SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Utrogestan 200 mg soft vaginal capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft vaginal capsule contains 200 mg progesterone (micronised).

Excipient with known effect:
Each soft vaginal capsule contains 2 mg of soybean lecithin.

For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Soft vaginal capsule

Slightly yellow, ovoid (approximately 15.1 mm x 9.1 mm),soft vaginal capsule, containing a whitish oily suspension..

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<invented name> is indicated in women for:
- Supplementation of the luteal phase during Assisted Reproductive Technology (ART) cycles.
- Prevention of preterm birth in women with a singleton pregnancy who have a short cervix (mid-trimester sonographic cervix ≤25 mm) and/or a history of spontaneous preterm birth (see section 4.4)

4.2 Posology and method of administration

Posology

For **supplementation of the luteal phase during Assisted Reproductive Technology cycles** - the recommended dose is 600 mg/day, given in three divided doses, one in the morning, one at midday and the third at bedtime. The treatment is started not later than the third day after oocyte retrieval. If pregnancy has been confirmed, continue treatment until at least the 7th week but no longer than the 12th week of pregnancy.

For **prevention of preterm birth in women with a singleton pregnancy who have a short cervix and/or a history of spontaneous preterm birth**, the recommended dosage is 200 mg per day in the evening at bedtime from around week 20 to week 34 of pregnancy. For information on shared decision making, see section 4.4.

Paediatric population
There is no relevant use of <invented name> in the paediatric population.

Elderly patients

There is no relevant use of <invented name> in the elderly.

Method of Administration:
Vaginal
Each capsule of <invented name> must be inserted deep into the vagina.

4.3 Contraindications

- Hypersensitivity to the active substance, soya, peanut (see section 4.4) or to any of the excipients listed in section 6.1,
- Jaundice,
- Severe hepatic dysfunction,
- Undiagnosed vaginal bleeding,
- Mammary or genital tract carcinoma,
- Thrombophlebitis,
- Thromboembolic disorders,
- Cerebral haemorrhage,
- Porphyria,
- Missed abortion,
- Premature rupture of membranes (PPROM) (see Section 4.4),

4.4 Special warnings and precautions for use

Warnings:

- A complete medical examination must be performed before starting and regularly during the treatment.
- <invented name> is not suitable as a contraceptive and must only be used in accordance with the indications in section 4.1.
- In rare cases, the use of micronised progesterone during the second and third trimester of pregnancy may lead to the development of gravidic cholestasis or hepatocellular liver disease.
- Treatment should be discontinued upon diagnosis of a missed abortion.

Warning specific for supplementation of the luteal phase during Assisted Reproductive Technology cycles:

- <invented name> should only be used during the first three months of pregnancy and must only be administrated by vaginal route.
- <invented name> is not intended to treat an **imminent** premature delivery.

Precautions:

- Any vaginal bleeding should always be investigated.

Precautions specific for prevention of preterm birth in women with a singleton pregnancy who have a short cervix and/or a history of spontaneous preterm birth:
Before treatment is initiated:

- The risks and benefits of the options available, should be discussed with the patient. The physician and patient should make a shared decision on which treatment is most suitable (see section 5.1).
- Premature rupture of membranes (PPROM) should be excluded (see section 4.3). Should rupture of membranes occur during treatment, further treatment with <invented name>

should be discontinued.

Excipient

<invented name> contains soybean lecithin and may cause hypersensitivity reactions (urticaria and anaphylactic shock) in hypersensitive patients. As there is a possible relationship between allergy to soya and allergy to peanut, patients with peanut allergy must avoid using this medicine (see Section 4.3).

<invented name> contains highly refined sunflower oil, for which the incidence of hypersensitivity is very rare in adults.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs known to induce the hepatic CYP450-3A4 such as barbiturates, anti-epileptic agents (phenytoin, carbamazepine), rifampicin and also herbal products containing St. John's wort (Hypericum perforatum) may increase the elimination of progesterone. Ketoconazole and other inhibitors of CYP450-3A4 may increase the plasma exposure of progesterone.

4.6 Fertility, pregnancy and lactation

Natural progesterone may be given orally, vaginally or by the intramuscular route to treat luteal phase deficiency until at least the 7th week of pregnancy and not later than the 12th week of pregnancy. Natural progesterone may also be given vaginally for prevention of preterm birth, from the 20th week of pregnancy to the 34th week of pregnancy.

Pregnancy
No association has been found between the maternal use of natural progesterone in early pregnancy and foetal malformations.

Breastfeeding
<invented name> is not indicated during breast-feeding.
Detectable amounts of progesterone enter the breast milk.

Fertility
As this medicinal product is indicated to support luteal deficiency in sub-fertile or infertile women, there is no deleterious known effect on fertility.

4.7 Effects on ability to drive and use machines

This medicine has no or negligible influence on the ability to drive and use machines. However, dizziness or fatigue may occur in some individuals. If affected, patients should not drive or operate machines.

4.8 Undesirable effects

Local intolerance (burning, itching or oily discharge) has been observed in clinical studies and has been reported in publications, but the incidence is extremely rare.

When used as recommended, transient fatigue or dizziness may occur within 1 – 3 hours of taking the medicine.

Reporting of suspected adverse reactions after authorisation

The information given below is based on extensive post marketing experience from vaginal administration of progesterone.

Adverse effects have been ranked under headings of frequency using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); frequency not known (cannot be estimated from the available data).

System organ class (SOC)	**Frequency Not known (cannot be estimated from the available data)**
Skin and subcutaneous tissue disorders	Pruritus
Reproductive system and breast disorders	Vaginal haemorrhage Vaginal discharge
General disorders and administrative site conditions	Fatigue Burning sensation
Nervous System Disorders	Dizziness

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Symptoms of overdosage may include somnolence, dizziness, euphoria or dysmenorrhoea. Treatment is observation and, if necessary, symptomatic and supportive measures should be provided.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sex hormones and modulators of the genital system, progestogens, ATC code: G03DA04.

Mechanism of action
Supplementation of the luteal phase during ART:
Progesterone is a natural progestogen, the main hormone and most important hormone of the corpus luteum and the placenta. It acts on the endometrium by converting the proliferating phase to the secretory phase. <invented name> have all the properties of endogenous progesterone with induction of a full secretory endometrium and in particular gestagenic, antiestrogenic, slightly anti-androgenic and antialdosterone effects.

Prevention of preterm birth

Progesterone is important during pregnancy in maintaining uterine quiescence by limiting the production of stimulatory prostaglandins responsible for uterine contractions. Progesterone also limits the release of matrix metalloproteinases that can cause cervical effacement and softening by inhibiting the expression of contraction-associated protein genes (ion channels, oxytocin and prostaglandin receptors, and gap junctions) within the myometrium.
Although levels of progesterone in the maternal circulation do not change significantly in the weeks preceding labour, the onset of labour at term and preterm is associated with a functional withdrawal of progesterone activity at the level of the uterus.

Clinical efficacy/safety studies

A meta-analysis of individual participant data from randomised controlled trials (EPPPIC 2021) concluded that vaginal progesterone reduced birth before 34 weeks' gestation in high-risk singleton pregnancies. Trials in singleton pregnancies included mostly women with previous spontaneous preterm birth or short cervix. Preterm birth before 34 weeks was reduced in such women who received vaginal progesterone (nine trials, 3769 women; relative risk [RR] 0·78, 95% CI 0·68–0·90). Given increased underlying risk, absolute risk reduction was greater for women with a short cervix, hence treatment might be most useful for these women. Shared decision making with woman with high-risk singleton pregnancies should discuss an individual's risk, potential benefits, harms and practicalities of intervention. Treatment of unselected multifetal pregnancies with a progestogen was not supported by the evidence.

5.2 Pharmacokinetic properties

Absorption

Micronised progesterone is rapidly absorbed following vaginal administration. Unlike oral progesterone, vaginal progesterone does not undergo first pass metabolism in the gastrointestinal tract and liver. As a result of the "uterine first pass effect", relatively high concentrations occur in uterine and nearby tissues with low systemic exposure to progesterone and its metabolites.

The plasma exposure following administration of different vaginal dosages (e.g. 200 mg to 600 mg) is non-linear and increase less than proportional to dose. In a reported clinical study, administration of a 600 mg daily vaginal dose of progesterone resulted in stable plasma concentrations throughout administration times with the highest average plasma concentration equal to around 11.6 ng/ml.

Distribution

Micronised progesterone administered into the vagina undergoes the first metabolic cycle in the uterus, causing higher hormone levels in the uterus and nearby tissues.

The small amount of progesterone that is absorbed is transported via the lymph and blood vessels and approximately 96 - 99% is bound to serum proteins, mainly into serum albumin (50 - 54%) and transcortin (43 - 48%).

Biotransformation

After vaginal administration observable plasma levels of pregnenolone and 5α-dihydroprogesterone are very low due to the lack of first-pass metabolism.

Elimination

95% of systemically absorbed progesterone is eliminated from the urine as glucuronide conjugate metabolites.

Pharmacokinetic/pharmacodynamic relationship(s)

<invented name> provides a local effect on the vagina and uterus. The efficacy of vaginal progesterone is related to the overall amount of progesterone accumulating in the endometrium and not to the amount that is systemically absorbed.

5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of safety

pharmacology and toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:
Sunflower oil, refined
Soybean lecithin (E322)

Capsule shell:
Gelatin (E441)
Glycerol (E422)
Titanium dioxide (E171)
Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

The product is supplied in PVC/Aluminium blisters contained in cartons.
Pack sizes: Blister pack containing 15, 21, 45 or 90 soft vaginal capsules.
Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

<To be completed Nationally>

8. MARKETING AUTHORISATION NUMBERS

<To be completed Nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

10. DATE OF REVISION OF THE TEXT

<To be completed Nationally>

2026-02-04