NAME OF MEDICINE

SUSTANON 250

250mg/mL for injection
Oily solution for intramuscular use

Presentation

A clear, pale yellow solution.

Each ampoule or vial contains 1 mL arachis oil containing the following active substances:

testosterone proprionate	30mg
testosterone phenylpropionate	60mg
testosterone isocaproate	60mg
testosterone decanoate	100mg

The total amount of testosterone per mL is 176mg.

Uses

Actions

Pharmacotherapeutic group: Androgens. ATC code G03B A03.

Treatment of hypogonadal men with SUSTANON results in a clinically significant rise of plasma concentrations of testosterone, dihydrotestosterone, oestradiol and androstenedione, as well as a decrease of SHBG (sex hormone binding globulin). Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) are restored to the normal range. In hypogonadal men, treatment with SUSTANON results in an improvement of testosterone deficiency symptoms. Moreover, treatment increases bone mineral density and lean body mass, and decreases body fat mass. Treatment also improves sexual function, including libido and erectile function. Treatment decreases serum LDL-C, HDL-C and triglycerides, increases haemoglobin and hematocrit, whereas no clinically relevant changes in liver enzymes and PSA have been reported. Treatment may result in an increase in prostate size, but no adverse effects on prostate symptoms have been observed. In hypogonadal diabetic patients, improvement of insulin sensitivity and/or reduction in blood glucose have been reported with the use of androgens. In boys with constitutional delay of growth and puberty, treatment with androgens accelerates growth and induces development of secondary sex characteristics.

In female-to-male transsexuals, treatment with androgens/SUSTANON induces masculinization.

Pharmacokinetics

SUSTANON 250 contains four esters of testosterone with different durations of action. The esters are hydrolyzed into the natural hormone testosterone as soon as they enter the general circulation.

Absorption

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

Distribution

Testosterone displays a high (over 97%) non-specific binding to plasma proteins and sex hormone binding globulin in *in vitro* tests.

Biotransformation

Testosterone is metabolized to dihydrotestosterone and oestradiol, which are further metabolized via the normal pathways.

Elimination

Excretion mainly takes place via the urine as conjugates of etiocholanolone and androsterone.

Preclinical Safety Data

Preclinical data reveal no hazard for humans.

Indications

Testosterone replacement therapy in males for conditions associated with primary and secondary hypogonadism, either congenital or acquired.

In female to male transsexuals:

- masculinization

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

Dosage and Administration

In general, the dose should be adjusted according to the response of the individual patient.

Adults (incl. elderly):

Usually, one injection of 1ml per three weeks is adequate.

SUSTANON should be administered by deep intramuscular injection.

Paediatric population:

Safety and efficacy have not been adequately determined in children and adolescents. Pre-pubertal children treated with SUSTANON should be treated with caution (see **Warnings and Precautions**). SUSTANON contains benzyl alcohol and should not be given to children under 3 years of age.

Contraindications

- Pregnancy
- Known or suspected carcinoma of prostate or breast cancer
- Breastfeeding
- Hypersensitivity to the active substance or to any of the excipients, including arachis oil. SUSTANON is therefore contraindicated in patients allergic to peanuts or soya (see **Warnings and Precautions**).

Warnings and Precautions

Medical Examination:

Testosterone level should be monitored at baseline and at regular intervals during treatment. Clinicians should adjust the dosage individually to ensure maintenance of eugonadal testosterone levels.

Physicians should consider monitoring patients receiving SUSTANON before the start of treatment, at quarterly intervals for the first 12 months and yearly thereafter for the following parameters:

- digital rectal examination (DRE) of the prostate and PSA to exclude benign prostate hyperplasia or a sub-clinical prostate cancer (see **Contraindications**)
- hematocrit and haemoglobin to exclude polycythemia.

Conditions that need supervision:

Patients, especially the elderly, with the following conditions should be monitored for:

- **Tumours** – Mammary carcinoma, hypernephroma, bronchial carcinoma and skeletal metastases. In these patients hypercalcemia may develop spontaneously, also during androgen therapy. The latter can be indicative of a positive tumour response to the hormonal treatment. Nevertheless, the hypercalcemia should first be treated appropriately and after restoration of normal calcium levels, hormone therapy can be resumed.
- **Pre-existing conditions** – In patients with pre-existing cardiac, renal or hepatic insufficiency/disease androgen treatment may cause complications characterized by edema

with or without congestive heart failure. In such cases treatment must be stopped immediately. Patients who experienced myocardial infarction, cardiac-, hepatic- or renal insufficiency, hypertension, epilepsy, or migraine should be monitored due to the risk of deterioration of or reoccurrence of disease. In such cases treatment must be stopped immediately. There is insufficient long-term safety data to assess a potentially increased risk of cardiovascular disease.

- **Diabetes mellitus** – Androgens in general and SUSTANON can improve glucose tolerance in diabetic patients (see **Interactions**).
- **Anti-coagulant therapy** – Androgens in general and SUSTANON can enhance the anti-coagulant action of coumarin-type agents (see **Interactions**).
- **Sleep apnea** – There is insufficient evidence for a recommendation regarding the safety of treatment with testosterone esters in men with sleep apnea. Good clinical judgment and caution should be employed in patients with risk factors such as adiposity or chronic lung diseases.

Adverse events:

If androgen-associated adverse reactions occur (see **Adverse Effects**), treatment with SUSTANON should be discontinued and, upon resolution of complaints, resumed with a lower dose.

Virilization:

Patients should be informed about the potential occurrence of signs of virilization. In particular, singers and women with speech professions should be informed about the risk of deepening of the voice. The voice changes may be irreversible. If signs of virilisation develop, the risk/benefit ratio has to be newly assessed with the individual patient.

(Mis)use in sports:

Patients who participate in competitions governed by the World Anti-Doping Agency (WADA) should consult the WADA-code before using this product as SUSTANON can interfere with anti-doping testing. The misuse of androgens to enhance ability in sports carries serious health risks and is to be discouraged.

Excipients:

SUSTANON contains arachis oil (peanut oil) and should not be taken/ applied by patients known to be allergic to peanut. As there is a possible relationship between allergy to peanut and allergy to soya, patients with soya allergy should also avoid Sustanon (see **Contraindications**).

SUSTANON contains 100 mg benzyl alcohol per ml solution and must not be given to premature babies or neonates. Benzyl alcohol may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years old.

Paediatric Population:

In pre-pubertal children statural growth and sexual development should be monitored since androgens in general and Sustanon in high dosages may accelerate epiphyseal closure and sexual maturation.

Pregnancy and Lactation

SUSTANON is contraindicated in women who are pregnant (see Contraindications).

There are no adequate data for the use of SUSTANON in pregnant women. In view of the risk of virilization of the foetus, SUSTANON should not be used during pregnancy. Treatment with SUSTANON should be discontinued when pregnancy occurs.

There are no adequate data for the use of SUSTANON during lactation. Therefore, SUSTANON should not be used during lactation.

Effects on Fertility

In men, treatment with androgens can lead to fertility disorders by repressing sperm-formation (see **Adverse Effects**).

In women, treatment with androgens can lead to an infrequent or repressed menstrual cycle (see **Adverse Effects**).

Effects on Ability to Drive and Use Machines

SUSTANON has no influence on the ability to drive and use machines.

Adverse Effects

Due to the nature of SUSTANON, side effects cannot be quickly reversed by discontinuing medication. Injectables in general, may cause a local reaction at the injection site.

The following adverse reactions have been associated with androgen therapy in general.

System Organ Class	MedDRA term*
Neoplasms benign, malignant and unspecified	Prostatic cancer[1]
Blood and lymphatic system disorders	Polycythaemia
Metabolism and nutrition disorders	Fluid retention
Psychiatric disorders	Depression, nervousness, mood altered, libido increased, libido decreased
Musculoskeletal and connective tissue	Myalgia
Vascular disorders	Hypertension
Gastrointestinal disorders	Nausea
Hepatobiliary disorders	Hepatic function abnormal
Skin and subcutaneous tissue	Pruritus, acne
Reproductive system and breast disorders	Gynaecomastia, oligozoospermia, priapism, Benign prostatic hyperplasia[2]
Investigations	Haematocrit increased Red blood cell count increased Haemoglobin increased Lipids abnormal[3], PSA increased

MedDRA version 15.0
[1] Progression of a sub-clinical prostatic cancer
[2] Prostatic growth (to eugonadal state)
[3] Decrease in serum LDL-C, HDL-C and triglycerides

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

In a few patients, diarrhoea and abdominal pain or discomfort have been reported during use of SUSTANON.

Treatment in women:
Treatment with SUSTANON may induce signs of virilization in women (see **Warnings and Precautions**). Symptoms of virilization may include hoarseness, acne, hirsutism, menstrual irregularity and alopecia.

Paediatric population:
The following undesirable effects have been reported in pre-pubertal children using androgens (see **Warnings and Precautions**): precocious sexual development, an increased frequency of erections, phallic enlargement and premature epiphyseal closure.

Interactions

Enzyme-inducing agents may decrease and enzyme-inhibiting drugs may increase testosterone levels. Therefore, adjustment of the dose of Sustanon may be required.

Insulin and other antidiabetic medicines:

Androgens may improve glucose tolerance and decrease the need for insulin or other anti-diabetic medicines in diabetic patients (see **Warnings and Precautions**). Patients with diabetes mellitus should therefore be monitored especially at the beginning or end of treatment and at periodic intervals during SUSTANON treatment.

Anti-coagulant therapy:

High doses of androgens may enhance the anti-coagulant action of coumarin-type agents (see **Warnings and Precautions**). Therefore close monitoring of prothrombin time and if necessary a dose reduction of the anti-coagulant is required during therapy.

ACTH or corticosteroids:

The concurrent administration of testosterone with ACTH or corticosteroids may enhance oedema formation; thus these active substances should be administered cautiously, particularly in patients with cardiac or hepatic disease or in patients predisposed to oedema (see **Warnings and Precautions**).

Laboratory test interactions:

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.

Overdosage

The acute toxicity of testosterone is low. If symptoms of chronic overdose occur (e.g. polycythemia, priapism) treatment should be discontinued and after disappearance of the symptoms, be resumed at a lower dosage.

Pharmaceutical Precautions

Ampoules: 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.

Vials: Single use in one patient only. The solution should be injected immediately after withdrawing the contents from the vial using a sterile syringe and needle.

Shelf-life 36 months. SUSTANON may be used until the expiration date indicated on the package.

Incompatibilities

Not applicable.

Special precautions for storage

Store below 30°C; do not refrigerate or freeze. Store in original package and keep container in outer carton.

Discard any unused product or waste material.

List of excipients

Arachis (peanut) oil; benzyl alcohol.

Medicine Classification

Prescription Medicine.

Package Quantities

Each package contains one ampoule or one vial, containing 1mL of oily solution for injection.

Further Information

All four compounds are esters of the natural hormone testosterone. The solution also contains 10 per cent benzyl alcohol.

Name and Address

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