IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA0261/003/001
Case No: 2036546

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Organon Laboratories Limited

Cambridge Science Park, **Milton Road**, **Cambridge CB4 0FL**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Deca Durabolin 100mg/ml, Solution for Injection (ampoule)

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **08/06/2007** until **28/08/2010**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Deca Durabolin 100mg/ml, Solution for Injection (ampoule)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains nandrolone decanoate 100mg.
For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A clear, pale yellow, oily solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the management of the refractory anaemias associated with such conditions as chronic renal failure (including patients on haemodialysis) aplastic anaemia, anaemia due to cytotoxic therapy associated with malignant disease.

4.2 Posology and method of administration

Dosage
Adults:

Anaemia of chronic renal failure:
Males: 200mg weekly
Females: 100mg weekly

Aplastic anaemia:
The usual dose is 50 to 150mg weekly.

Anaemia due to cytotoxic therapy:
The usual dose is 200mg weekly commencing 2 weeks prior to the course of cytotoxic therapy. This treatment should be continued throughout cytotoxic therapy and thereafter during the recovery period until the blood count has returned to normal.

Children:
There is insufficient clinical experience to permit specific recommendations.

Administration
Deep Intramuscular injection.

4.3 Contraindications

1. Use in women who are pregnant or at risk of becoming pregnant.
2. Use in patients with known or suspected prostatic or testicular carcinoma or male mammary carcinoma.
3. Use in patients allergic to peanuts or soya.
4. Known hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and precautions for use

1. Anabolic steroids may interfere with growth in children with acceleration of bone maturation.
2. This product may induce virilisation in female patients, particularly in high doses and inhibition of spermatogenesis in males.
3. This product should only be used with great caution in patients with renal, cardiac or liver dysfunction, or in those with a history of coronary artery disease, epilepsy or migraine.
4. Alterations in glucose tolerance may occur, requiring surveillance for latent diabetes, and possible changes in control for diabetic patients.
5. Fluid retention may occur.
6. The appearance of unexplained amenorrhoea, hypercalcaemia or hypercalciuria requires discontinuation of therapy. Patients with skeletal metastases or the elderly should be carefully monitored.
7. This product should only be used under specialist supervision and regular surveillance.

4.5 Interaction with other medicinal products and other forms of interaction

Anabolic steroids may improve glucose tolerance and decrease the need for insulin or other antidiabetic medicines in diabetes.

Concurrent administration with rifampicin, barbiturates, phenytoin, dichloralphenazone, phenylbutazone, carbamazepine may decrease its effect. Use with an anticoagulant may alter the effect of the latter. Concomitant use with heparin should be avoided.

4.6 Pregnancy and lactation

This medicine is contraindicated during pregnancy because of possible masculinisation of the foetus. There are insufficient data on the use of this medicine during breast-feeding to assess potential harm to the infant or a possible influence on milk production.

4.7 Effects on ability to drive and use machines

As far as is known Deca Durabolin 100 has no effect on alertness and concentration.

4.8 Undesirable effects

Dependent on the dose, frequency and total period of administration of Deca-Durabolin the following undesirable effects may occur (see also Section 4.4):

System Organ Class	MedDRA term*
Endocrine disorders	Virilism Hirsutism
Metabolism and nutrition disorders	Hyperglycaemia Hyperlipidaemia
Psychiatric disorders	Libido increased
Vascular disorders	Hypertension
Respiratory, thoracic and mediastinal disorders	Hoarseness Dysphonia
Gastrointestinal disorders	Nausea
Hepato-biliary disorders	Hepatic function abnormal Peliosis hepatis
Skin and subcutaneous tissue disorders	Acne Rash Pruritus
Musculoskeletal, connective tissue and bone disorders	Epiphyses premature fusion
Renal and urinary disorders	Urine flow decreased
Reproductive system and breast disorders	Benign prostatic hyperplasia Priapism Penis enlarged Enlarged clitoris Oligomenorrhoea
General disorders and administration site conditions	Oedema Injection site reaction
Investigations	High density lipoprotein decreased Sperm count decreased Haemoglobin increased
Injury, poisoning and procedural complications	Intentional misuse

*MedDRA version 7.1

The terms used to describe the undesirable effects are also meant to include synonyms and related terms.

Liver tumors have been reported occasionally on prolonged treatment with orally active C17-alpha-alkylated anabolic steroids. A relationship between liver tumors and non C17-alpha-alkylated anabolic steroids such as Nandrolone esters appears to be highly unlikely but cannot be absolutely excluded.

4.9 Overdose

The acute toxicity of nandrolone decanoate in animals is very low. There are no reports of acute overdosage with Deca-Durabolin "100" in man.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

DECA-DURABOLIN "100" is a high dosage form of nandrolone decanoate designed especially for adjuvant therapy in the treatment of certain blood disorders. Nandrolone, the pharmacologically active substance of the preparation, is

chemically related to testosterone. Compared to testosterone, it has an enhanced anabolic and a reduced androgenic activity. This has been demonstrated in animal bioassays and explained by receptor binding studies. The low androgenicity of nandrolone is confirmed in clinical use.

In animals, nandrolone decanoate possesses an erythropoiesis-stimulating effect probably by directly stimulating the haematopoietic stem cells in the bone marrow and by increasing the release of erythropoietin. It also affords protection against the bone marrow depression caused by cytotoxic agents.

In the human, DECA-DURABOLIN "100" stimulates erythropoiesis as demonstrated by rises in the red blood cell mass, and in the haemoglobin and haematocrit values. This effect is utilised therapeutically in the treatment of anaemia due to a decreased production of erythropoietin, bone marrow depression induced by chemotherapy, or hypoplasia of the stem cells in the bone marrow. In the latter condition (e.g. aplastic anaemia) the erythropoiesis response is frequently accompanied by a positive effect on leucopoiesis and thrombopoiesis. Androgenic effects (e.g. virilisation) are relatively uncommon at the recommended dosages. Nandrolone lacks the C17alpha-alkyl group which is associated with the occurrence of liver dysfunction and cholestasis.

5.2 Pharmacokinetic properties

Nandrolone decanoate 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 of hydrolysis of nandrolone decanoate and of 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.

5.3 Preclinical safety data

Pharmacological studies in animals on the toxicity after repeated dosing, genotoxicity and carcinogenicity did not indicate a safety risk for humans. No animal data on reproduction are available. The use of androgens in different species has demonstrated to result in masculinisation of the external genitals of female fetuses.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Arachis oil, refined (peanut oil)

6.2 Incompatibilities

None known.

6.3 Shelf Life

Unopened: 5 years.
The ampoules are intended for single use only.
Once opened, any unused solution should be discarded.

6.4 Special precautions for storage

Do not store above 25^{o}C.
Do not refrigerate.
Keep the ampoules in the outer carton.

6.5 Nature and contents of container

A clear Type I glass ampoule containing 1ml of solution, packed in boxes of 3 ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Organon Laboratories Limited
Cambridge Science Park
Milton Road
Cambridge
CB4 0FL
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 261/3/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 August 1975.

Date of last renewal: 29 August 2005.

10 DATE OF REVISION OF THE TEXT

February 2006.