SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Prefemin®

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 film coated tablet contains:

20 mg Agni casti fructus (agnus castus) dry extract, Native (DER 6-12 : 1).

Excipient with known effect

40 mg lactose monohydrate

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet.

Round, white, biconvex.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of PMS (premenstrual syndrome) complaints recurring monthly prior to menstruation, in adults.

4.2 Posology and method of administration

Posology

Adult women

1 film coated tablet daily in the morning.

Children and adolescents

Prefemin is not indicated for children and adolescents below 18 years of age due to lack of adequate data.

Method of administration

Oral

The film coated tablet is taken unchewed with a sufficient amount of liquid.

The film coated tablet should preferably be taken at the same time each day.

Duration of use

To achieve an optimal treatment effect, continued use over three months is recommended.

If the symptoms worsen or no improvement occurs after three months, a doctor should be consulted.

4.3 Contraindication

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Patients who suffer or suffered from an oestrogen-sensitive cancer should consult their doctor before using Prefemin.

Patients who are using dopamine agonists, dopamine antagonists, oestrogens and antioestrogens should consult their doctor before using Prefemin (see section 4.5).

Agnus castus extract is thought to act on the pituitary-hypothalamic axis and therefore, patients with a history of a pituitary disorder should consult a doctor before use.

In cases of prolactin secreting tumours of the pituitary gland the intake of Agnus castus extract can mask symptoms of the tumour.

If the symptoms worsen during the use of the medicinal product or persist after continued use over three months, a doctor should be consulted.

The film coated tablets contain lactose monohydrate.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

No interactions are known to date.

Because of the possible dopaminergic and oestrogenic effects of Agnus castus extracts, interactions with dopamine agonists, dopamine antagonists, oestrogens and antioestrogens cannot be excluded.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no indication for the use during pregnancy.

There are no data from the use of Agnus castus extract in pregnant women available. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). The use is not recommended during pregnancy.

Breastfeeding

It is unknown whether Agnus castus extract or its metabolites are excreted in human milk. Data from reproductive studies suggest that Agnus castus extract may affect lactation. A risk to the suckling child cannot be excluded. The use during lactation is not recommended.

Fertility

No fertility data are available.

4.7 Effects on the ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The frequency is not unknown.

Immune system disorders

Severe allergic reactions with face swelling, dyspnoea and swallowing difficulties

Nervous system disorders

Headache, dizziness

Gastrointestinal disorders

Nausea, abdominal pain

Skin and subcutaneous tissue disorders

Allergic skin reactions such as rash and urticaria, acne

Reproductive system and breast disorders

Menstrual disorders

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form http://sideeffects.health.gov.il

4.9 Overdose

No cases of overdose has been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other gynecologicals ATC code: G02CX03

The mode of action is not known.

Inhibitory influences on prolactin release and the dopaminergic (dopamine-agonistic) effects were seen in preclinical studies by different working groups. In human pharmacology a reduction of elevated prolactin levels by Agnus castus extract has not been conclusively proven.

There are contradictory results concerning binding to oestrogen receptor in general and the preferential binding to β- or α-receptors. Furthermore, there are some references concerning β-endorphin-like activity (possibly via the μ-opiate receptor binding).

Clinical efficacy

In a randomised, double-blind, study 170 women with a diagnosis of PMS were treated with *Vitex agnus-castus* extract (laboratory code: Ze 440) or placebo for the duration of three menstruation cycles. Treatment with *Vitex agnus-castus* extract Ze 440 led to a significant reduction of the symptoms of PMS (irritability, mood swings, anger outbursts and headache) vs. placebo in the women.

5.2 Pharmacokinetic properties

No data available.

5.3 Preclinical safety data

There are only limited preclinical safety data on *Vitex agnus castus* L., fructus (Agnus castus fruit) or preparations thereof.

In two repeat dose toxicity studies in rats (4 weeks, 26 weeks) signs of liver toxicity have been observed.

In vitro and *in vivo* tests conducted with the Agnus castus dry extract did not demonstrate genotoxic potential.

Tests on carcinogenicity and adequate tests on reproductive toxicity have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose, Lactose monohydrate, Silica colloidal anhydrous, Hypromellose,
Titanium dioxide, Magnesium stearate, Macrogol 400, Propylene glycol, Macrogol 20,000.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25 °C. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

PVC/PVdC aluminium blisters with 30 or 90 film coated tablets.
It is possible that not all pack sizes are marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MANUFACTURER

MAX Zeller Sohne AG, Romanshorn, Switzerland

8 REGISTRATION HOLDER

Rafa Laboratories Ltd., P.O.Box 405, Jerusalem 9100301

Drug registration number: 164-38-35417

Revised in April 2024