HCP-MEPPO
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TESTOVIRON®-DEPOT 250 mg / 1 ml

Bayer Middle East

injection solution
Active ingredient: Testosterone enanthate

1. WHAT IS TESTOVIRON-DEPOT AND WHAT IS IT USED FOR?

Testoviron-Depot contains a derivative of testosterone, the male sexual hormone (androgen) that occurs naturally in the human organism.

Testoviron-Depot is administered

- as a testosterone substitution treatment in the presence of male hypogonadism (diminished testicular function) Testoviron-Depot may only be administered in cases where the testosterone deficiency has been confirmed in clinical and medical laboratory tests and where other possible causes of the symptoms and signs have been excluded (cf. also Section 2. «Special caution is required with the administration of Testoviron-Depot»).
- To induce puberty among boys with delayed puberty.

2. WHAT DO YOU NEED TO BE AWARE OF BEFORE ADMINISTRATION OF TESTOVIRON-DEPOT?

Testoviron-Depot may not be administered:

- if you oversensitive (allergic) to testosterone enanthate or one of the excipients of Testoviron-Depot,
- in cases of tumours of the prostate or of the male mammary gland if their growth would be stimulated by male sexual hormones (androgens),
- in cases of previous or existing liver tumours,
- in cases of nephrotic syndrome,
- to new-borns and small children,
- to women.

Special caution is required with the administration of Testoviron-Depot

Testoviron-Depot should only be administered with caution to cancer patients who are at risk for elevated calcium levels in the blood (hypercalcinaemia) because of bone metastases and for whom, as a result of this, more calcium is excreted with the urine (hypercalciuria). In such cases it is recommended that the calcium level be monitored at regular intervals.

The emergence of benign and malignant liver tumours among patients who receive testosterone substitution treatment has been observed in rare cases.

Patients who suffer from a severe cardiac, liver or renal function disorder or from heart disease caused by reduced perfusion (ischemic heart disease) may experience serious complications resulting from the treatment with testosterone caused by the development of oedemas (water retention in tissue) which may be accompanied by backflow of the blood (congestive cardiac insufficiency), with or without cardiac insufficiency. Immediate termination of the treatment is required in such cases.

No investigations have been carried out to date regarding the efficacy and harmlessness of Testoviron-Depot for patients with limited kidney or liver function. Testosterone substitution treatment for these patients should therefore only be performed with great caution.

The restrictions governing the use of intramuscular injections for patients with acquired or congenital coagulation disorders must be observed at all times. Testoviron-Depot should be administered only with great caution to patients with epilepsy or migraine, because these illnesses could worsen as a result.

Patients who achieve normal testosterone levels in the blood after the testosterone substitution treatment may experience an improved sensitivity to insulin.

Certain signs may indicate an overly strong effect of Testoviron-Depot, including among them irritability, nervousness, weight gain, excessively long-lasting or frequent erections.

Consult your physician if this is the case.

Testoviron-Depot should be discontinued if the complaints persist as a result of an overly strong drug

action or reappear during treatment with the recommended dosage.

Pre-existing sleep apnoea (occurrence of brief respiratory arrest during sleep) could become more severe.

Testoviron-Depot is not suitable for treating male sterility.

In the presence of male hypogonadism (diminished testicular function)

Testoviron-Depot may only be used to treat confirmed cases of diminished testicular function (hypergonadotropic or hypogonadotropic hypogonadism), and then only after previous exclusion of other causes which could be the reason for the symptoms and signs. The testosterone deficiency must be unambiguously confirmed by clinical indications such as degeneration of the secondary sex characteristics, changes in physical constitution, rapid fatigue, reduction of libido and erectile dysfunction and verified by two determinations of the concentration of testosterone in the blood that are independent of one another.

Medical examination/check-up examinations

A thorough medical examination is required before beginning treatment with Testoviron- Depot. The possibility of prostate cancer must be excluded at this time. Careful and regular medical examinations of the prostate and the breast in accordance with currently recognised examination methods must be performed during the treatment (at least once per year as well as twice per year for older patients and risk patients).

In addition to the regular verification of testosterone concentrations in the blood, the following laboratory parameters should also be monitored during treatment with Testoviron- Depot: Haemoglobin (red haemoglobin) and haematocrit (total volume of red blood corpuscles), as well as liver function tests. Determinations of testosterone should always be performed in the same laboratory.

Tumours

Androgens such as testosterone can accelerate the progress of existing prostate cancers that are already in their early stages or of benign enlargements of the prostate (benign prostatic hyperplasia).

Children and adolescents

As a result of its conversion to oestrogen, a female sexual hormone, testosterone can accelerate bone maturation, thus resulting in a reduction of the final size of the bones.

Radiological bone age determinations should therefore be performed at regular intervals in cases of prolonged or higher-dosage administration.

Older people

It should be taken into account with older patients (over 65 years of age) that serum testosterone levels fall off in terms of physiology with increasing age.

Effects in the event of misuse for doping purposes

The use of Testoviron-Depot can lead to positive doping test results.

Androgens, such as those contained in Testoviron-Depot, are not suitable for promoting muscle development or physical performance capability in healthy individuals.

The effects on one's health caused by the use of Testoviron-Depot as a doping agent are unpredictable, the possibility of grave health hazards cannot be excluded (see Section 4. "What are the potential side effects?").

When using Testoviron-Depot with other drugs:

Please inform your physician or your pharmacist if you are taking or applying other medicinal products and/or have taken or applied them recently, even it they were ones that did not require a prescription.

The action of the pharmacons and/or preparations groups listed below can be influenced by simultaneous treatment with Testoviron-Depot.

<u>Oral anticoagulants (blood-clotting drugs)</u>

Testosterone and its derivatives can enhance the action of drugs used for inhibiting blood clotting (oral anticoagulants). Tight monitoring of clotting status (more frequent verification of prothrombin time

and more frequent INR determinations) is therefore required for patients undergoing treatment with oral anticoagulants, particularly at the beginning and end of treatment with Testoviron-Depot.

Other interactions

The simultaneous administration of testosterone and ACTH (adrenocorticotropic hormone

- a particular pituitary hormone) or corticosteroids (adrenal cortex hormones) can increase the risk of the formation of oedemas (accumulation of fluid in the tissue). For this reason, these active ingredients may only with great caution be administered simultaneously, particularly to patients with cardiac or liver disorders or to patients who have a tendency to develop oedemas.

Influence of Testoviron-Depot on laboratory parameters of the thyroid

Androgens can influence the investigation results of thyroid function tests. If such tests are to be performed on you, be sure to inform your physician that you are receiving a testosterone substitution treatment.

However, in view of the fact that the concentrations of the effective thyroid hormones are not altered by Testoviron-Depot, you need not fear that you will experience any symptoms, e.g. those connected with hyperthyroidism.

Driving ability and the operation of machinery:
Testoviron-Depot has no effect on driving skills or on the ability to operate machinery.

3. HOW SHOULD TESTOVIRON-DEPOT BE ADMINISTERED?

Testoviron-Depot is generally administered by a physician. Please consult your physician if your are not entirely sure of the correct administration procedure.

This drug should be administered in accordance with the following dosage recommendations:

Adult

1 ampoule or 1 ready-to-use syringe is administered by intramuscular injection at intervals of 2-3 weeks for initial treatment of deficits with respect to male hypogonadism.

The interval between injections should remain within the recommended range of 2-3 weeks in order to maintain a sufficient androgen effect in adult men. Shorter injection intervals may be necessary, depending on individual hormone requirements.

Boys

In order to induce puberty among boys with delayed adolescence, a dosage of 50 mg to a maximum of 100 mg of testosterone enanthate is administered every 4 weeks for 4-6 months, followed by a treatment intermission of 3 months. The course of treatment is repeated if necessary. (Note: If a monthly dosage of 100 mg is to be administered, then it is preferable to administer 50 mg every two weeks.)

Type of application:
Injection solution.

Testoviron-Depot must be administered exclusively by intramuscular injection. The injection solution is to be injected very slowly deep into the muscle of the buttock while observing at the same time the usual precautionary measures for intramuscular injections. Special care must be taken to ensure that the injection is not made into a blood vessel (intravascular injection). Experience has shown that the temporary reactions (urge to cough, fits of coughing, difficult breathing) that occur in rare cases either during or immediately after injections of oily solutions can be avoided by very slow injection.

Please consult your physician or pharmacist if you have the impression that the effect of Testoviron-Depot is either too strong or too weak.

If you are administered more than the recommended dose of Testoviron-Depot, then no special therapeutic measures are required other than the discontinuation of the drug.
If you have any further questions regarding the use of this drug, please consult your doctor or pharmacist.

4. WHAT ARE THE POTENTIAL SIDE EFFECTS?

As is the case with all medicinal products, Testoviron-Depot could cause side effects, although these need not be experienced by every patient.
The following categories are used as a basis for the

information provided regarding the frequency of side effects:

Very common:	**Experienced by more than 1 treated patient out of 10**
Common:	**1 to 10 treated patients out of 100**
Occasional:	**1 to 10 treated patients out of 1000**
Rare:	**1 to 10 treated patients out of 10,000**
Very rare:	**Experienced by fewer than 1 treated patient out of 10,000**
Unknown:	**Frequency cannot be estimated on the basis of available data**

Possible side effects:

Pain at the site of the injection was observed very frequently. The following side effects caused by drugs containing testosterone have been reported in medical publications:

System organ class	Side effects
Diseases of the blood and of the lymphatic system	A considerable increase in red blood corpuscle counts in the blood (polycythaemia, erythrocytosis) in rare cases
Metabolic and nutritional disorders	Weight gain, changes in electrolyte values (retention of sodium, chloride, potassium, calcium and inorganic phosphate and water) with high dosage and/or long-term treatment
Musculoskeletal system	Muscle cramps
Nervous system	Nervousness, aggressiveness, Depression
Respiratory tract	Brief respiratory arrest during sleep (sleep apnoea)
Diseases of the liver and gall bladder	Jaundice and abnormal liver function tests in very rare cases
Skin and skin appendages	A variety of different skin reactions could appear, including acne, increased sebum production (seborrhoea) and hair loss
Diseases of the reproductive organs and of the mammary gland	Change in sexual desire (libido), increased erection frequency; highdosage administration of testosterone preparations generally causes a reversible interruption or reduction in sperm formation and a resulting diminishment of testicle size; testosterone substitution treatment for testicular subfunction (hypogonadism) can in rare cases cause painful continuous erections (priapism), malformations of the prostate, prostate cancer* and urinary obstruction. Breast pain, enlargement of the mammary gland (gynacomastia)
General illnesses and complaints at the administration site	High dosage treatment or long-term treatment with testosterone sometimes lead to cumulative occurrence of water retention and water build-up in the tissue (oedemas); Oversensitivity reactions could occur Pain and haematomas at the injection site

* The data is unclear with respect to the risk of the emergence of prostate cancer in connection with testosterone treatment.

Countermeasures

If you experience side effects following the administration of Testoviron-Depot, then please inform your attending physician, who will then decide about countermeasures that may possibly need to be initiated.

Side effects which may make it necessary for you to consult a physician immediately or which make termination of treatment imperative are listed in Section 2. “Special caution is required with the administration of Testoviron-Depot”.

Please inform your doctor or pharmacist if one of the side effects listed is considerably inhibiting for you or if you notice other side effects that are not specified in these Instructions for Use.

5. HOW SHOULD TESTOVIRON-DEPOT BE STORED?

Keep drugs out of the reach of children.

Do not use the drug after the expiration date stated on the ready-to-use syringe or the ampoule label and on the collapsible cardboard box. The expiration date refers to the last day of the respective month.

Storage conditions:

Store below 30°C. Store the ready-to-use syringes and the ampoules in the outer packaging in order to shield the contents against light.

6. FURTHER INFORMATION

What Testoviron-Depot contains:

The active substance is Testosterone enanthate.

1 ampoule for ready-to-use syringe, each for 1 ml, contains 250 mg of testosterone enanthate in oily solution.

The excipients are: benzyl benzoate and virgin castor oil.

Appearance of Testoviron-Depot and contents of the package:

Testoviron-Depot is a clear, yellowish oily solution.

Testoviron-Depot is obtainable in packings with 1 ampoule containing 1 ml; also Testoviron-Depot is obtainable in packings with 1 ready-to-use syringe, containing 1 ml; and with 3 ready-to-use syringes, each containing 1 ml, and with 3 ampoules, each containing 1 ml.

Manufacturer
Bayer Schering Pharma AG
D-13342 Berlin - Germany

These Instructions for Use were last revised in September, 2008.

The following information is intended solely for the use of physicians and/or specialised medical personnel:

Additional specifications
More detailed information concerning the preparation that is required by the physician is contained in special brochures.

Handling instruction for the ready-to-use syringes:

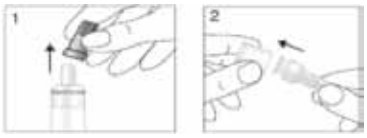
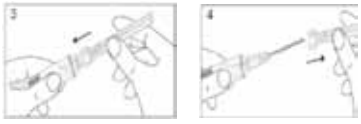


Fig. 1: Pull the rubber stopper off the easy-to-use syringe
Fig. 2: Hold the cannula firmly on the protective covering and pull off the cap completely.



Figs. 3 and 4: Insert cannula into the syringe and remove protective cover.

Specifications concerning the sterile cannula for one-time use:
To avoid needle puncture injuries, throw the cannula into a suitable cannula disposal box.