAILABILITY OF DOSAGE FORMS

DECA-DURABOLIN® (nandrolone decanoate injection) (in sterile sesame oil solution for intramuscular injection) is available in a potency of 100 mg/ml with 10% benzyl alcohol (preservative): 2 ml multiple dose vial (100mg/ml)

PHARMACOLOGY

The action of nandrolone decanoate is primarily protein anabolic. This could be demonstrated in pharmacological trials. As measured by the weight increase of the musculus levator ani of castrated young male rats, this substance had a marked, long-lasting protein anabolic or rather myotrophic effect, whilst the androgenic activity, as measured by the weight increase of the seminal vesicles, was very slight. Also only weak anti-oestrogenic and gonad-inhibiting activities could be demonstrated.

Experiments carried out on rats revealed that the long-acting effect of nandrolone esters, in this case nandrolone decanoate, is due to the length of the fatty acid molecule -- the decanoate molecule -- causing slow absorption of the ester from an intramuscular depot.

Following release from the depot, the nandrolone esters are rapidly hydrolized in the blood and the resulting nandrolone was found to be the ultimate active compound affecting the levator ani-muscle and seminal vesicles. The rate and concentration at which nandrolone reaches these receptors is fully determined by the rate of absorption of the ester.

In humans, the protein anabolic action was clear from the extensive and strictly controlled nitrogen balance tests in which the quantity of retained nitrogen can be considered as a parameter of protein anabolic activity. It appeared that DECA-DURABOLIN® (nandrolone decanoate injection) administered at clinical dose levels, has a powerful nitrogen retaining or protein-sparing effect of at least three weeks duration. This effects was especially clear in patients who had a negative nitrogen balance resulting from treatment with protein-catabolism-promoting corticosteroids (anti-catabolic action).

TOXICOLOGY

Toxicity studies were performed in rats and beagle dogs.

In acute toxicity studies castrated male rats were given a single subcutaneous dose of 8 mg (equivalent to 140 mg/kg body weight) and groups were sacrificed at 2, 4, and 6 weeks. The only changes noted were increases in the size of seminal vesicles and the levator ani muscles which are consistent with androgenic activity. In another experiment groups of male and female rats were given weekly subcutaneous injections of either 1 mg/kg, 5 mg/kg or 25 mg/kg for 16 weeks. There were no abnormal findings on autopsy except for the expected androgenic and gonadal inhibiting effects.

A group of beagle dogs were treated with weekly subcutaneous doses of 25 mg for a period of six months. Biochemical tests remained normal throughout the course of the study. Again there were no abnormal pathological findings except for the expected androgenic and gonadal inhibiting effects.

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