NEW ZEALAND DATA SHEET

1. PRODUCT NAME

DEPO-TESTOSTERONE® 100mg/mL Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL solution for injection contains 100 mg/mL testosterone cypionate.

Excipients with known effects:

- Benzyl alcohol

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection

DEPO-TESTOSTERONE is a slightly yellow viscous solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DEPO-TESTOSTERONE is indicated for replacement therapy in males in conditions associated with symptoms of deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired)-testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome; or orchidectomy.

Hypogonadotropic hypogonadism (congenital or acquired)-idiopathic gonadotropin or LHRH deficiency, or pituitary-hypothalamic injury from tumours, trauma, or radiation.

4.2 Dose and method of administration

Prior to initiating DEPO-TESTOSTERONE, confirm the diagnosis of hypogonadism by ensuring that serum testosterone concentrations have been measured in the morning on at least two separate days and that these serum testosterone concentrations are below the normal range.

DEPO-TESTOSTERONE is for intramuscular use only.

It should not be given intravenously. Intramuscular injections should be given deep in the gluteal muscle.

Dose

The suggested dosage for DEPO-TESTOSTERONE varies depending on the age, sex, and diagnosis of the individual patient. Dosage is adjusted according to the patient's response and the appearance of adverse reactions.

Various dosage regimens have been used to induce pubertal changes in hypogonadal males; some experts have advocated lower dosages initially, gradually increasing the dose as puberty progresses, with or without a decrease to maintenance levels. Other experts emphasise that higher dosages are needed to induce pubertal changes and lower dosages can be used for maintenance after puberty. The chronological and skeletal ages must be taken into consideration, both in determining the initial dose and in adjusting the dose.

For replacement in the hypogonadal male, 50 mg to 400 mg should be administered every two to four weeks.

Method of administration

Parenteral drug product should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Warming and shaking the vial should redissolve any crystals that may have formed during storage at temperatures lower than recommended.

4.3 Contraindications

Known hypersensitivity to the drug.

Males with carcinoma of the breast.

Males with known or suspected carcinoma of the prostate gland.

Women who are pregnant (see section 4.6).

Patients with serious cardiac, hepatic or renal disease (see section 4.4).

4.4 Special warnings and precautions for use

Hypercalcaemia may occur in immobilised patients. If this occurs, the drug should be discontinued.

Prolonged use of high doses of androgens (principally the 17-α alkyl-androgens) has been associated with development of hepatic adenomas, hepatocellular carcinoma, and peliosis hepatis - all potentially life-threatening complications.

Testosterone should be used with caution in patients with thrombophilia or risk factors for venous thromboembolism (VTE). There have been post-marketing reports of venous thromboembolic events, including deep vein thrombosis (DVT) and pulmonary embolism (PE), in patients using testosterone products, such as DEPO-TESTOSTERONE. Evaluate patients who report symptoms of pain, oedema, warmth and erythema in the lower extremity for DVT and those who present with acute shortness of breath for PE.In thrombophilic patients, VTE cases have been reported even under anticoagulation treatment. If a venous thromboembolic event is suspected, discontinue treatment with DEPO-TESTOSTERONE and initiate appropriate workup and management. 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.

Long term clinical safety trials have not been conducted to assess the cardiovascular outcomes of testosterone replacement therapy in men. To date, epidemiologic studies and randomised

controlled trials have been inconclusive for determining the risk of major adverse cardiovascular events (MACE), such as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death, with the use of testosterone compared to non-use. Some studies, but not all, have reported an increased risk of MACE in association with use of testosterone replacement therapy in men. Patients should be informed of this possible risk when deciding whether to use or to continue to use DEPO-TESTOSTERONE.

Testosterone has been subject to abuse, typically at doses higher than recommended for the approved indication and in combination with other anabolic androgenic steroids. Anabolic androgenic steroid abuse can lead to serious cardiovascular and psychiatric adverse reactions (see section 4.8).

If testosterone abuse is suspected, check serum testosterone concentrations to ensure they are within therapeutic range. However, testosterone levels may be in the normal or subnormal range in men abusing synthetic testosterone derivatives. Counsel patients concerning the serious adverse reactions associated with abuse of testosterone and anabolic androgenic steroids. Conversely, consider the possibility of testosterone and anabolic androgenic steroid abuse in suspected patients who present with serious cardiovascular or psychiatric adverse events.

Oedema with or without congestive heart failure, may be a serious complication in patients with pre-existing cardiac, renal or hepatic disease.

Gynaecomastia may develop and occasionally persists in patients being treated for hypogonadism.

Safety and efficacy of DEPO-TESTOSTERONE in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established. Age-related hypogonadism refers to men with serum testosterone concentrations below the normal range for no apparent reason other than age, and who experience signs and symptoms of aging that overlap with those of hypogonadism.

Androgen therapy should be used cautiously in healthy males with delayed puberty. The effect on bone maturation should be monitored by assessing bone age of the wrist and hand every 6 months. In children, androgen treatment may accelerate bone maturation without producing compensatory gain in linear growth. This adverse effect may result in compromised adult stature. The younger the child, the greater is the risk of compromising final mature height.

This drug has not been shown to be safe and effective for the enhancement of athletic performance. Because of the potential risk of serious adverse health effects, this drug should not be used for such purpose.

The preservative benzyl alcohol has been associated with serious adverse events, including the “gasping syndrome”, and death in paediatric patients. Although normal therapeutic doses of this product ordinarily deliver amounts of benzyl alcohol that are substantially lower than those reported in association with the “gasping syndrome”, the minimum amount of benzyl alcohol at which toxicity may occur is not known. The risk of benzyl alcohol toxicity depends on the quantity administered and the liver and kidneys’ capacity to detoxify the chemical. Premature and low-birth weight infants may be more likely to develop toxicity.

General

Patients with benign prostatic hypertrophy may develop acute urethral obstruction. Priapism or excessive sexual stimulation may develop. Oligospermia may occur after prolonged administration or excessive dosage. If any of these effects appear, the androgen should be stopped and if restarted, a lower dosage should be utilised.

Testosterone cypionate should not be used interchangeably with testosterone propionate because of differences in duration of action.

Testosterone cypionate is not for intravenous use.

Information for patients

Patients should be instructed to report any of the following: nausea, vomiting, changes in skin colour, ankle swelling, too frequent or persistent erections of the penis.

Paediatric population

Safety and effectiveness in paediatric patients below the age of 12 years have not been established.

Use in the elderly

Elderly patients treated with androgens may be at an increased risk of developing prostatic hypertrophy and prostatic carcinoma although conclusive evidence to support this concept is lacking (see section 5.3).

4.5 Interaction with other medicines and other forms of interaction

Androgens may increase sensitivity to oral anticoagulants. Dosage of the anticoagulant may require reduction in order to maintain satisfactory therapeutic hypoprothrombinaemia.

Concurrent administration of oxyphenbutazone and androgens may result in elevated serum levels of oxyphenbutazone.

In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, insulin requirements.

Effect on laboratory tests

Haemoglobin and haematocrit levels (to detect polycythaemia) should be checked periodically in patients receiving long-term androgen administration.

Serum cholesterol may increase during androgen therapy.

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.

4.6 Fertility, pregnancy and lactation

Fertility

In men, treatment with androgens can lead to fertility disorders by repressing sperm-formation (testosterone induced suppression of spermatogenesis).

See pregnancy section.

Pregnancy

The use of testosterone in women who are pregnant is contraindicated. (see section 4.3). Testosterone is teratogenic and may cause fetal harm. Testosterone is known to cause virilization of the female fetus when administered to pregnant women. A study has shown the degree of virilization of the genitalia of the female fetus following treatment with androgens is directly related to the amount of hormone given between the 8th and 13th weeks of pregnancy, which is the sensitive period.

Benzyl alcohol can cross the placenta (see section 4.4).

Lactation

DEPO-TESTOSTERONE is not recommended for use in nursing mothers.

4.7 Effects on ability to drive and use machines

The effects of DEPO-TESTOSTERONE on driving and using machines has not been studied. However, it is not expected to have an impact on the ability to drive and use machines.

4.8 Undesirable effects

The following adverse reactions in the male have occurred with some androgens:

Blood and lymphatic system disorders

Haematologic: Suppression of clotting factors II, V, VII and X, bleeding in patients on concomitant anticoagulant therapy, and polycythaemia.

Endocrine disorders

Endocrine and urogenital: Gynaecomastia and excessive frequency and duration of penile erections. Oligospermia may occur at high dosages.

Nervous system disorders

Increased or decreased libido, headache, anxiety, depression, and generalised paraesthesia.

Eye disorders

Rare cases of central serous chorioretinopathy (CSCR).

Cardiac disorders

Myocardial infarction, stroke.

Fluid and electrolyte disturbances

Retention of sodium, chloride, water, potassium, calcium and inorganic phosphates.

Vascular disorders

Venous thromboembolism, including deep vein thrombosis and pulmonary embolism.

Gastrointestinal disorders

Nausea, cholestatic jaundice, alterations in liver function tests, rarely hepatocellular neoplasms and peliosis hepatis (see section 4.4)

Skin and subcutaneous tissue disorders

Skin and appendages: Hirsutism, male pattern of baldness, seborrhoea, and acne.

Allergic

Hypersensitivity, including skin manifestations and anaphylactoid reactions.

Miscellaneous

Weight increase, inflammation and pain at the site of intra-muscular injection.

Drug abuse and dependence

Abuse

Drug abuse is intentional non-therapeutic use of a drug, even once, for its rewarding psychological and physiological effects. Abuse and misuse of testosterone are seen in male and female adults and adolescents. Testosterone, often in combination with other anabolic androgenic steroids (AAS), and not obtained by prescription through a pharmacy, may be abused by athletes and bodybuilders. There have been reports of misuse by men taking higher doses of legally obtained testosterone than prescribed and continuing testosterone despite adverse events or against medical advice.

Abuse-related adverse reactions

Serious adverse reactions have been reported in individuals who abuse anabolic androgenic steroids and include cardiac arrest, myocardial infarction, hypertrophic cardiomyopathy, congestive heart failure, cerebrovascular accident, hepatotoxicity, and serious psychiatric manifestations, including major depression, mania, paranoia, psychosis, delusions, hallucinations, hostility and aggression.

The following adverse reactions have also been reported in men: transient ischemic attacks, convulsions, hypomania, irritability, dyslipidemias, testicular atrophy, subfertility, and infertility.

The following additional adverse reactions have been reported in women: hirsutism, virilisation, deepening of voice, clitoral enlargement, breast atrophy, male-pattern baldness, and menstrual irregularities.

The following adverse reactions have been reported in male and female adolescents: premature closure of bony epiphyses with termination of growth, and precocious puberty.

Because these reactions are reported voluntarily from a population of uncertain size and may include abuse of other agents, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Dependence

Behaviours associated with addiction

Continued abuse of testosterone and other anabolic steroids, leading to addiction is characterised by the following behaviours:

- Taking greater dosages than prescribed
- Continued drug use despite medical and social problems due to drug use
- Spending significant time to obtain the drug when supplies of the drug are interrupted
- Giving a higher priority to drug use than other obligations
- Having difficulty in discontinuing the drug despite desires and attempts to do so
- Experiencing withdrawal symptoms upon abrupt discontinuation of use

Physical dependence is characterised by withdrawal symptoms after abrupt drug discontinuation or a significant dose reduction of a drug. Individuals taking supratherapeutic doses of testosterone may experience withdrawal symptoms lasting for weeks or months which include depressed mood, major depression, fatigue, craving, restlessness, irritability, anorexia, insomnia, decreased libido and hypogonadotropic hypogonadism.

Drug dependence in individuals using approved doses of testosterone for approved indications has not been documented.

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 professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

There have been no reports of acute overdosage with the androgens.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Endogenous androgens are responsible for normal growth and development of the male sex organs and the maintenance of secondary sex characteristics. These effects include growth and maturation of the prostate, seminal vesicles, penis, and scrotum; development of male hair distribution, such as beard, pubic, chest, and axillary hair; laryngeal enlargement, vocal cord thickening, and alterations in body musculature and fat distribution. Drugs in this class also

cause retention of nitrogen, sodium, potassium, and phosphorus, and decreased urinary excretion of calcium. Androgens have been reported to increase protein anabolism and decrease protein catabolism. Nitrogen balance is improved only when there is sufficient intake of calories and protein.

Androgens are responsible for the growth spurt of adolescence and the eventual termination on linear growth, brought about by fusion of the epiphyseal growth centres. In children, exogenous androgens accelerate linear growth rates, but may cause disproportionate advancement in bone maturation. Use over long periods may result in fusion of the epiphyseal growth centres and termination of the growth process. Androgens have been reported to stimulate production of red blood cells by enhancing production of erythropoietic stimulation factor.

During exogenous administration of androgens, endogenous testosterone release is inhibited through feedback inhibition of pituitary luteinizing hormone (LH). At large doses of exogenous androgens, spermatogenesis may also be suppressed through feedback inhibition of pituitary follicle stimulating hormone (FSH).

There is a lack of substantial evidence that androgens are effective in fractures, surgery, convalescence, and functional uterine bleeding.

5.2 Pharmacokinetic properties

Absorption

Testosterone esters are less polar than free testosterone. Testosterone esters in oil injected intramuscularly are absorbed slowly from the lipid phase; thus, testosterone cypionate can be given at intervals of two to four weeks.

Distribution

Testosterone in plasma is 98 percent bound to a specific testosterone-oestradiol binding globulin, and about 2 percent is free. Generally, the amount of this sex-hormone binding globulin in the plasma will determine the distribution of testosterone between free and bound forms, and the free testosterone concentration will determine its half-life.

Excretion

About 90 percent of a dose of testosterone is excreted in the urine as glucuronic and sulphuric acid conjugates of testosterone and its metabolites; about 6 percent of a dose is excreted in the faeces, mostly in the unconjugated form. Inactivation of testosterone occurs primarily in the liver. Testosterone is metabolised to various 17-keto steroids through two different pathways.

The half-life of testosterone cypionate when injected intra-muscularly is approximately eight days.

In many tissues the activity of testosterone appears to depend on reduction to dihydrotestosterone, which binds to cytosol receptor proteins. The steroid-receptor complex is transported to the nucleus where it initiates transcription events and cellular changes related to androgen action.

5.3 Preclinical safety data

Carcinogenicity

Animal Data: Testosterone has been tested by subcutaneous injection and implantation in mice and rats. The implant induced cervical-uterine tumours in mice, which metastasised in some cases. There is suggestive evidence that injection of testosterone into some strains of female mice increases their susceptibility to hepatoma. Testosterone is also known to increase the number of tumours and decrease the degree of differentiation of chemically-induced carcinomas of the liver in rats.

Human Data: There are rare reports of hepatocellular carcinoma in patients receiving long-term therapy with androgens in high doses. Withdrawal of the drugs did not lead to regression of the tumours in all cases.

Elderly patients treated with androgens may be at an increased risk of developing prostatic hypertrophy and prostatic carcinoma although conclusive evidence to support this concept is lacking.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Benzyl benzoate,
- Cottonseed oil,
- Benzyl alcohol.

6.2 Incompatibilities

None stated.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at 20°C - 25°C (see USP Controlled Room Temperature) and protect from light.

6.5 Nature and contents of container

DEPO-TESTOSTERONE is available in 10 mL multi-dose vials.

6.6 Special precautions for disposal and other handling

None stated.

7. MEDICINE SCHEDULE

Prescription Medicine.

8. SPONSOR

Pfizer New Zealand Limited
P O Box 3998
Auckland, New Zealand, 1140.

Toll Free Number: 0800 736 363.

9. DATE OF FIRST APPROVAL

31 December 1969

10. DATE OF REVISION OF THE TEXT

24 December 2024

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.6	Added information on testosterone induced suppression of spermatogenesis.
4.7	Added information regarding ability to drive and use machines.
4.8	Update to the ADR reporting URL.