AUSTRALIAN PRODUCT INFORMATION
PRIMOTESTON® DEPOT

1 NAME OF THE MEDICINE

Testosterone enantate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL Primoteston Depot contains 250 mg testosterone enantate (equivalent to approximately 180 mg testosterone).

Primoteston Depot contains: benzyl benzoate

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Solution for injection

Clear, yellowish oily solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Androgen replacement therapy for confirmed testosterone deficiency in males.

4.2 DOSE AND METHOD OF ADMINISTRATION

Like all oily solutions, Primoteston Depot must be injected intramuscularly, and extremely slowly (see 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

For the development and stimulation of still underdeveloped androgen-dependent target organs and for the initial treatment of deficiency symptoms: 1 prefilled syringe i.m. every 2-3 weeks.

To maintain an adequate androgenic effect: 1 prefilled syringe i.m. every 3-4 weeks. Shorter injection intervals may be necessary depending on the individual requirement for hormone, but longer intervals of up to 6 weeks are also sufficient in many cases.

Serum testosterone levels should be measured before the start of treatment and periodically during treatment as recommended by current treatment guidelines.

The product should be inspected visually for particles prior to administration. Only clear solution free from particles should be used.

4.3 CONTRAINDICATIONS

Prostatic carcinoma, mammary carcinoma in males.

Hypercalcaemia accompanying malignant tumours.

Previous or existing liver tumours.

Hypersensitivity to any of the ingredients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The general aim of androgen replacement therapy for confirmed testosterone deficiency in males is to keep serum testosterone levels within the reference range for the age group concerned. Over-replacement should be avoided.

Androgens are not indicated for enhancing muscular development in healthy individuals or for increasing physical ability.

Older patients treated with androgens may be at increased risk for the development of prostatic hyperplasia. Androgens can enhance the growth of an existing prostatic carcinoma. Therefore, carcinoma of the prostate has to be excluded before starting therapy with testosterone preparations.

As a precaution, regular examinations of the prostate are recommended. Haemoglobin and haematocrit should be checked periodically in patients on long-term androgen therapy to detect cases of polycythaemia (see 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)).

In general, the risk of bleeding from using intramuscular injections in patients with acquired or inherited bleeding disorders always has to be taken into account. Testosterone and its derivatives have been reported to increase the activity of coumarin-derived oral anticoagulants (see also 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

Testosterone should be used with caution in patients with thrombophilia, as there have been post-marketing studies and reports of thrombotic events in these patients during testosterone therapy.

Cases of benign and malignant liver tumours, which may lead to life-threatening intra-abdominal haemorrhage, have been observed after the use of hormonal substances such as the one contained in Primoteston Depot. The doctor must therefore be informed of the occurrence of unusual upper abdominal complaints which do not disappear spontaneously within a short time as it may then be necessary to withdraw the preparation. A hepatic tumour should be considered in the differential diagnosis when severe upper abdominal pain, liver enlargement or signs of intra-abdominal haemorrhage occur in men using Primoteston Depot.

Caution should be exercised in patients predisposed to oedema, e.g. in case of severe cardiac, hepatic, or renal insufficiency or ischaemic heart disease, as treatment with androgens may result in increased retention of sodium and water. In case of severe complications characterised by oedema with or without congestive heart failure, treatment must be stopped immediately (see 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)).

Testosterone may cause a rise in blood pressure and Primoteston Depot should be used with caution in men with hypertension.

Primoteston Depot must not be used in women, due to possible virilising effects.

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.

Testosterone abuse may result in dependence and withdrawal symptoms upon significant dose reduction or abrupt discontinuation of use.

Abuse of testosterone along with other anabolic androgenic steroids can lead to serious adverse reactions including: cardiovascular (with fatal outcomes in some cases), hepatic and/or psychiatric events.

Pre-existing sleep apnoea may be potentiated.

As with all oily solutions, Primoteston Depot must be injected intramuscularly and extremely slowly. Pulmonary microembolism of oily solutions can lead to signs and symptoms such as cough, dyspnoea and chest pain. There may be other signs and symptoms including vasovagal reactions

such as malaise, hyperhidrosis, 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 oxygen.

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.

Use in Hepatic Impairment

No formal studies have been performed in patients with liver impairment. The use of Primoteston Depot is contraindicated in men with past or present liver tumours.

Use in Renal Impairment

See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Use in the Elderly

Limited data do not suggest the need for a dosage adjustment in elderly patients.

Paediatric Use

Primoteston Depot is not indicated for use in children and adolescents.

In addition to causing masculisation in children, testosterone can cause accelerated growth, bone maturation and premature epiphyseal closure, thereby reducing adult height.

Effects on Laboratory Tests

See section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Drugs that affect testosterone

Barbiturates and Other Enzyme Inducers

Interactions can occur with drugs that induce microsomal enzymes which can result in increased clearance of testosterone.

Effects of androgens on other drugs

Oxyphenbutazone
Increased oxyphenbutazone serum levels have been reported.

Oral Anticoagulants

Testosterone and its derivatives have been reported to increase the activity of coumarin-derived oral anticoagulants, possibly requiring dose adjustment. Independently of this finding, the risk of

bleeding from using intramuscular injections in patients with acquired or inherited bleeding disorders always has to be taken into account as a general rule.

Hypoglycaemic agents

Androgens may enhance the blood sugar reducing effects of hypoglycaemic agents including oral antidiabetic drugs and insulin. Therefore, the dosage of the hypoglycaemic agent may need to be lowered.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

See Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS).

Use in Pregnancy

Primoteston Depot is intended for use in men only. Primoteston Depot is not indicated for use in pregnant women.

Use in Lactation

Primoteston Depot is intended for use in men only. Primoteston Depot is not indicated for use in breast feeding women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not known.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The most commonly reported adverse reactions with Primoteston Depot are injection site pain, injection site erythema, and cough and/or dyspnoea during or immediately after the injection.

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. Cases suspected by the company or the reporter representing oily pulmonary microembolism have been reported from postmarketing experience (see section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

High-dosed or long-term administration of testosterone, including Primoteston Depot, increases the tendency to water retention and oedema.

Spermatogenesis is reversibly interrupted or reduced by long-term and high-dosed treatment with Primoteston Depot.

If, in individual cases, frequent or persistent, painful erections (priapism) occur, the dose should be reduced or the treatment discontinued in order to avoid injury to the penis.

Various skin reactions including injection site reactions (injection site pain, injection site erythema, injection site induration, injection site swelling, injection site inflammation) may occur.

Other events reported with Primoteston Depot include benign and malignant liver tumours, polycythaemia, hypersensitivity reactions, libido increased, libido decreased, depression, insomnia, restlessness, aggression, irritability, headache, dizziness, hot flush, hypertension, cough, dyspnoea,

dysphonia, diarrhoea, nausea, jaundice, acne, alopecia, rash, urticaria, pruritus, erythema, hyperhidrosis, arthralgia, pain in extremity, myalgia, various kinds of injection site reactions, fatigue, asthenia, Prostatic Specific Antigen (PSA) increased, weight increased, liver function test abnormal, haematocrit increased, red cell blood count increased, haemoglobin increased, blood pressure increased, blood testosterone increased, gynaecomastia, testicular pain and post marketing reports of venous thromboembolism.

Hostility, nervousness and increased hair growth have been reported under treatment with testosterone-containing preparations.

Regarding adverse effects associated with the use of androgens, please also refer to Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

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

Acute toxicity data show that testosterone enantate, the ester contained in Primoteston Depot, can be classified as non-toxic following single intake. Even following single administration of a multiple of the dose required for therapy, no toxicity risk is to be expected.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

Primoteston Depot contains a derivative of the natural male sex hormone testosterone as its active ingredient. The general aim of androgen replacement therapy for confirmed testosterone deficiency in males is to keep serum testosterone levels within the reference range for the age group concerned.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

The depot effect of testosterone enantate permits long intervals between injections. This ester not only has a long-lasting, but also a very intensive androgenic effect. The duration of action of 1 mL Primoteston Depot is approximately 2-4 weeks depending on the initial hormonal status.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Benzyl benzoate, castor oil.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine Please see Section 4.5 – INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Primoteston Depot should be stored below 25 °C. Keep out of reach of children. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

1 mL prefilled syringe containing 250 mg testosterone enantate.

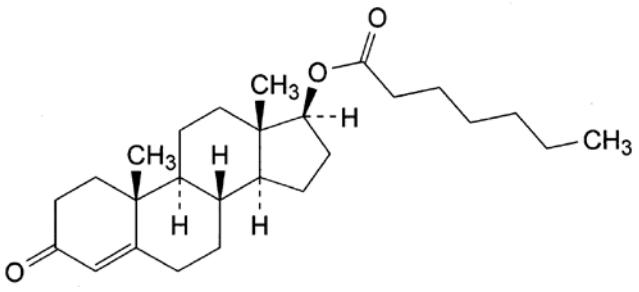
Pack sizes of 1 x 1 mL and 3 x 1 mL pre-filled syringes. Not all pack sizes may be available.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical Structure



CAS Number

315-37-7

Testosterone enantate is designated chemically as 17 beta-heptanoyloxy-4-androstene-3-one.

The empirical formula of testosterone enantate is $C_{26}H_{40}O_3$ and its molecular weight is 400.66 g/mol.

7 MEDICINE SCHEDULE (POISONS STANDARD)

PRESCRIPTION ONLY MEDICINE

8 SPONSOR

Bayer Australia Ltd
ABN 22 000 138 714
875 Pacific Highway
Pymble NSW 2073
Australia

9 DATE OF FIRST APPROVAL

19 August 1991

10 DATE OF REVISION

13 March 2025

Summary Table of Changes

Section Changed	Summary of New Information
4.5	Update on interaction with hypoglycaemic agents.
4.8	Expansion of class effects of testosterone.
All	Editorial changes.

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