IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA0261/009/003
Case No: 2037733

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

Sustanon '250' Ampoule Solution for Injection

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 **17/07/2007** until **31/03/2009**.

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

Sustanon 250 Ampoule Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule of Sustanon 250 contains 30 mg/ml testosterone propionate, 60 mg/ml testosterone phenylpropionate, 60 mg/ml testosterone isocaproate and 100 mg/ml testosterone decanoate. Sustanon 250 has a content equivalent to 176 mg of testosterone.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
A clear pale yellow solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In men testosterone therapy may be indicated in osteoporosis caused by androgen deficiency.

In males: Testosterone replacement therapy for primary or secondary hypogonadal disorders, for example:
- After castration,
- Eunuchoidism,
- Hypopituitarism,
- Endocrine impotence.

In female to male transsexuals:
- Masculinization.

4.2 Posology and method of administration

In general, dosing frequency should be adjusted according to the response of the individual patient.
Usually, one injection of 1 ml per three weeks is adequate. Sustanon 250 should be administered by deep intramuscular injection.
Safety and efficacy has not been determined in children. Since Sustanon 250 contains benzyl alcohol as an excipient, it should not be used in children younger than 3 years.

4.3 Contraindications

- Known or suspected prostatic carcinoma or breast carcinoma in the male.
- Pregnancy.
- Breast-feeding.
- Hypersensitivity for any of the excipients.
- Hypercalciuria, hypercalcaemia, nephrosis and ischaemic heart disease.
- Use in patients allergic to peanuts and soya.
- Use of androgens to enhance ability in sports is contraindicated.

4.4 Special warnings and precautions for use

- Initiation of testosterone therapy and its overall direction should only be carried out by specialists.
- Androgens should be used with caution in (pre) pubertal boys to avoid premature epiphyseal closure or precocious sexual development. Skeletal maturation should be monitored regularly.
- Patients with latent or overt cardiac failure, renal dysfunction, hypertension, epilepsy or migraine (or a history of these conditions) should be kept under close medical supervision, since aggravation or recurrence may occasionally be induced.
- Androgens should be used with caution in men suffering from benign prostatic hypertrophy.
- If androgen-associated adverse reactions occur, Sustanon treatment should be interrupted and, after disappearance of the symptoms, be resumed at a lower dosage.
- The use of steroids may influence the results of certain laboratory tests.
- Sustanon 250 contains arachis oil (peanut oil). If you are allergic to peanut or soya, do not use this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Enzyme-inducing agents may exert increasing or decreasing effects on testosterone levels. Therefore adjustment of dose, and/or intervals between injections may be required.

Since Sustanon is administered intramuscularly, interactions with food, drinks or physical activity is not likely.

4.6 Pregnancy and lactation

This medicine is contraindicated during pregnancy (section 4.3) because of possible masculinization of the foetus. There are insufficient data on the use of this medicine during breast-feeding to access potential harm to the infant or a possible influence on milk production.

4.7 Effects on ability to drive and use machines

Up to now no reference has been made to any influence on alertness and powers of concentration, during the use of Sustanon.

4.8 Undesirable effects

The following adverse reactions have been associated with androgen therapy, in general with high dosages, prolonged treatment and/or too frequent administration:

- In prepubertal boys:
  Precocious sexual development, increased frequency of erections, phallic enlargement and premature epiphyseal closure.
- In men:
  Priapism and other signs of excessive sexual stimulation, oligospermia and decreased ejaculatory volume.
- In women:
  Androgens have been described to cause symptoms of virilisation such as hirsutism, acne and voice changes (deepening, hoarsening). The voice changes may be irreversible. If unwanted signs of virilisation develop treatment should be discontinued.
- In all patients:
  Water and sodium retention.
- Hypertrichosis.
- Myalgia.
- Hypertension.
- Mood disturbances.
- Changes in liver function tests.
- Injectables in general, may cause local reactions at the injection site such as pain and oedema.

- With high doses and prolonged treatment, electrolyte changes (sodium, potassium, calcium, inorganic phosphate and water retention), polycythemia and changes in lipid profile may occur.

If deemed appropriate, treatment should be interrupted until symptoms have disappeared and reintroduced at a lower rate.

4.9 Overdose

The acute intramuscular toxicity of Sustanon is very low. Priapism in men is a symptom of chronic overdosage. If this occurs, Sustanon treatment should be interrupted and, after disappearance of the symptom, be resumed at a lower dosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Testosterone and all testosterone esters have the ATC code: G03B A03.

Testosterone is the principal endogenous hormone essential for normal growth and development of the male sex organs and male secondary sex characteristics. During adult life testosterone is essential for the functioning of the testes and accessory structures, and for the maintenance of libido, sense of well-being, erectile potency, prostate and seminal vesicle function.
Treatment of hypogonadal men with Sustanon results in a clinically significant rise of plasma concentrations of testosterone, dihydrotestosterone and androstenedione, as well as a decrease of SHBG (sex hormone binding globulin). In males with primary (hypergonadotropic) hypogonadism treatment with Sustanon results in a normalization of gonadotropin levels.

Treatment of female-to-male transsexuals with Sustanon results in a clinically significant rise of plasma testosterone levels, a decrease of LH (luteinizing hormone) and FSH (follicle stimulating hormone) levels and a decrease in SHBG level.

5.2 Pharmacokinetic properties

Sustanon contains a number of esters of testosterone with different durations of action. The esters are hydrolysed into the natural hormone testosterone as soon as they enter the general circulation.

A single dose of Sustanon 250 leads to an increase of total plasma testosterone with peak levels of approximately 70 nmol/l (Cmax), which are reached approximately 24-48 h (t-max) after administration. Plasma testosterone levels return to the lower limit of the normal range in males in approximately 21 days.

Testosterone is metabolised via the normal pathways. Excretion mainly takes place via the urine as conjugates of etiocholanolone and androsterone.

5.3 Preclinical safety data

No particulars.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
Arachis Oil

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

5 years.
Since an opened ampoule cannot be resealed in such a way to further guarantee the sterility of the contents, the solution should be used immediately.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze. Store the ampoules in the original package.

6.5 Nature and contents of container

Each ml of Sustanon is filled in colourless hydrolytic glass Type I ampoule Ph. Eur. Sustanon is available in pack sizes of 1 ml x 3 ampoules and 1 ml x 6 ampoules.

Not all pack sizes may be marketed.

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 261/9/3

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1979

Date of last renewal: 01 April 2004

10 DATE OF REVISION OF THE TEXT

May 2005