SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Utrogestan 400 mg soft vaginal capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft vaginal capsule contains 400 mg progesterone (micronized).

Excipient with known effect:

Each soft vaginal capsule contains 4 mg soybean lecithin.

For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Soft vaginal capsule.

Yellowish, oblong (approximately 25 mm x 9 mm), soft vaginal capsule, containing a whitish oily suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

<invented name> is indicated for the prevention of miscarriage in women presenting with bleeding in the first trimester of pregnancy and have a history of recurrent miscarriages (see sections 4.2 and 5.1).

4.2 Posology and administration

Treatment should always be individualised to the patient. The decision to treat women who have experienced recurrent miscarriages should follow further investigation and is at the discretion of the clinician.

Posology

Vaginal use only.

The recommended dose is 800 mg/day, given in two divided doses, one in the morning and the other at bedtime. Treatment should be initiated during the first trimester of pregnancy, at first sign of vaginal bleeding (see Section 4.4 Special Warnings and Precautions for Use) and should continue to the 16th week of gestation.

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 <invented name> capsule 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

4.4 Special warnings and precautions for use

Warnings:

A complete medical examination must be performed before starting the treatment and regularly during the treatment.

<invented name> should only be used for threatened miscarriage during the first trimester; up to the 16th week of pregnancy and must only be administered by the vaginal route.

<invented name> is not suitable as a contraceptive and must only be used in accordance with the indications in section 4.1.

Treatment should be discontinued upon diagnosis of a missed abortion.

<invented name> is not intended to treat an imminent premature delivery

Precautions:

Any vaginal bleeding should always be investigated.

Excipient:

<invented name> contains soybean lecithin and may cause hypersensitivity reactions (urticarial 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 <invented name> (see Section 4.3).

<invented name> contain 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

Pregnancy

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

Breast-feeding

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

Fertility

As this medicinal product is indicated to prevent miscarriage in women, there is no known deleterious 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, 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.

The following frequency conventions are used in the rating of undesirable effects: Very common (≥1/10); Common (≥1/100 to < 1/10); Uncommon (≥1/1000 to < 1/100); Rare (≥1/10000 to < 1/1000); Very rare (< 1/10000); 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

Progesterone is a natural endogenous hormone of the corpus luteum and is the 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> has all the properties of endogenous progesterone with induction of a full secretory endometrium and in particular has a gestagenic, antiestrogenic, slightly anti-androgenic and antialdosterone effects.

The pharmacodynamic effects for threatened and recurrent miscarriage are that progesterone modulates maternal immune responses to protect the foetus, improves the utero-placental circulation, maintains cervical integrity throughout pregnancy, promotes myometrial relaxation, inhibits prostaglandin production, and possesses anti-inflammatory properties.

Clinical efficacy/safety studies

The efficacy and safety of micronized progesterone in preventing miscarriage in women, with dual risk factors of early pregnancy bleeding and previous history of miscarriages, was evaluated in the PRISM study. The benefit of treatment with vaginal progesterone 400 mg twice daily increased with an increasing number of prior miscarriages. The benefit reached statistical significance in the prespecified subgroup of women with three or more previous miscarriages and current pregnancy bleeding; live birth rate was 72% (98/137) with progesterone vs 57% (85/148) with placebo (rate difference 15%; risk ratio, 1.28, 95% CI, 1.08-1.51; P=.004). For this group, the number needed to treat was 8 (95% CI, 7-10). From a safety perspective, progesterone 400 mg was well tolerated.

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 reveal no special hazard for humans based on conventional studies of safety pharmacology and toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Content of capsule:

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 temperature storage conditions.

Store in the original packaging.

6.5 Nature and contents of container

<invented name>, is packed in a white HDPE bottle of 15 soft vaginal capsules, with a white Polypropylene (PP) child-resistant screw cap and a tearable silver coloured seal. The bottle is supplied in a cardboard carton.

PVC/Aluminium blisters containing 15, 30 or 45 capsules.

Not all pack sizes may be marketed

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

<To be completed Nationally>

8. MARKETING AUTHORISATION NUMBER(S)

<To be completed Nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<To be completed Nationally>

10. DATE OF REVISION OF THE TEXT

2026-02-04