Name of the product

Cimidona 6.5 mg

Cimidona Forte 13 mg

Tablet.

Composition

Active substance:

Cimidona 6.5 mg: Dry extract from cimicifugae rhizoma (black cohosh) 6.5 mg

Cimidona Forte 13 mg: Dry extract from cimicifugae rhizoma (black cohosh) 13 mg

Therapeutic indications:

Alleviation of menopausal complaints (hot flashes, excessive perspiration, sleep disorders, nervousness and depressive moods).

Dosage:

1 tablet to be taken once daily, unchewed, with some fluid, preferably always at the same time of the day (in the morning or in the evening). The intake of the tablets does not depend on meals.

The effect does not set in immediately. Intake of Cimidona is recommended for a period of at least 6 weeks.

It is recommended to take Cimidona over several months; however, it should not be used for more than 6 months without medical advice.

Contraindications:

- Hypersensitivity to the active substance, to Ranunculaceae (buttercup plants) or to any of the excipients
- Cimidona is contraindicated for patients with a current or previous liver disorder.

Special warnings and precautions:

- This preparation has an effect on physical and psychological complaints during the menopause. Since there is no clinical data so far with regard to a positive effect on bones, this preparation cannot be used for the prevention of osteoporosis.
- In prospective clinical trials involving more than 1200 patients, black cohosh was not associated with serum enzyme elevations during treatment and no cases of

clinically apparent liver injury were reported. However, Products labeled as black cohosh have been linked to more than fifty instances of clinically apparent liver injury that have ranged in severity from symptomatic elevations in serum enzymes without jaundice, to acute self-limited hepatitis, prolonged hepatitis with cholestasis, autoimmune hepatitis, and acute liver failure requiring liver transplantation or with a fatal outcome. The latency to onset of liver injury ranged from 1 to 48 weeks, but was usually within 2 to 12 weeks.

- liver function test should be performed according to clinical judgment.

- Patients should stop taking Cimidona and consult their doctor immediately if they develop signs and symptoms suggestive of liver injury (such as unusual tiredness, loss of appetite, weight loss, yellowing of skin and eyes or severe upper stomach pain with nausea and vomiting, diarrhoea or dark urine).

- A doctor should be consulted in the case of a feeling of tension and swelling of the breasts as well if intracyclic bleeding, spotting, or recurrence of menstrual bleeding occurs.

- Cimidona 6.5 mg/Cimidona forte 13 mg contains lactose. Patients with rare heredity problems of fructose intolerance, galactose intolerance, galactosaemia or glucose-galactose malabsorption should not take this medicine.

- Cimidona 6.5 mg/Cimidona forte 13 mg contains croscarmellose sodium: this medicine contains less than 1 mmol sodium (23 mg) per tablet that is to say almost "sodium-free".

Interactions:

None known.

Pregnancy/ lactation:

The use of preparations containing Black Cohosh (Cimicifugae rhizome) is indicated for menopausal women. Administration during pregnancy and lactation is not intended.

There are no adequate animal or human data, which can exclude a potential risk with sufficient certainty.

Effect on the ability to drive and operate machines:

No relevant studies have been performed.

Undesirable effects:

In the following the undesirable effects are listed, which were observed for Cimidona during usage in clinical trials and market surveillance.

Immune system: Oedema in the face and the body (frequency unknown).

Gastrointestinal dysfunction: In rare cases, gastric complaints, nausea, dyspepsia and diarrhoea can occur.

Liver and bile: In single cases, there is evidence for partly severe liver injury (e.g. abnormal liver function tests, icterus, hepatitis).

Skin: Rash, pruritus, urticaria (frequency unknown).

Reproductive system and breast: Tension and swelling of the breasts, spotting, intracyclic bleeding as well as recurrence of menstrual bleeding can be observed in single cases.

Reporting of suspected adverse reactions

Reporting 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

https://sideeffects.health.gov.il/

Overdose:

No cases of overdose were reported.

Characteristics / effects:

ATC-Code

G02CX04

Mode of action:

Ethanolic extracts of the Cimicifuga rhizome contain triterpene glycosides, flavone derivatives and aromatic acids.

The effect of Cimicifuga extracts on human oestrogen receptor-positive and receptor-negative breast cancer cell lines was tested in different *in-vitro* experiments. The

results are equivocal. The majority of published studies, among others a study with Cimicifuga extract Ze 450, an inhibition of proliferation respectively no cell proliferation could be shown.

It could be shown that the substances contained in the Cimicifuga extract have a certain binding affinity to the oestrogen receptor, but lack an oestrogenic effect.

Safety pharmacodynamic:

In a clinical trial with 400 postmenopausal women, the thickness of the endometrium was determined by transvaginal sonography. Over a time period of one year, no increase in endometrial thickness was observed. Also, hormonal parameters (LH, FSH, oestradiol and prolactin) remained unchanged.
This data indicates that the observed Cimicifuga extract effects do not seem to directly affect these hormonal parameters.

Clinical efficacy:

The efficacy of Cimidona for the treatment of climacteric complaints was examined in a prospective, placebo-controlled, randomised clinical study.
In this 3-arm study, the superiority of Cimidona as compared to placebo was demonstrated over a time period of 12 weeks. The primary target variable, the Kupperman index, showed a dose-dependent efficacy in the intent-to-treat collective (N = 153). Women treated for menopausal complaints, for which a dosage of 6.5 mg is not sufficient, can be successfully treated with the13 mg dose.

Pharmacokinetics:

No pharmacokinetic studies were conducted for the galenic formulation present in Cimidona.

<u>Absorption</u>

No data available

<u>Distribution</u>

No data available

<u>Metabolism</u>

No data available

Elimination

No data available

Pre-clinical data:

In a toxicity study with rats with repeated oral administration of Cimicifuga dry extract (Ze 450) over a period of 7 days, no toxic reactions could be found in histological or microscopic examinations either.

The salmonella microsome assay according to Ames did not reveal any indication of a mutagenic effect of the dry extract Ze 450 from Black cohosh (Cimicifuga rhizome).

There is no knowledge on reproduction toxicology and carcinogenicity.

Additional information:

Excipients:

Cellulose microcrystalline, lactose monohydrate (44 mg), croscarmellose sodium (corresponds to max. 0.65 mg sodium), povidone, magnesium stearate, silica colloidal anhydrous.

The product contains approx. 44 mg digestible carbohydrates per single dose.
this medicine is suitable for diabetics.

Galenic form and active substance per unit:

Cimidona 6.5 mg: 6.5 mg dry extract (Ze 450) from rhizomes of Cimicifuga racemosa, DER 4.5 – 8.5:1, extraction solvent 60% ethanol (V/V).

Cimidona Forte 13 mg: 13 mg dry extract (Ze 450) from Cimicifugae rhizoma DER 4.5 – 8.5:1, extraction solvent 60% ethanol (V/V).

Incompatibilities

Not applicable.

Influence on diagnostic methods

Not known.

Shelf-life

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

Special storage information

Store below 25 °C.

Packages:

30 tablets

90 tablets

Not all package sizes may be marketed.

Manufacturer

MAX Zeller Söhne AG, Romanshorn, Switzerland

Registration holder

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

Drug registration number:
Cimidona 6.5 mg: 153-88-34027

Cimidona Forte 13 mg: 163-70-35388

Revised in November 2021 according to MOH's guidelines