A Division of Bayer East Africa Ltd

NAME OF THE MEDICINAL PRODUCT

Proviron

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet Proviron contains 25 mg mesterolone.

PHARMACEUTICAL FORM

White tablets

CLINICAL PARTICULARS

Therapeutic indications

- Reduced efficiency in middle and advanced age

Complaints attributable to androgen-deficiency, such as reduced efficiency, easy fatigability, lack of concentration, weak memory, disturbances of libido and potency, irritability, disturbances of sleep, depressive moods, and general vegetative complaints, can be overcome or improved by the use of Proviron tablets.

- Potency disturbances

Potency disorders based on an androgen deficiency are eliminated by administration of Proviron. If other factors are the sole cause or if they contribute to the disorders, Proviron may be administered in support of other therapeutic measures.

- Hypogonadism

Growth, development and function of androgen-dependent target organs are stimulated by Proviron. It promotes development of secondary male sex characteristics in cases of prepuberal androgen-deficiency.

Proviron eliminates deficiency symptoms in cases where a loss of gonadal function has occurred postpuberally.

- Infertility

Oligozoospermia and deficient Leydig-cell secretion may be the cause of infertility. With Proviron sperm count and sperm quality as well as the fructose concentration in the ejaculate can be improved or normalized, thus increasing the chances of procreation.

Dosage and method of administration

The tablets are to be swallowed whole with some liquid.

The following dosages are recommended:

- Reduced efficiency and potency disturbances

Commencement of treatment: 1 Proviron tablet 3 times per day.

After satisfactory clinical improvement it can be tried to reduce the dose.

Continuation of treatment: 1 Proviron tablet twice or once per day.

According to type and severity of the complaints, the dose for further treatment is to be adjusted to individual requirements. Continuous treatment over a period of several months is recommended.

- Hypogonadism requires continuous therapy

For development of secondary male sex characteristics 1 - 2 Proviron tablets 3 times per day for several months.

As maintenance dose 1 Proviron tablet 2 - 3 times per day will often be sufficient.

- Infertility - for the improvement of sperm quantity and quality

1 Proviron tablet 2 - 3 times per day for a cycle of spermatogenesis, i. e. for about 90 days. If necessary, Proviron treatment is to be repeated after an interval of several weeks.

To achieve a higher fructose concentration in the ejaculate in cases of postpuberal Leydig-cell insufficiency: 1 Proviron tablet twice per day over several months.

Contraindications

Carcinoma of the prostate, previous or existing liver tumours. Hypersensitivity to the active substances or to any of the excipients.

Special warnings and special precautions for use

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

Proviron is for use in male patients only.

Regular examinations of the prostate should be carried out prophylactically.

In rare cases benign and in even rarer cases malignant liver tumours leading in isolated cases to life-threatening intraabdominal haemorrhage have been observed after the use of hormonal substances such as the one contained in Proviron. If severe upper abdominal complaints, liver enlargement or signs of intra-abdominal haemorrhage occur, a liver tumour should be included in the differential-diagnostic considerations.

Interaction with other medicaments and other forms of interaction

Not applicable.

Pregnancy and lactation

Not applicable.

Effects on ability to drive and use machines

Not applicable.

Undesirable effects

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

Overdose

Acute toxicity studies using single administration showed that Proviron is to be classified as non-toxic. No risk of toxicity is to be expected even after inadvertent single administration of a multiple of the dose required for therapy.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Proviron balances a deficiency of androgen formation which begins to fall gradually with increasing age. Therefore, Proviron is suitable for the treatment of all conditions caused by

deficient endogenous androgen formation. In the recommended therapeutic dosage, Proviron will not impair spermatogenesis. Proviron is especially well tolerated by the liver.

Pharmacokinetic properties

Following oral ingestion mesterolone is rapidly and almost completely absorbed in a dose range of 25 - 100 mg. The intake of Proviron generates maximum serum drug levels of 3.1 ± 1.1 ng/ml after 1.6 ± 0.6 hours. Thereafter, drug levels in serum decrease with a terminal half-life of 12 - 13 hours. Mesterolone is bound to serum proteins by 98 %. Binding to albumin accounts for 40 % and binding to SHBG (sex hormone binding globulin) to 58 %.

Mesterolone is rapidly inactivated by metabolism. The metabolic clearance rate from serum accounts for 4.4 ± 1.6 $ml \cdot min^{-1} \cdot kg^{-1}$. There is no renal excretion of unchanged drug. The main metabolite has been identified as 1α-methyl-androsterone, which - in conjugated form - accounts for 55 - 70 % of renally excreted metabolites. The ratio of main metabolite glucuronide to sulphate was about 12:1. As a further metabolite 1α-methyl-5α-androstane-3α,17β-diol has been recognized, which accounted for about 3 % of renally eliminated metabolites. No metabolic conversion into estrogens or corticoids has been observed. In form of metabolites mesterolone is excreted by about 80% of dose with the urine and by about 13 % of dose with the feces. Within 7 days 93 % of dose have been recovered in excreta, the half of which had been excreted with urine within 24 hours.

The absolute bioavailability of mesterolone was determined to about 3 % of the oral dose.

The daily intake of Proviron 25 will lead to an about 30 % increase in drug serum levels.

Preclinical safety data

In systemic tolerance studies after repeated administration of Proviron no findings were observed which raise objections to its use at the doses required for therapy.

Experimental investigations into possible sensitizing effects of Proviron have not been carried out.

Investigations into embryotoxic effects have not been carried out with Proviron, since the preparation is prescribed for the therapeutic use in male patients. Fertility studies to clarify a possible deleterious effect on sperm cells have not been carried out with Proviron. On the basis of long-term systemic tolerance studies, these results do not indicate a toxic effect on sperm cells, but a central mediated inhibition of spermatogenesis. Although generally known in animal experiments, this effect has not been observed in humans even after years of usage at the recommended therapeutic dose levels.

Investigations into the mutagenic effect have not been carried out. On the basis of the negative results with other steroid hormones in in vitro and in vivo mutagenicity tests, no such potential is to be expected.

Systemic tolerance studies after repeated administration in rats and dogs over a period of 6 and 12 months did not produce any indications of a substance-related tumorigenic effect. Therefore, a further characterization with regard to a possible tumorigenic potential has not been carried out. However, it must be kept in mind that sex steroids can promote the growth of certain hormone dependent tissues and tumours.

On the whole, the results of toxicological investigations do not raise objections to the prescribed use of Proviron in humans for the indications and at the doses given.

PHARMACEUTICAL PARTICULARS

List of excipients

Lactose monohydrate
maize starch
polyvidone 25 000
methyl parahydroxybenzoate
propyl parahydroxybenzoate
magnesium stearate.

Local variation is possible.

Incompatibilities

None so far known.

Shelf life

5 years.

Special precautions for storage

None.

Nature and contents of container

Proviron 25 tablets are contained in blister packs consisting of transparent films made of polyvinyl chloride and metallic foils made of aluminum (mat side hot sealable) or in amber glass bottles (type III) with tamperproof closure made of polyethylene.

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Presentations:, 2 x 10 tablets

Instructions for use/handling

Do not store above 30°C.
Keep out of reach of children.
Only on prescription.

DATE OF REVISION OF THE TEXT AND DECISION BY CMAB

13.07.13

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