SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Proviron 25 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 25 mg mesterolone.

Excipient with known effect

Each tablet contains 60.050 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Disturbances due to androgen deficiency.

- Disturbances due to androgen deficiency, such as easy fatigability, lack of concentration, gradual retreat of memory and concentration ability, disturbances of libido and potency, irritability, disturbances of sleep, depressive mental states, general vegetative disturbances that can be eliminated or improved taking Proviron tablets.

- Potency disturbances attributable to androgen deficiency are treated with Proviron. If other factors are the sole cause or if they contribute to the disturbances, Proviron may be prescribed as an additional medicine.

- Hypogonadism

- Growth, progression and function of androgen-dependent target organs are stimulated by Proviron, as well as the development of secondary male sexual characteristics in cases of prepuberal androgen-deficiency.

- Proviron eliminates deficiency symptoms in cases where a loss of gonadal function has occurred after puberty.

- Infertility
Oligozoospermia and insufficient Leydig-cell secretion may be the cause of infertility. Proviron increases the sperm count and improves its quality by increasing and normalizing the fructose concentration of the ejaculate, thus increasing the chances of procreation.

4.2 Posology and method of administration

The tablets are swallowed whole with some liquid.

The following dosages are recommended:

- Disturbances due to androgen deficiency

1 Proviron tablet 3 times per day.

After satisfactory clinical improvement is achieved, a dose reduction can be attempted .

Maintenance: 1 Proviron tablet twice or once per day.

Depending on the type and severity of the disturbances or symptoms, the maintenance dose should be adjusted to individual needs for the continuation of the treatment. Continuous treatment over a period of several months is recommended.

- Hypogonadism requires continuous treatment:

Start: For the stimulation of the development of secondary male sexual characteristics, 1 - 2 tablets of Proviron must be administered 3 times per day for several months.
Maintenance: 1 tablet of Proviron 2- 3 times per day could be sufficient as a maintenance dose.

- Infertility - for the improvement of sperm quantity and quality

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

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

4.3 Contraindications

- Prostate cancer

- Previous or existing liver tumours.

- Hypersensitivity to the active substance or any of the other excipients mentioned in section 6.1

4.4 Special warnings and precautions for use

Proviron is for use in male patients only.

Drug abuse and dependency:
Mesterolone has been abused, typically in combination with other anabolic-androgenic steroids. Abuse of mesterolone and other anabolic-androgenic steroids carries serious health risks (e.g. cardiovascular events with a fatal outcome in some cases, hepatic and/or psychiatric events and dependency), therefore it must be discouraged.

Proviron must be used exclusively in male patients.

If in isolated cases, frequent or very prolonged erections are observed, the dose should be reduced or treatment suspended to avoid damage to the penis.

Regular examinations of the prostate should be carried out as precaution measures.

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 abdominal pain, hepatomegaly or signs of intra-abdominal haemorrhage occur, then a liver tumour should be included in the differential-diagnostic considerations.

Proviron contains lactose
Patients with rare genetic conditions such as galactose intolerance, total lactase deficiency or glucose-galactose malabsorption must not use this medication.

4.5 Interaction with other medicinal products and other forms of interaction

No studies have been conducted on pharmacokinetic interactions with mesterolone.

4.6 Fertility, pregnancy and lactation

Proviron is not indicated in women.

At the recommended therapeutic dose, Proviron will not damage spermatogenesis.

With Proviron, sperm count and quality, as well as the concentration of fructose in the ejaculation, can be improved or normalized, thus increasing the reproduction hypothesis (also see section 4.1).

4.7 Effects on ability to drive and use machines

No effects were observed on the ability to drive and use machines.

4.8 Undesirable effects

The table below includes adverse reactions from spontaneous reporting and scientific literature, the frequency of which cannot be estimated from the available data.

System organ class	Unknown
Gastrointestinal disorders	Abdominal pain
Skin and subcutaneous tissue disorders	Acne Alopecia
Nervous system disorders	Headache
Reproductive system and breast disorders	Increased erection* Priapism

* increased number of erections

Reporting of suspected adverse reactions
It is important to report suspected adverse reactions in the post-marketing phase as it enables the risk/benefit ratio of the medicine to be continuously monitored.
Health professionals are asked to report any suspected adverse reactions directly to:

Jordan:
Tel: +962-6-5632000
JFDA email : jpc@jfda.jo
JFDA website: www.jfda.jo
http://primaryreporting.who-umc.org/JO

Egypt:
Egyptian Pharmaceutical Vigilance Centre
Hotline: 15301
Email: pv.followup@edaegypt.gov.eg
Website: www.edaegypt.gov.eg

United Arab Emirates (UAE):
Pharmacovigilance & Medical Device section
Tel: 80011111 / +971 42301000
Email: pv@mohap.gov.ae
Website: www.mohap.gov.ae
P.O.Box 1853 Dubai

Oman:
Tel: +968 - 2444 1999
Fax: +968 - 24602287
Email: pharma-vigil@moh.gov.om
Website: www.moh.gov.om

Kuwait:
Drug &Food Control, Ministry of Health
Tel.: +965-24811532
Fax: +965-24811507
Email : Adr_reporting@moh.gov.kw
Website: http://eservices.moh.gov.kw/SPCMS/DrugCmp.aspx

Other Countries:
Please contact the relevant competent authority

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 8.5.2 Androgens and anabolics,
ATC code: G03BB01

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 well tolerated by the liver.

5.2 Pharmacokinetic properties

Absorption
Following oral ingestion, mesterolone is rapidly and almost completely absorbed in a dose range of 10 - 100 mg. The intake of Proviron 25 mg generates maximum serum drug levels of 3.1 ± 1.1 ng/ml after 1.6 ± 0.2 hours. Absolute bioavailability of mesterolone was determined in approximately 3 % of oral dose.

Distribution
Mesterolone is bound to serum proteins by 98 %. Binding to albumin accounts for 40 % and binding to SHBG (sex hormone binding globulin) to 58 %.

Biotransformation
Mesterolone is rapidly inactivated by metabolism. The metabolic clearance rate from serum is 4.4 ± 1.6 ml/min^{-1}/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 conjugate) to sulphate conjugate was about 12:1. As a further metabolite 1α-metyl-5α-androstane-3α,17ß-diol, has been recognized, which accounted for about 3 % of renally eliminated metabolites. No metabolic conversion into oestrogens or corticoids has been observed.

Elimination
The serum levels of mesterolone decrease with a terminal half- life of 12-13 hours. In form of metabolites, mesterolone is excreted by approximately 80 % of dose with the urine and by approximately 13 % of dose with the faeces. Within 7 days, 93 % of dose was excreted, half of which in urine within 24 hours.

Linearity/non-linearity
The daily intake of Proviron 25 mg leads to approximately 30 % increase of the mesterolone serum concentration.

5.3 Preclinical safety data

Repeated-dose toxicity
Based on conventional repeated-dose toxicity studies, non-clinical data do not show any specific danger to humans in necessary treatment doses.

Genotoxicity and carcinogenicity
No trials have been conducted on the mutagenic or carcinogenic effect of mesterolone. A toxicity assessment based on the structure did not show any evidence on a mutagenic potential.

The results of repeated-dose toxicity studies with systemic administration in rats and in dogs for a 6- and 12-month period did not indicate a drug-related tumorigenic effect. However, it has to be taken into account that sex steroids can stimulate the growth of certain hormone-dependent tissues and tumours.

Toxicity in reproduction

There have been no investigations for embryotoxic effects of mesterolone, since this medicinal product is intended for therapeutic use only by male patients.

Fertility studies with mesterolone have not been conducted in order to elucidate its harmful effect on the sperm. Based on long-term studies of systemic tolerability, the results obtained do not indicate a toxic effect on sperm cells, but a central moderate inhibition of spermatogenesis. Although this is known from experiments in animals, this effect has not been observed in humans, even after many years of use of the proposed therapeutic dosage.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose mono-hydrate

Maize starch

Povidone 25.000

Methyl hidroxybenzoate

Propyl hidroxybenzoate

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not store above 30ºC.

6.5 Nature and contents of container

Blister of polyvinyl chloride and aluminium, heat-sealed.

Pack contains 20 tablets.

6.6 Special precautions for disposal

There are no special requirements.

7. MARKETING AUTHORISATION HOLDER

Bayer AG,
Leverkusen, Germany.

8. MARKETING AUTHORISATION NUMBER(S)

Registration No.: 824 24 04 – 20 tablets, 25 mg, blister

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9 October 1970
Date of last renewal: 22 May 2023

10. DATE OF REVISION OF THE TEXT

17/11/2023