1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

SUSTANON 250 injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule of SUSTANON 250 contains 1 ml arachis oil containing the following active substances:

Testosterone propionate 30 mg

Testosterone phenylpropionate 60 mg

Testosterone isocaproate 60 mg

Testosterone decanoate 100 mg

All four compounds are esters of the natural hormone testosterone. The total amount of testosterone per ml is 176 mg.

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Injection

An ampoule marked with a red and yellow ring on the neck, containing a clear yellow oily solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SUSTANON 250 is indicated in adults for:

- Testosterone replacement therapy in males for conditions associated with primary and secondary hypogonadism (either congenital or acquired), only when testosterone deficiency has been confirmed by clinical features and biochemical tests.

4.2 Posology and method of administration

Posology

In general, the dosage should be adjusted according to the response of the individual patient. Safety and efficacy have not been determined in children.

Adults

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

Paediatric population

Safety and efficacy have not been determined in children and adolescents. Pre-pubertal children treated with SUSTANON 250 should be treated with caution (see section 4.4).

Method of administration

SUSTANON 250 should be administered by deep intramuscular injection.

4.3 Contraindications

SUSTANON 250 is contraindicated in:

- Patients with hypersensitivity to testosterone or any of the excipients of SUSTANON 250, including arachis oil,in SUSTANON 250, is therefore contraindicated in patients allergic to peanuts or soya (see section 4.4 and section 6.1).
- Patients with known or suspected prostatic carcinoma or breast carcinoma.
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

Medical examination

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

Medical practitioners should consider monitoring patients receiving SUSTANON 250 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.
- haematocrit and haemoglobin to exclude polycythemia.

Conditions that need supervision:

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

Tumours

Patients especially the elderly should be monitored for mammary carcinoma, hypernephroma, bronchial carcinoma and skeletal metastases. In these patient's

hypercalcaemia may develop spontaneously, also during SUSTANON 250 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.

SUSTANON 250 should be used with caution in men suffering from benign prostatic hypertrophy.

Pre-existing conditions

Middle aged and elderly males on treatment for angina pectoris or other circulatory disease should receive SUSTANON 250 only under very careful supervision.

Patients on treatment for 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 be induced, by treatment with SUSTANON 250. In such cases treatment must be stopped immediately.

In patients with pre-existing cardiac, renal or hepatic insufficiency/disease, androgen treatment with SUSTANON 250 may cause complications characterised by oedema with or without congestive heart failure. In such cases treatment must be stopped immediately.

Approved testosterone treatment, such as SUSTANON 250 possibly may increase risk of heart attack and strokes. Patients should not stop taking SUSTANON 250 without first discussing any questions or concerns with their health care professionals. Health care

professionals should consider whether the benefits of treatment are likely to exceed the potential risks of treatment.

Diabetes mellitus

SUSTANON 250 can improve glucose tolerance and blood glucose control in diabetic patients (see section 4.5).

Anti-coagulant therapy

SUSTANON 250 can enhance the anti-coagulant action of warfarin (see section 4.5).

Sleep apnoea

There is insufficient evidence for a recommendation regarding the safety of treatment with testosterone esters in men with sleep apnoea. Good clinical judgment and caution should be employed in patients with risk factors such as adiposity or chronic lung diseases. SUSTANON 250 in obese males with chronic obstructive pulmonary disease (COPD) may cause sleep apnoea.

Adverse events

If androgen associated adverse reactions occur (see section 4.8), treatment with SUSTANON 250, should be discontinued, and, upon resolution of complaints, and after disappearance of the symptoms, be resumed at a lower dosage.

A decrease in protein bound iodine (PBI) may occur, but this has no clinical significance.

Clotting disorders

Testosterone should be used with caution in patients with thrombophilia or risk factors for venous thromboembolism (VTE), as there have been post-marketing studies and reports

of thrombotic events (e.g. deep-vein thrombosis, pulmonary embolism, ocular thrombosis) in these patients during testosterone therapy. In thrombophilic patients, VTE cases have been reported even under anticoagulation treatment, therefore continuing testosterone treatment after first thrombotic event should be carefully evaluated. In case of treatment continuation, further measures should be taken to minimise the individual VTE risk.

(Mis)use in sports

The misuse of SUSTANON 250 to enhance ability in sports carries serious health risk.

Patients who participate in competitions governed by the World Anti-Doping Agency (WADA) should consult the WADA-code before using this SUSTANON 250, as SUSTANON 250 can interfere with anti-doping testing. The misuse of androgens to enhance ability in sports carries serious health risks and is to be discouraged.

Polycythaemia

Treatment with testosterone, as in SUSTANON 250 decreases serum LDL-C, HDL-C and triglycerides and increases haemoglobin and haematocrit, which may lead to polycythaemia.

Virilisation

Patients should be informed about the potential occurrence of signs of virilisation. 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.

Drug abuse and dependence

Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indications and in combination with other anabolic androgenic steroids. Abuse of testosterone and other anabolic androgenic steroids can lead to serious adverse reactions including: cardiovascular (with fatal outcomes in some cases), hepatic and/or psychiatric events. Testosterone abuse may result in dependence and withdrawal symptoms upon significant dose reduction or abrupt discontinuation of use. The abuse of testosterone and other anabolic androgenic steroids carries serious health risks and is to be discouraged (see section 4.8).

Elderly people

There is limited experience on the safety and efficacy of the use of SUSTANON 250 in patients over 65 years of age. Currently, there is no consensus about age specific testosterone reference values.It should be taken into account that physiologically testosterone serum levels are lower with increasing age.

Paediatric population

SUSTANON 250 should not be used in pre-pubertal boys as premature epiphyseal closure or precocious sexual development may occur.

In pre-pubertal children statural growth and sexual development should be monitored since SUSTANON 250 in high dosages may accelerate epiphyseal closure and sexual maturation.

Excipients

SUSTANON 250 contains arachis oil (peanut oil) and should not be administered to patients known to be allergic to peanuts. As there is a possible relationship between allergy to peanut and allergy to soya, patients with soya allergy should also avoid SUSTANON 250 (see section 4.3).

SUSTANON 250 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.

4.5 Interaction with other medicines and other forms of interaction

Enzyme-inducing medicines may decrease, and enzyme-inhibiting medicines may increase testosterone levels. Therefore, adjustment of the dose of SUSTANON 250, and/or intervals between injections may be required.

Insulin and other anti-diabetic medicines

SUSTANON 250 may improve glucose tolerance and decrease the need for insulin or other anti-diabetic medicines in diabetic patients, with hypogonadism (see section 4.4). Patients with diabetes mellitus should therefore be monitored especially at the beginning or end of treatment and at periodic intervals during SUSTANON 250 treatment.

Anti-coagulant therapy

High doses of SUSTANON 250 may enhance the anticoagulant action of warfarin and other anti-coagulants(see section 4.4). Therefore, close monitoring of prothrombin time and if necessary, a dose reduction of the warfarin is required during therapy.

ACTH or corticosteroids

The concurrent administration of SUSTANON 250 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 section 4.4).

Laboratory test interactions

SUSTANON 250 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 non clinical evidence of thyroid dysfunction.

4.6 Fertility, pregnancy, lactation

SUSTANON 250 is contraindicated in pregnancy and lactation.

Pregnancy

SUSTANON 250 is not indicated for treatment in women and therefore must not be used by pregnant or breastfeeding women. If used during pregnancy SUSTANON 250 poses a risk of virilisation of the foetus (see section 4.3).

Breastfeeding

There are no adequate data for the use of SUSTANON 250 during lactation. Therefore, SUSTANON 250 should not be used during lactation.

Fertility

In men, treatment with SUSTANON 250 can lead to fertility disorders by repressing sperm-formation (see section 4.8).

4.7 Effects on ability to drive and use machines

SUSTANON 250 can cause mood disturbances, paranoia and delusion which may influence the ability to drive and operate machines.

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that SUSTANON 250 does not adversely affect their ability to do so safely (see section 4.8).

4.8 Undesirable effects

a) Summary of the safety profile

Due to the nature of SUSTANON 250, side effects cannot be quickly reversed by discontinuing SUSTANON 250. SUSTANON 250 may cause a local reaction at the injection site.

The following adverse reactions have been associated with SUSTANON 250. Frequencies are unknown.

b) Tabulated list of adverse reactions

System Organ Class	Frequency unknown (cannot be estimated from the available data)
Neoplasms benign and malignant (including cysts and polyps)	Prostatic cancer[1]
Blood and the lymphatic system disorders	Polycythaemia
Metabolism and nutrition disorders	Fluid retention
Psychiatric disorders	Depression, nervousness, mood disturbances, increased libido, decreased libido, aggression
Vascular disorders	Hypertension
Gastrointestinal disorders	Nausea
Skin and subcutaneous tissue disorders	Pruritus, acne
Musculoskeletal, connective tissue and bone disorders	Myalgia
Reproductive system and breast disorders	Gynaecomastia, oligozoospermia, decreased ejaculatory volume, priapism, benign prostatic disorder[2] In pre-pubertal boys: precocious sexual development, an increased frequency of erections, priapism, phallic enlargement and premature epiphyseal closure
Investigations	Hepatic function abnormal, abnormal lipids[3], PSA increased, increased haematocrit, increased red blood cell count, increased haemoglobin
[1] Progression of a sub-clinical prostatic cancer [2] Prostatic growth (to eugonadal state) [3] Decrease in serum LDL-C, HDL-C and triglycerides	

c) *Description of selected adverse reactions*

Drug abuse and dependence:

Testosterone, often in combination with other anabolic androgenic steroids (AAS), has been subject to abuse at doses higher than recommended for the approved indication

(see section 4.4). The following additional adverse reactions have been reported in the context of testosterone/AAS abuse:

Endocrine disorders: Secondary hypogonadism[1]

Psychiatric disorders: Hostility, aggression[1], psychotic disorder[1], mania, paranoia and delusion.

*Cardiovascular disorders***:** Myocardial infarction[1], cardiac failure[1], cardiac failure chronic[1],[2], cardiac arrest, sudden cardiac death, cardiac hypertrophy[1],[2], cardiomyopathy[1], ventricular dysrhythmia, ventricular tachycardia[1], venous/arterial thrombotic and embolic events (including deep venous thrombosis[1], pulmonary embolism[1], coronary artery thrombosis, carotid artery occlusion[1],[2], intracranial venous sinus thrombosis[1],[2]), cerebrovascular accident and ischaemic stroke.

Hepatobiliary disorders: Peliosis hepatis[1], cholestasis, liver injury, jaundice[1] , hepatic failure.

Skin and subcutaneous tissue disorders: Alopecia[1].

Reproductive system and breast disorders: Testicular atrophy, azoospermia, infertility (in males), enlarged clitoris and breast atrophy (in females).

[1] Has been reported with SUSTANON

[2] With fatal outcomes in some cases

d) Paediatric population

The following undesirable effects have been reported in pre-pubertal children using androgens (see section 4.4): precocious sexual development, an increased frequency of erections, phallic enlargement and premature epiphyseal closure.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to to **SAHPRA** via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9 Overdose

Symptoms

The acute toxicity of testosterone is low.

If symptoms of chronic overdose occur (e.g. polycythaemia, priapism) treatment should be discontinued and after disappearance of the symptoms, be resumed at a lower dosage (see section 4.8).

Treatment

Treat symptomatically.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: 21.6 Anabolic steroids

Pharmacotherapeutic group: Hormones

ATC code: G03BA03

Mechanism of action

The formulation contains four esters of testosterone, the main androgen in males responsible for maintaining androgenic hormone functions in males. The esters are hydrolysed into testosterone.

5.2 Pharmacokinetic properties

Absorption

A single dose of 1 mL, (175 mg testosterone) leads to an increase of total plasma testosterone, with peak levels of approximately 70 nmol/l (C_{max}), which are reached approximately 24 to 48 hrs (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 metabolised to dihydrotestosterone and estradiol, which are further metabolised via the normal pathways.

Elimination

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

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Arachis oil and benzyl alcohol 10 % *v/v.*

6.2. Incompatibilities

None

6.3. Shelf life

60 months

6.4. Special precautions for storage

Store at or below 30 °C. Do not refrigerate or freeze.

Store in the original package in order to protect from light.

6.5. Nature and contents of container

Box of 1 ml clear glass ampoule packed as a single unit.

6.6. Special precautions for disposal

None

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

G3208 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION

Old Medicine

10. DATE OF REVISION OF TEXT

21 December 2023

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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