Summary of Product Characteristics

Cyclodynon® Film-Coated Tablets

1. Name of the medicinal product

Cyclodynon® Film-Coated Tablets
Active substance: Dry extract derived from chaste tree fruit
（agni casti fructus)

2. Qualitative and quantitative composition

1 film-coated tablet contains:
4.0 mg dry extract derived from chaste tree fruit (7-11:1);
extracting agent: ethanol 70 % (V/V)

Excipients:
Lactose monohydrate 25.0 mg

For a full list of excipients see section 6.1.

3. Pharmaceutical form

Film-coated tablet

The film-coated tablets are greenish blue, round, biconvex with dull surface.

4. Clinical particulars

4.1 Therapeutic indications

Cyclodynon® film-coated tablets constitute the phytogenous therapeutic agent, which is used for complex therapy (see interactions with other medicinal products and other forms of interactions), in the cases as follows:

menstrual cycle disturbances

premenstrual syndrome

cyclic mastodynia (cyclic breast pain)

In cases of tension and tumescence in the area of mammary glands as well as with menstrual disturbances, medical advice should be sought, to investigate whether there are other diseases that need additional medical research.

4.2 Posology and method of administration

Take 1 times daily 1 film-coated tablet.

To achieve an optimal treatment effect, continued use – even during menstruation over three months is recommended.

If the symptoms persist after a continued use over three months, a doctor or a qualified health care practitioner should be consulted.

The use in children and adolescents under 18 years of age is not rcommended (see section 4.4 “Special warnings and precautions for use!).

Swallow film-coated tablets with sufficient liquid (e.g. a glass of water). Do not chew tablets.

4.3 Contraindications

Cyclodynon Film-Coated Tablets must not be taken in case of hypersensitivity to the active substance or to any of the excipients of the medicinal product.

4.4 Special warnings and precautions for use

Patients who suffer or suffered from an oestrogen-sensitive cancer should consult their doctor before using Vitex agnus castus.
Patients who are using dopamine agonists, dopamine antagonists, oestrogens and antioestrogens should consult their doctor before using Vitex agnus-castus. (see section 4.5 ‘Interactions with other medicinal products and other forms of interaction’)

The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.

If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Vitex agnus castus, fructus is thougt 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 sectreting tumours of the pituitary gland the intake of Vitex agnus castus, fructus can mask symptoms of the tumour.

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

4.5 Interactions with other medicinal products and other forms of interaction

Because of the possible dopaminergic and oestrogenic effects of Vitex agnus-castus, fructus interactions with dopamine agonists, dopamine antagonists, oestrogens and antioestrogens cannot be excluded.

4.6 Pregnancy and lactation

There is no indication for the use during pregnancy.
Data from reproductive studies suggest that extracts of Vitex agnus-castus, fructus may affect lactation.
Cyclodynon film-coated tablets must not be taken during pregnancy and lactation

4.7 Effects on 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

Like all other medications, Cyclodynon® film-coated tablets may also have side effects – severe allergic reactions with face swelling, dyspnoea and swallowing difficulties. Allergic skin reactions (such as rash and urticaria), headache, dizziness, gastrointestinal disorders (such as nausea, abdominal pain), acne, menstrual disorders have been reported. The frequency is not known.
At the first signs of a hypersensitivity / allergic reaction Cyclodynon® film-coated tablets must not be taken again.

At the first signs of a hypersensitivity / allergic reaction Agnucaston® film-coated tablets must not be taken again.

If other adverse reactions not mentioned above occur, a doctor or a qualified health care

practitioner should be consulted.

4.9 Overdose

No case of overdose has been reported.

Treatment of overdose:
If symptoms of overdose occur, symptomatic treatment should be initiated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: herbal medicine for the treatment of menstrual rhythm anomalies

ATC code: G02CX

There is evidence that aqueous alcoholic Agnus castus extracts inhibit prolactin release *in vitro*. The inhibitory effect on prolactin release was also confirmed in animal studies. A reduction of increased prolactin levels has not yet been shown for humans. However, several clinical studies showed evidence that slightly elevated prolactin levels in women and increased prolactin release due to stress (so-called "latent hyperprolactinemia") are reduced through administration of Agnus castus extract.

In vitro studies showed that the location where the effects take place are the lactotrophic pituitary cells. The active principle is dopaminergic.

Bicyclic diterpenes have been identified as a substance group that contributes to the prolactin reducing effects of Agnus castus extract BNO 1095. These substances bind to the human dopamine receptor subtype 2 and lower in a dose-dependent manner the prolactin release in cultured rat pituitary cells.

5.2 Pharmacokinetic properties

No data available.

5.3 Preclinical safety data

Acute toxicity

The Agnus castus extract BNO 1095 that is contained in Cyclodynon Film-Coated Tablets has a low toxicity. One-time administration resulted in no fatalities in rats and mice. The LD_{50} values surpass the highest dose as defined in the guidelines.

Species	Mode of application	LD_{50} (mg/kg body weight)
Rat	Oral	>2,000
Rat	Intraperitoneal	>2,000
Mouse	Oral	>2,000
Mouse	Intraperitoneal	>2,000

Subacute toxicity

The toxicity of BNO 1095 applied in repeated doses to rats was examined up to a dose of 1,000 mg/kg. Oral administration over four weeks resulted in a no-observed-effect-level („NOEL“) of 50 mg extract/kg body weight which is a multiple above the recommended human dose of 4 mg/patient and day.

Chronic toxicity

Oral administration to rats over 26 weeks with doses up to 1,000 mg/kg resulted in no substance-related changes for the therapeutic dose range. The no-observed-adverse-effect-level (“NOAEL”) in this study was 40 mg extract/kg body weight.

Mutagenicity

Four different test approaches for the identification of the genotoxic potential yielded no evidence for bacterial strains as for mammal cells or the whole animal for any mutagenic or chromosome-damaging effects of the Agnus castus extract BNO 1095. In five bacterial strains (*Salmonella typhimurium*) and cultivated mammal cells (mouse lymphoma cells) this extract caused no mutations neither without nor with metabolic activition. Oral administration to rats did not result in increased DNA synthesis in liver cells which would otherwise indicate repair of possible cell damage. The micronucleus test in the mouse that is used to identify chromosome damage after in vivo administration was also negative.

Reproduction toxicity

There are no studies available on the influence of the extract on embryo toxicity and fertility.

Carcinogenicity

There are no studies available on the tumorigenic potential of Agnus castus extracts after long-term administration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ammonium methacrylate-copolymer (type A)
iron (III) oxide (E 172)
indigo carmine (E 132) aluminium salt
potato starch,
lactose monohydrate
magnesium stearate,
Macrogol 6000,
microcrystalline cellulose,
povidone,
highly disperse silicon dioxide,
talcum,
titanium dioxide (E171)

Note for diabetics:
Cyclodynon Film-Coated Tablets contain per single dose less than 0.01 carbohydrate exchange units (CEU)

6.2 Incompatibilities

None known.

6.3 Shelf life

5 years

6.4 Special precautions for storage

Not applicable.

Keep medicine out of reach and sight of children.

6.5 Nature and contents of container

Package with 30 (N1) film-coated tablets
Package with 60 (N2) film-coated tablets
Package with 90 (N3) film-coated tablets

6.6 Special precautions for disposal

No special requirements.

7. Marketing authorisation holder

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Internet: www.bionorica.de
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8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of the revision of the text

February 2017

11. General classification for supply

Available only in pharmacies