Package leaflet: Information for the patient
Testoviron Depot 250
250 mg/1 mL solution for injection
testosterone enantate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Testoviron Depot 250 is and what it is used for
Testoviron Depot 250 contains a derivative of testosterone, the male sex hormone (androgen) that occurs naturally in the human body.

Testoviron Depot 250 is used:
Testoviron Depot 250 is used in adult men for testosterone replacement to treat various health problems caused by a lack of testosterone (male hypogonadism). This should be confirmed by two separate blood testosterone measurements and also include clinical symptoms such as:
- Impotence
- Infertility
- Low sex drive
- Tiredness
- Depressive moods
- Bone loss caused by low hormone levels

- Testoviron Depot 250 may be used only when testosterone deficiency has been confirmed clinically and by laboratory tests and when other possible underlying causes of the symptoms have been ruled out (see also section 2. “Take special care with Testoviron Depot 250”).
- <u>for treating delayed puberty in boys.</u>
  Puberty induction with Testoviron Depot 250 should be performed only by an experienced doctor specialising in paediatric and adolescent medicine in cooperation with a paediatric endocrinologist. The dosing schedule is determined by the underlying clinical picture and should be guided by the relevant recommendations by professional associations.

2. What you need to know before you use Testoviron Depot 250
Do not use Testoviron Depot 250:
- if you are allergic to testosterone enantate or any of the other ingredients of this medicine (listed in section 6),
- in the presence of prostate or male breast tumours whose growth is stimulated by male sex hormones (androgens),

- in patients with a past or present history of liver tumours,
- in patients with high blood calcium levels in the presence of cancerous (malignant) tumours,
- in newborn infants,
- in young children,
- in women.

Warnings and precautions
Talk to your doctor or pharmacist before you are administered Testoviron Depot 250, or if you have suffered from any of the following conditions:
- epilepsy
- heart, kidney or liver disease
- migraine
- temporary pauses in your breathing while you are asleep (sleep apnoea), as these may get worse
- cancer, as calcium levels in your blood may have to be regularly checked
- high blood pressure or if you are being treated for high blood pressure, as testosterone can lead to a rise in blood pressure.
- blood clotting problems
  - bleeding disorders (i.e. haemophilia)
  - thrombophilia (a blood clotting disorder that increases the risk of blood clots forming in the blood vessels).
  - Factors that increase your risk for blood clots in a vein: previous blood clots in a vein; smoking; obesity; cancer; immobility; if one of your immediate family has had a blood clot in the leg, lung or other organ at a young age (e.g. below the age of about 50); or as you get older.

How to recognise a blood clot: painful swelling of one leg or sudden change in colour of the skin, e.g. turning pale, red or blue, sudden breathlessness, sudden unexplained cough which may bring up blood; or sudden chest pain, severe light headedness or dizziness, severe pain in your stomach, sudden loss of vision. Seek urgent medical attention if you experience one of these symptoms.

Take special care with Testoviron Depot 250
Male hormones may enhance the growth of prostate cancer and prostate enlargement (benign prostatic hyperplasia). Before administering Testoviron Depot 250, your doctor should check you for the presence of prostate cancer. If you are elderly, there may be an increased risk of developing prostate enlargement when androgens such as Testoviron Depot 250 are used. There is no clear evidence that androgens actually cause prostate cancer, but androgens can enhance the growth of existing prostate cancer.
For the treatment of reduced testicular function, Testoviron Depot 250 may be used only in confirmed (hyper- or hypogonadotropic) dysfunction and after prior exclusion of other underlying causes of the symptoms. Testosterone deficiency must be clearly shown to be present by clinical signs, such as regression of secondary sex characteristics, changes in body composition, rapid onset of fatigue, reduced sex drive and erection problems (erectile dysfunction), and must be confirmed by two independent measurements of blood testosterone levels.
Testoviron Depot 250 should be injected into muscle only. Based on experience, the brief reactions that occur in rare cases during or immediately after injection of oily solutions (tickly cough, coughing fits, shortness of breath) can be avoided by injecting the solution very slowly.

<u>Medical examination/check-ups</u>
A thorough medical examination is required before starting treatment with Testoviron Depot 250. Prostate cancer must be ruled out at this time. During treatment, careful and regular medical examinations of the prostate and breast must be performed in accordance with currently established examination/testing methods (at least once a year, or twice a year in the elderly and patients at risk).
In addition to regular checks on blood testosterone levels, the following laboratory parameters should also be monitored during treatment with Testoviron Depot 250: haemoglobin (red blood pigment) and haematocrit (total volume of red blood cells), as well as liver enzymes. Testosterone measurements should always be performed in the same laboratory.

Tumours

Androgens such as testosterone can speed up the progression of pre-existing prostate cancer or non-cancerous prostate enlargement (benign prostatic hyperplasia).

Cancer patients with bone metastases may have high calcium levels in the blood and urine. Caution should therefore be exercised during treatment with Testoviron Depot 250; see also "Do not use Testoviron Depot 250". For this reason, it is recommended that calcium levels be regularly monitored in these patients during treatment with Testoviron Depot 250.

Cases of both benign (non-cancerous) and malignant (cancerous) liver tumours have been observed after the use of testosterone depot preparations. In isolated cases, these tumours may cause internal bleeding, which might be life-threatening. Tell your doctor if you experience unusual pain in your upper abdomen that does not stop within a short period of time.

Other illnesses

If you are suffering from severe heart, liver or kidney disease treatment with Testoviron-Depot 250 may cause serious complications in the form of water retention in your body sometimes accompanied by (congestive) heart failure. In such cases, treatment must be stopped immediately.

The following blood checks should be carried out by your doctor before and during treatment: testosterone blood level, full blood count.

Tell your doctor if you have high blood pressure or if you are treated for high blood pressure, as testosterone may cause a rise in blood pressure.

Caution should be exercised in patients predisposed to fluid accumulation in the tissues (oedema), as treatment with androgens such as testosterone can increase sodium retention (see also section 4. "Possible side effects").

The restrictions on the use of intramuscular injections that apply to patients with acquired or congenital blood clotting disorders must be observed at all times.

Testoviron Depot 250 should be used only with caution in patients with epilepsy or migraine, as these disorders may worsen.

Testosterone and its derivatives can increase insulin sensitivity, thereby reducing the doses of insulin or other antidiabetic medications needed for treatment. If you are being treated with insulin or other antidiabetic agents, your doctor will therefore monitor your blood sugar level closely, especially at the start and end of treatment with Testoviron Depot 250.

Pre-existing sleep apnoea (brief suspension of breathing during sleep) may get worse.

Certain signs, such as irritability, nervousness, weight gain, persistent or excessively frequent erections, may indicate that the effect of Testoviron Depot 250 is too strong. In this case, please talk to your doctor.

Testoviron Depot 250 should no longer be used if symptoms of too strong an effect persist or return during treatment at the recommended dosage.

Testoviron Depot 250 is not suitable for the treatment of male sterility.

Effect of Testoviron Depot 250 on thyroid laboratory tests

Androgens can affect the results of certain laboratory tests (thyroid test). If you are scheduled for such a test, tell the doctor in charge that you are receiving testosterone treatment. However, the concentrations of the hormones investigated in the above tests and responsible for the hormone effect remain unchanged. This means that symptoms such as those associated with an underactive thyroid are unlikely.

Special groups

Elderly individuals (65 years and older)

If you are over 65 years of age, your doctor will generally not adjust (increase) the dose.

If your liver is no longer working properly

No formal studies have been conducted in patients with impaired liver function. Testosterone treatment must therefore proceed with caution if your liver is no longer working properly. If you have or have ever had a liver tumour, you will not be prescribed Testoviron Depot 250 (see "Do not use Testoviron Depot 250").

If your kidneys are no longer working properly

No formal studies have been conducted in patients with impaired kidney function. Testosterone treatment must therefore proceed with caution if your kidneys are no longer working properly.

Children and adolescents
The safety and efficacy of Testoviron Depot 250 in children aged up to 12 years have not been established.
In boys, Testoviron Depot 250 may be used only after careful consideration of the benefit/risk balance.
Testosterone may speed up bone maturation as a result of conversion to oestrogen, a female sex hormone, thereby reducing adult height. In longer-term or higher-dose administration, radiological bone age measurements should therefore be conducted at regular intervals.

Effects when misused for doping purposes
The use of Testoviron Depot 250 can lead to positive results in doping tests.
Androgens such as those contained in Testoviron Depot 250 are not suitable for enhancing muscular development in healthy individuals or for boosting physical performance.
It is impossible to predict the health consequences of using Testoviron Depot 250 as a doping agent; serious health risks cannot be ruled out (see section 4. "Possible side effects").

Drug abuse and dependence
Always take this medicine exactly as your doctor or pharmacist has told you.
Abuse of testosterone, especially if you take too much of this medicine alone or with other anabolic androgenic steroids, can cause serious health problems to your heart and blood vessels (that can lead to death), mental health and/or the liver.
Individuals who have abused testosterone may become dependent and may experience withdrawal symptoms when the dosage changes significantly or is stopped immediately. You should not abuse this medicine alone or with other anabolic androgenic steroids because it carries serious health risks (see "Possible side effects").

Other medicines and Testoviron Depot 250
Tell your doctor or pharmacist if you are taking/using, have recently taken/used or might take/use any other medicines.

The effect of the following active substances or groups of medicines can be influenced if treatment with Testoviron Depot 250 is combined with:
- medicines used to treat nervousness and sleep disorders (barbiturates and other enzyme inducers)
- medicines used to treat pain or inflammation (oxyphenbutazone)
- Testosterone can enhance the effect of medicines that prevent the blood from clotting (oral anticoagulants). In patients receiving treatment with oral anticoagulants, close monitoring of the clotting status (more frequent checks on prothrombin time and more frequent INR tests) is therefore required, especially at the start and end of treatment with Testoviron Depot 250.
- medicines used to treat diabetes. It may be necessary to adjust the dose of medicines used to regulate blood glucose levels, because testosterone, like other insulins, may enhance the effect of insulin.
- ACTH (a certain pituitary hormone) or corticosteroids (adrenal cortex hormones) Co-administration of testosterone and ACTH (adrenocorticotropic hormone - a certain pituitary hormone) or corticosteroids (adrenal cortex hormones) can increase the risk of oedema formation (accumulation of fluid in the tissues). For this reason, these active substances may be used only with caution, especially in patients with heart or liver disease or in patients prone to oedema.

Please make sure you tell your doctor if you have a bleeding disorder, because it is important for your doctor to know this before deciding to inject Testoviron.
Androgens can affect the results of thyroid function tests (see also section 2. "Take special care with Testoviron Depot 250").

Pregnancy, breast-feeding and fertility
Testoviron Depot 250 is not intended for use in women and must not be used in pregnant or breast feeding women.
Testosterone treatment can temporarily suppress sperm production, thereby impairing fertility.

Driving and using machines
Testoviron Depot 250 has no or negligible influence on the ability to drive and use machines.

Testoviron Depot 250 contains benzyl benzoate
This medicine contains 342.0 mg of benzyl benzoate in each 1 mL ampoule/pre-filled syringe.

3. How to use Testoviron Depot 250

Always use this medicine exactly as your doctor or pharmacist has told you. Use of Testoviron Depot 250 is performed or arranged by a doctor. Check with your doctor if you are not quite sure about its use.
For intramuscular injection. Your doctor will inject Testoviron Depot 250 into the buttock muscle. The injection must be given very slowly to reduce the risk of physical reactions (see section 4). The intramuscular injection must be given immediately after the ampoule/pre-filled syringe is opened.
Your doctor will measure the testosterone level in your blood before the start of treatment, occasionally during treatment and at the end of the injection interval. If the testosterone level is too low, your doctor may decide to give you more frequent injections. If your testosterone level is too high, your doctor may decide to give you injections less often. Do not miss your injection appointments. Otherwise, your optimum testosterone level cannot be maintained.
If you have the impression that the effect of Testoviron Depot 250 is too strong or too weak, also talk to your doctor.

The recommended dose is:
<u>For reduced male testicular function</u>
For long-term replacement in reduced testicular function, 1 mL Testoviron Depot 250 (equivalent to 250 mg testosterone enantate) is recommended every 2 to 3 weeks as a guide. The individual dosage can be modified, depending on the clinical picture and the serum testosterone levels measured.
In rare cases, persistent and painful erections of the penis may occur during treatment. In such cases, the dose must be reduced or the therapy temporarily discontinued.

<u>For treatment of delayed puberty in boys</u>
Treatment of delayed puberty in boys should be performed only by an experienced specialist. The recommended dosage is guided by the cause of the delayed puberty.

a) Disorders due to reduced testicular function (hypogonadotropic hypogonadism, complete hypergonadotropic hypogonadism):
A gradual increase in the testosterone dose is recommended, starting with 50 mg every four weeks up to 250 mg every three weeks over a period of three years:
Months 1 - 6: 50 mg testosterone enantate every 4 weeks IM
Months 7 - 12: 100 mg testosterone enantate every 4 weeks IM
Year 2: 250 mg testosterone enantate every 4 weeks IM
Year 3: 250 mg testosterone enantate every 3 weeks IM

b) Partial impairment of testicular function (partial hypergonadotropic hypogonadism (e.g. Klinefelter syndrome):
Start treatment with 100 – 250 mg testosterone enantate IM every 4 weeks in cases where there is a reduction in the morning blood testosterone level below the age norm at pubertal age.

c) Physical/biological delay in development:
Administration of 100 mg testosterone enantate in months 1 - 6 every 4 weeks IM, break in treatment from months 7 - 12. Re-examination/check-ups at the end of month 12.

Instructions for handling
The solution for injection must be visually inspected prior to use. Only clear, particle-free solutions must be used.

Testoviron Depot 250 is intended for single use. Any unused remaining portions must be discarded.
In the absence of compatibility studies, Testoviron Depot 250 must not be mixed with other medicines.

If more than the recommended dose of Testoviron Depot 250 has been administered,
no special therapeutic measures are required other than discontinuing the medicine.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Pain and itching (redness) at the injection site, as well as cough and/or shortness of breath, have been most frequently observed during or immediately after the injection.
The side effects listed in the following table have been reported.

System organ class	**Side effect**		
	Common (may affect up to 1 in 10 patients treated)	**Rare (may affect up to 1 in 1,000 patients treated)**	**Unknown (Frequency cannot be estimated from the available data)**
Neoplasms benign and malignant (incl. cysts and polyps)			Benign (non-cancerous) and malignant (cancerous) liver tumours
Blood and lymphatic system disorders	Increase in red haematocrit, increase in red blood cell count, and increase in haemoglobin		Significant increase in red blood cells (polycythaemia, erythrocytosis)
Immune system disorders			Hypersensitivity reactions
Metabolism and nutrition disorders			Weight gain, electrolyte changes (retention of sodium, chloride, potassium, calcium and inorganic phosphate and water) at high doses and/or during long-term therapy
Nervous system disorders			Nervousness, aggressiveness, depression, headache and fatigue
Respiratory, thoracic and mediastinal disorders			Brief suspension of breathing during sleep (sleep apnoea), upper airway infections
Gastrointestinal disorders			Constipation, diarrhoea, bloating, abdominal pain
Hepatobiliary disorders			Abnormal liver function tests, yellowing of the skin and eyes (jaundice)
Skin and subcutaneous tissue disorders			Various skin reactions (including acne, redness, nettle rash, itching and hair loss)
Musculoskeletal and connective tissue disorders			Muscle cramps

Reproductive system and breast disorders			Altered sex drive (libido), increased erection frequency; high-dose use of testosterone preparations generally causes a reversible interruption or reduction in sperm production and hence a decrease in testicular size; in rare cases, testosterone replacement therapy in reduced testicular function (hypogonadism) can cause painful and persistent erection (priapism), prostate abnormalities, prostate cancer* as well as urinary outflow obstruction. Breast pain, male breast enlargement (gynaecomastia)
General disorders and administration site conditions			Various types of reaction at the injection site, including pain, itching, skin hardening, swelling and inflammation
Investigations			Increase in prostate-specific antigen
Injury, poisoning and procedural complications		Pulmonary microembolism caused by oily solutions	

* *Data are inconclusive as regards the risk of developing prostate cancer in association with testosterone treatment.*

Testoviron Depot 250, an oily liquid, can get into the lungs (pulmonary microembolism caused by oily solutions), which, in rare cases, can lead to signs and symptoms such as coughing, shortness of breath, generally feeling unwell, intense sweating, chest pain, dizziness, “pins and needles” or fainting.
These reactions can occur during or immediately after the injection and are reversible.
Hostility/aggression has been reported to occur, as well as increased growth of body and facial hair, on treatment with testosterone-containing medicines.

Corrective measures
If you experience side effects after the use of Testoviron Depot 250, please tell your doctor, who will decide on any corrective measures to be taken.
Side effects for which you may need to consult a doctor at once, or which require discontinuation of treatment, are listed in section 2. “Take special care with Testoviron Depot 250”.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Testoviron Depot 250

Keep this medicine out of the sight and reach of children.
Keep the pre-filled syringes/ampoules in the folding box in order to protect from light.
Do not use this medicine after the expiry date which is stated on the pre-filled syringe/ampoule label and folding box. The expiry date refers to the last day of that month. The solution for injection must be visually inspected prior to use. Testoviron Depot 250 may be used only if the solution for injection is clear and free from particles.
Store below 30°C.

6. Contents of the pack and other information

What Testoviron Depot 250 contains

- The active substance is: testosterone enantate
- The other ingredients are: benzyl benzoate and castor oil refined.

1 ampoule or 1 pre-filled syringe with 1 mL solution for injection contains 250 mg testosterone enantate, equivalent to 180.0 mg testosterone.

What Testoviron Depot 250 looks like and contents of the pack

Testoviron Depot 250 is a clear, yellowish, oily solution.
Testoviron Depot 250 is available in packs of 1x1 mL ampoule and 3x1 mL ampoules.
It is also available in packs of 1 x 1 mL pre filled syringe and 3 x 1 mL pre filled syringes.
Not all pack sizes may be marketed

Manufacturer

Bayer AG
Müllerstrasse 178
13353 Berlin, Germany

Marketing Authorisation Holder

Bayer AG
Kaiser-Wilhelm-Allee 1
51373 Leverkusen, Germany

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This is a medicament

- A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists

The following information is intended for medical or healthcare professionals only:

Further information

More detailed information on the product, as required by the doctor, is contained in special publications.
Like all oily solutions, Testoviron Depot 250 must be injected precisely and very slowly via the intramuscular route. A pulmonary microembolism with oily solutions can lead to symptoms such as cough, dyspnoea and chest pain. Other symptoms may occur, including vasovagal reactions such as malaise, hyperhidrosis, dizziness, paraesthesia or syncope. These reactions can occur during or immediately after the injection and are reversible. Treatment is usually carried out with supportive measures, e.g. with additional oxygen administration.
During testosterone treatment, careful and regular check-ups of the prostate and breast must be performed in accordance with currently established examination/testing methods (digital rectal examination and measurement of serum PSA) at least once yearly and twice yearly in elderly patients and in patients at risk (with certain clinical or familial risk factors).
In addition to laboratory tests to determine testosterone concentrations, the following laboratory parameters should also be regularly checked in patients before and during long-term androgen therapy: haemoglobin, haematocrit and liver enzymes.