SUMMARY OF PRODUCT CHARACTERISTICS

UTROGESTAN soft capsules

1. NAME OF THE MEDICINAL PRODUCT

Utrogestan 200 mg soft capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

200 mg Progesterone (micronised)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Soft capsules

Ovoid and slightly yellow soft capsules, containing whitish oily suspension

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Gynaecological:

- Disorders related to progesterone insufficiency,
  In particular:
  - premenstrual syndrome,
  - menstrual disorders due to poor ovulation or anovulation,
  - benign breast disease,
  - premenopause.
- Treatment of the menopause (as an adjuvant to oestrogen therapy).
- Sterility due to luteal phase deficiency.

Obstetric:

- Threat of miscarriage or prevention of recurrent miscarriages due to proven luteal phase deficiency.

- Threat of premature delivery.

4.2 Posology and method of administration

Posology

On average, the dosage is 200 to 300 mg progesterone per day, divided into one or two doses, i.e. 200 mg in the evening at bedtime plus 100 mg in the morning, if needed..

- For **luteal phase deficiency** (premenstrual syndrome, menstrual irregularities, premenopause, benign breast disease): the treatment is used for 10 days per cycle, usually from **days 17 to 26** inclusive.

- In **the treatment of menopause**: as oestrogen therapy alone is not recommended, progesterone is added during the last two weeks of each treatment schedule, followed by a one-week suspension of all replacement therapy, during which withdrawal bleeding may be observed.
- For **threatened premature delivery**: 400 mg of progesterone every 6 to 8 hours, depending on the clinical results obtained during the acute phase, followed by a maintenance dosage (e.g. 3 x 200 mg per day) up until week 36 of pregnancy.

Method of administration

Oral administration.

4.3 Contraindications

This medicinal product must not be prescribed in the following situations:

- serious changes in liver function.
- hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- neoplasm of the breast or genital organs, suspected or confirmed.

4.4 Special warnings and precautions for use

This treatment, under the recommended conditions for use, **IS NOT A CONTRACEPTIVE.**
If the treatment schedule is initiated too early in the month, particularly before day 15 of the cycle, this may shorten the cycle or bleeding may occur.

- In the case of uterine bleeding, do not prescribe until a definite cause has been established, preferably via endometrial investigations.
- Due to the thromboembolic and metabolic risks which cannot totally be eliminated, treatment must be discontinued at the onset of:
  - eye disorders, such as loss of vision, diplopia, vascular lesions of the retina;
  - venous thromboembolisms or thrombotic events, regardless of the region;
  - severe headaches
- Patients with a history of thrombophlebitis should be closely monitored.
- If amenorrhoea should occur during treatment, pregnancy must be excluded.

More than half of spontaneous abortions are due to genetic complications. Furthermore, infectious manifestations and mechanical disorders may be responsible for miscarriages; in which case, the sole effect of administering progesterone would be a delay in the expulsion of a dead ovum. Progesterone administration must therefore only be reserved for cases where corpus luteum secretion is insufficient.

Utrogestan contains soya lecithin and may cause hypersensitivity reactions (urticaria, anaphylactic shock).

4.5 Interaction with other medicinal products and other forms of interaction

With HRT involving oestrogens, administration of progesterone over a minimum of 12 days per cycle is strongly recommended.

Combination with other medicinal products may increase the metabolism of progesterone, which may lead to a modification in its effect.

This applies in the case of:
- potent enzyme inducers such as barbiturates, antiepileptic agents (phenytoin), rifampicin, phenylbutazone, spironolactone and griseofulvin. These medicines cause increased metabolism in the liver.
- certain antibiotics (ampicillin, tetracyclines): variations in the intestinal flora, leading to a change in the enterohepatic circulation of steroids.

Given that these interactions can differ from one individual to another, it is not always possible to predict clinical results.

Progestins may cause a reduction in glucose tolerance and, as a result, may increase the need for insulin and other antidiabetic agents in patients with diabetes.

Smoking may reduce the bioavailability of progesterone and alcohol abuse may increase it.

4.6 Fertility, pregnancy and lactation

Pregnancy
The use of Utrogestan is not contraindicated during pregnancy, including the first few weeks (see section 4.1: Therapeutic indications – Obstetric).

Breastfeeding
The passage of progesterone into milk has not been studied in detail. Its prescription should therefore be avoided during the breastfeeding period.

4.7 Effects on ability to drive and use machines

Attention should be drawn to the risks of drowsiness and/or dizziness associated with the oral use of this medicine, particularly in the case of patients who drive or operate machinery. Ingestion of the capsules at bedtime will avoid such problems.

4.8 Undesirable effects

The following effects have been observed:

System organ class	Common undesirable effects ≥1/100; <1/10	Uncommon adverse effects ≥1/1000; ≤1/100	Rare undesirable effects ≥1/10 000; ≤1/1 000	Very rare undesirable effects ≤1/10 000
Reproductive system and breast disorders	Altered periods Amenorrhoea Intercurrent bleeding	Mastodynia		
Central nervous system disorders	Headaches	Drowsiness Fleeting dizzy sensations		Depression
Gastrointestinal disorders		Vomiting Diarrhoea Constipation	Nausea	
Hepatobiliary disorders		Cholestatic jaundice		

Immune system disorders				Urticaria
Skin and subcutaneous tissue		Pruritus Acne		Chloasma

Drowsiness and/or transient dizziness are observed particularly with concomitantly low levels of oestrogen. These effects are immediately reversible upon reduction of the dosage or escalation of the oestrogen dose, without compromising the therapeutic benefit.

If the treatment schedule is initiated too early in the month, particularly before day 15 of the cycle, this may shorten the cycle or intermenstrual bleeding may occur.

Altered menstrual cycles, amenorrhoea and intermenstrual bleeding have been observed and reported in association with general progestin use.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

More often than not, the undesirable effects described above are signs of an overdose. They resolve spontaneously when the dosage is reduced.

In some individuals, the usual dosage may prove to be too high, as evidenced by the persistence or recurrence of unstable endogenous progesterone secretion, marked sensitivity to the product or concomitantly low blood levels of oestradiol. In these cases, the following measures should be taken:

- In the event of drowsiness or transient dizziness, the dosage amount should be reduced or progesterone should be administered IN THE EVENING AT BEDTIME, over 10 days per cycle.
- In the event of spotting/shortening of the menstrual cycle, initiation of treatment should be deferred until later into the cycle (e.g. day 19 instead of day 17).
- Perimenopausal women/women receiving HRT should be tested to ensure that blood oestradiol levels are sufficient.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Genitourinary system and sex hormones
ATC code: G03DA04

UTROGESTAN, which contains progesterone in micronised form, allows a significant increase in plasma progesterone levels following oral administration, thus making it possible to correct progesterone deficiency.

5.2 Pharmacokinetic properties

Elevation of blood progesterone levels starts from the first hour onwards, with peak plasma levels observed 1 to 3 hours post-dose. Owing to the tissue retention time of the hormone, it would appear necessary to divide the dosage into two doses, taken at approximately 12-hour intervals, in order to ensure that impregnation is obtained throughout the entire 24-hour period.

Metabolism: plasma and urinary metabolites are identical to those found during physiological corpus luteum secretion: in plasma, its main metabolites are 20-alpha-hydroxy-delta-4-pregnenolone and 5-alpha-dihydroprogesterone. Urinary elimination occurs at a rate of 95% in the form of glucuronide-conjugated metabolites, the main one being 3-alpha-5-beta pregnanediol (pregnandiol).

5.3. Preclinical safety data

No data supplied.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents: Sunflower oil, soya lecithin.
Capsule shell: Gelatin, glycerol, titanium dioxide (E171), purified water

6.2 Incompatibilities

No data supplied.

6.3 Shelf life

Three years in the sealed blister.

6.4 Special precautions for storage

Do not store above 30ºC. Store in the original packaging.

6.5 Nature and content of container

Boxes of 15 or 45 x 200 mg soft capsules, packed in PVC/Aluminium blisters, for oral use.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Besins Healthcare S.A.
Avenue Louise, 287
1050 Brussels
Belgium

8. MARKETING AUTHORISATION NUMBERS

TAN 20 HM 410

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25th September, 2020

10. DATE OF REVISION

Not applicable (First authorization)