PROFESSIONAL INFORMATION

TESTOSTERONE CIPLA

SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE

TESTOSTERONE CIPLA (1000 mg/4 mL, solution for injection).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 4 mL vial of TESTOSTERONE CIPLA solution for injection contains testosterone undecanoate 1000 mg.

Each mL contains 250 mg of testosterone undecanoate, corresponding to 157,9 mg of testosterone base form. Each 4 mL vial contains 1000 mg of testosterone undecanoate, corresponding to 631,5 mg of testosterone base form.

Sugar free.

For full list of excipients, see **section 6.1**

3 PHARMACEUTICAL FORM

Solution for injection.

TESTOSTERONE CIPLA, solution for injection, is a clear yellowish oily solution in a vial containing 1000 mg/4 mL (250 mg/mL) of testosterone undecanoate.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

TESTOSTERONE CIPLA is indicated for testosterone replacement therapy in primary and secondary male hypogonadism.

4.2 Posology and method of administration

Posology

TESTOSTERONE CIPLA (1 vial corresponding to 1000 mg testosterone undecanoate) is injected every 10 to 14 weeks. Injections with this frequency are capable of maintaining sufficient testosterone levels and do not lead to accumulation.

Start of treatment

Serum testosterone levels should be measured before the start of treatment. The first injection interval may be reduced to a minimum of 6 weeks. With this loading dose, steady-state levels will be reached quickly.

Individualisation of treatment

It is advisable to occasionally measure testosterone serum levels at the end of an injection interval. Serum levels below normal range would indicate the need for a shorter injection interval. In the case of high serum levels, an extension of the injection interval may be considered. The injection interval should remain within the recommended range of 10 to 14 weeks.

Special populations

Paediatric population

TESTOSTERONE CIPLA is not indicated for use in children and adolescents.

It has not been clinically evaluated in males below the age of 18 years **(see section**

4.4).

Elderly patients

Limited data do not suggest the need for a dosage adjustment in elderly patients **(see section 4.4).**

Patients with hepatic impairment

No formal studies have been performed in patients with hepatic impairment. The use of TESTOSTERONE CIPLA in men with past or present liver tumours **(see section 4.3).**

Patients with renal impairment

No formal studies have been performed in patients with renal impairment.

Method of administration

TESTOSTERONE CIPLA is strictly for intramuscular injection. Special care must be given to avoid intravasal injection. The injections must be administered very slowly (over 2 minutes). To avoid injury when opening, the contents of the vial are to be injected intramuscularly immediately after opening (**see section 6.6.).**

4.3 Contraindications

TESTOSTERONE CIPLA should not be used in:

- Patients with known hypersensitivity to testosterone or to any of the excipients in TESTOSTERONE CIPLA **(see section 6.1).**
- Androgen-dependent carcinoma of the prostate or of the male mammary gland.
- Hypercalcaemia accompanying malignant tumours.
- Past or present liver tumours.

The use of TESTOSTERONE CIPLA in women is contraindicated.

4.4 Special warnings and precautions for use

Children and adolescents

Clinical trials with TESTOSTERONE CIPLA in children or adolescents under the age of 18 have not been conducted.

In children, besides masculinisation, TESTOSTERONE CIPLA can cause accelerated growth and bone maturation and premature epiphyseal closure, thereby reducing final height.

Elderly population

Older patients treated with TESTOSTERONE CIPLA may be at an increased risk for the development of prostatic hyperplasia. Although there are no clear indications that TESTOSTERONE CIPLA actually generates prostatic carcinoma, it can enhance the growth of any existing prostatic carcinoma. Therefore, carcinoma of the prostate has to be excluded before starting therapy with TESTOSTERONE CIPLA.

As a precaution, regular examinations of the prostate are recommended in men.

Laboratory tests

Haemoglobin and haematocrit should be checked periodically in patients on long-term testosterone therapy to detect cases of polycythaemia (see **section 4.8**).

Tumours

Cases of benign and malignant liver tumours have been reported in users of hormonal substances such as androgen compounds. If severe upper abdominal complaints, liver enlargement or signs of intra-abdominal haemorrhage occur in men

using TESTOSTERONE CIPLA, a liver tumour should be included in the differential-diagnostic considerations.

Cardiac, hepatic or renal insufficiency

Caution should be exercised in patients predisposed to oedema, e.g., in cases of severe cardiac, hepatic or renal insufficiency or ischaemic heart disease, as treatment with androgens may results in increased retention of sodium and water. In cases of severe complications characterised by oedema with or without congestive heart failure, treatment must be stopped immediately (see **section 4.8**).
Testosterone may cause a rise in blood pressure and TESTOSTERONE CIPLA should be used with caution in men with hypertension.

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.

Other conditions

Pre-existing sleep apnoea may be potentiated.

Drug abuse and dependence

Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indication(s) 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.

Application

TESTOSTERONE CIPLA must be injected strictly intramuscularly and very slowly (over two minutes). Pulmonary microembolism of oily solutions can in rare cases lead to signs and symptoms such as couch, dyspnoea, malaise, hyperhidrosis, chest pain, dizziness, paraesthesia, or syncope. These reactions may occur during or immediately after the injection and are reversible. Treatment is usually supportive, e.g., by administration of supplemental oxygen.

Suspected anaphylactic reactions after TESTOSTERONE CIPLA injection have been reported.

4.5 Interaction with other medicines and other forms of interactions

Oral anti-coagulants

Testosterone and derivatives have been reported to increase the activity of coumarin derived oral anti-coagulants. Patients receiving oral anti-coagulants require close monitoring, especially at the beginning or end of androgen therapy. Increased

monitoring of the prothrombin time, and international normalised ratio (INR) determinations, are recommended.

Other interactions

The concurrent administration of testosterone with adrenocorticotropic hormone (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.

Laboratory test interactions: Androgens may decrease levels of thyroxin-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.

TESTOSTERONE CIPLA may enhance the blood-sugar reducing effects of insulin. The dosage of the hypoglycaemic medicine may need to be lowered.

Interactions can occur with medicines that induce microsomal enzymes, which can result in increased clearance of TESTOSTERONE CIPLA e.g., barbiturates.

TESTOSTERONE CIPLA may interfere with the metabolism of other medicines. Accordingly, plasma and tissue concentrations may be affected e.g., increased oxyphenbutazone serum levels have been reported. Moreover, testosterone and derivatives have been reported to increase the activity of oral anticoagulants, possibly requiring dose adjustment. Independently of this finding, as a general rule,

the limitations of using intramuscular injections in patients which acquired or inherited blood clotting irregularities always have to be observed.

4.6 Fertility, pregnancy and lactation

Pregnancy

TESTOSTERONE CIPLA is not indicated for use in women and must not be used in pregnant women.

Breastfeeding

TESTOSTERONE CIPLA is not indicated for use in women and must not be used in breastfeeding women.

Fertility

TESTOSTERONE CIPLA may reversibly reduce spermatogenesis (see **section 4.8**).

4.7 Effects on ability to drive and use machines

Dizziness has been reported as less frequent side effect (**see section 4.8).** Patients experiencing dizziness should avoid driving and use of machines.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequently reported undesirable effects during treatment with TESTOSTERONE CIPLA are acne and injection site pain.

Pulmonary microembolism of oily solution can in rare cases lead to signs and symptoms such as cough, dyspnoea, malaise, hyperhidrosis, chest pain, dizziness,

paraesthesia, or syncope. These reactions may occur during or immediately after the injection and are reversible.

Suspected anaphylactic reactions after TESTOSTERONE CIPLA injection have been reported.

Androgens may accelerate the progression of sub-clinical prostatic cancer and benign prostatic hyperplasia.

b. List of adverse reactions

Blood and lymphatic system disorders:

Frequent:	Polycythaemia
Less frequent:	Haematocrit increased
	Red blood cell count increased
	Haemoglobin increased

Immune system disorders:

Less frequent:	Hypersensitivity

Metabolism and nutrition disorders:

Frequent:	Weight increased
Less frequent:	Increased appetite
	Glycosylated haemoglobin increased
	Hypercholesterolaemia
	Blood triglycerides increased
	Blood cholesterol increased

Psychiatric disorders:

Less frequent:	Depression
	Emotional disorder
	Insomnia
	Restlessness
	Aggression
	Irritability

Nervous system disorders:

Less frequent:	Headache
	Migraine
	Tremor

Vascular disorders:

Frequent:	Hot flush.
Less frequent:	Cardiovascular disorder
	Hypertension
	Dizziness

Respiratory, thoracic and mediastinal disorders:

Less frequent:	Bronchitis
	Sinusitis
	Cough
	Dyspnoea
	Snoring

	Dysphonia

Gastrointestinal disorders:

Less frequent:	Diarrhoea
	Nausea

Hepatobiliary disorders:

Less frequent:	Liver function test abnormalities
	Aspartate aminotransferase increased

Skin and subcutaneous tissue disorders:

Frequent:	Acne.
Less frequent:	Alopecia
	Erythema
	Rash
	Papular rash
	Pruritis
	Dry skin

Musculoskeletal and connective tissue disorders:

Less frequent:	Arthralgia
	Pain in extremity
	Muscle spasm
	Muscle strain
	Musculoskeletal stiffness

	Blood creatinine phosphokinase increased

Renal and urinary disorders:

Less frequent:	Urine flow decreased
	Urinary retention
	Urinary tract disorder
	Nocturia
	Dysuria

Reproductive system and breast disorders:

Frequent:	Prostate specific antigen increased
	Prostate examination abnormal
	Benign prostate hyperplasia
Less frequent:	Prostatic intraepithelial neoplasia
	Prostate induration
	Prostatitis
	Prostatic disorder
	Decreased libido
	Increased libido
	Testicular pain
	Breast induration
	Breast pain
	Gynaecomastia
	Increased estradiol
	Testosterone increased

Frequency unknown:	Increased frequency of erections,
	Interruption or reduction in spermatogenesis
	Testicle size reduction
	Painful erections.

General disorders and administration site conditions:

Frequent:	Injection site pain
	Injection site discomfort
	Injection site pruritus
	Injection site erythema
	Injection site haematoma
	Injection site irritation
	Injection site reaction
Less frequent:	Fatigue
	Asthenia
	Hyperhidrosis
	Night sweats
Frequency unknown:	Water retention and oedema.

Injury, poisoning and procedural complications:

Frequency unknown:	Pulmonary oil microembolism.

c. Description of selected adverse reactions

Pulmonary microembolism of oily solutions can in rare cases lead to signs and symptoms such as cough, dyspnoea, malaise, hyperhidrosis, chest pain, dizziness, paraesthesia, or syncope. These reactions may occur during or immediately after the injections and are reversible.

In addition to the above, mentioned adverse reactions, nervousness, hostility, sleep apnoea, various skin reactions including seborrhoea, increased hair growth, increased frequency of erections and in very rare cases jaundice have been reported under treatment with testosterone containing preparations.

Therapy with high doses of testosterone preparations commonly reversibly interrupts or reduces spermatogenesis, thereby reducing the size of the testicles; testosterone replacement therapy of hypogonadism can in rare cases cause persistent, painful erections (priapism). High-dosed or long-term administration of testosterone occasionally increases the occurrences of water retention and oedema.

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.- Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website, or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9 Overdose

No special therapeutic measure apart from termination of therapy with the medicine or dose reduction is necessary after overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 21.7 – Male sex hormones.

ATC code: G03B A03

Testosterone undecanoate is an ester of the naturally occurring androgen, testosterone. The active form, testosterone, is formed by cleavage of the side chain.

Testosterone is the most important androgen of the male, mainly synthesised in the testicles, and to a small extent in the adrenal cortex.

Testosterone is responsible for the expression of masculine characteristics during foetal, early childhood, and pubertal development and thereafter for maintaining the masculine phenotype and androgen-dependent functions (e.g., spermatogenesis, accessory sexual glands). It also performs functions, e.g., in the skin, muscles, skeleton, kidney, liver, bone marrow and central nervous system.

Dependent on the target organ, the spectrum of activities of testosterone is mainly androgenic (e.g., prostate, seminal vesicles, epididymis) or protein-anabolic (muscle, bone, haematopoiesis, kidney, liver).

The effects of testosterone in some organs arise after peripheral conversion of

testosterone to estradiol, which then binds to estrogen receptors in the target cell nucleus e.g., the pituitary, fat, brain, bone, and testicular Leydig cells.

5.2 Pharmacokinetic properties

Absorption

TESTOSTERONE CIPLA is an intramuscularly administered depot preparation of testosterone undecanoate and thus circumvents the first-pass effect. Following intramuscular injection of testosterone undecanoate as an oily solution, the compound is gradually released from the depot and is almost completely cleaved by serum esterases into testosterone and undecanoic acid. An increase in serum levels of testosterone above basal values can already be measured one day after administration.

Distribution

Data from studies indicate that the mean maximum concentrations of testosterone of 24 and 45 nmol/L were measured about 14 and 7 days, respectively, after single intramuscular administration of 1000 mg of testosterone undecanoate in hypogonadal men. Post maximum testosterone levels declined with an estimated half-life of about 53 days.

In the serum of men, about 98 % of the circulating testosterone is bound to SHGB and albumin. Only the free fraction of testosterone is considered as biologically active. Following intravenous infusion of testosterone in elderly men, an apparent volume of distribution of about 1,0 L/kg was determined.

Biotransformation

Testosterone which is generated by ester cleavage from testosterone undecanoate is metabolised and excreted the same way as endogenous testosterone. The undecanoic acid is metabolised by β-oxidation in the same way as other aliphatic carboxylic acids. The major active metabolites of testosterone are oestradiol and dihydrotestosterone.

Elimination

Testosterone undergoes extensive hepatic and extrahepatic metabolism. After the administration of radio-labelled testosterone, about 90 % of the radioactivity appears in the urine as glucuronic and sulphuric acid conjugates and 6 % appears in the faeces after undergoing enterohepatic circulation. Urinary medicines include androsterone and etiocholanolone. Following intramuscular administration of this depot formulation the release rate is characterised by a half-life of 90 ± 40 days.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Benzyl benzoate
- Castor oil, refined.

6.2 Incompatibilities

In the absence of compatibility studies, TESTOSTERONE CIPLA must not be mixed with other medicines.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

- Store at or below 30 °C.

6.5 Nature and contents of container

TESTOSTERONE CIPLA 1000 mg/4 mL solution for injections is contained in 6R (amber glass) vials with a rubber stopper and aluminium flip-off cap.

Pack size is 1 x 4 mL vial.

6.6 Special precautions for handling

At cold storage temperatures the properties of this oil-based solution might temporarily change (e.g., higher viscosity, cloudiness). If stored at cold temperature, the product should be brought to room or body temperature before use.

The solution for intramuscular injection is to be visually inspected prior to use and only clear solution free from particles should be used.

The medicine is for single use only and any unused solution should be discarded in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer care: 080 222 6662

8 REGISTRATION NUMBER

57/21.7/0491

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 09 September 2025

Latest renewal: Not applicable.

10 DATE OF REVISION OF THE TEXT

Not applicable