Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Microgest 400mg soft gelatin capsules

2. Qualitative and quantitative composition

The Progesterone 400 mg Soft Gelatin Capsule are constituted by the active ingredient of Progesterone BP (Micronized).

Each Progesterone 400 mg Soft Gelatin Capsule contains 400 mg Progesterone BP (Micronized).

Excipients with known effect: soya bean lecithin
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Oblong shaped, off-white to yellowish colored soft gelatin capsule.
Approximately 26.2 mm x 10.5 mm

4. Clinical particulars

4.1 Therapeutic indications

Prometrium 400mg soft vaginal Capsules 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 method of administration

Posology

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.

Vaginal use only.

The recommended dose is 400 mg twice a day (morning and night). 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 Progesterone 400mg soft vaginal capsules in the paediatric population.

Elderly patients

There is no relevant use of Progesterone 400mg soft vaginal capsules in the elderly.

Method of administration

Vaginal
Each Progesterone 400mg soft vaginal capsule must be inserted deep into the vagina.

4.3 Contraindications

• Hypersensitivity to the active substance 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
• Allergy to nuts or soya (see Section 4.4)

4.4 Special warnings and precautions for use

Progesterone 200 mg soft gelatin Capsules should only be used during the first three months of pregnancy and must only be administrated by vaginal route. 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.
Progesterone 200 mg soft gelatin Capsules are not suitable in confirmed pregnancy (see section 4.6), in the treatment of premature labour, or as a contraceptive.
Treatment should be discontinued upon diagnosis of a missed abortion.

Precautions
A complete medical examination must be performed before starting the treatment and regularly during the treatment.
Progesterone 400mg soft vaginal capsules 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.
Progesterone 400mg soft vaginal capsules is not suitable as a contraceptive.
Treatment should be discontinued upon diagnosis of a missed abortion.

4.5 Interaction with other medicinal products and other forms of interaction

Enzyme inducers
Drugs known to induce the hepatic CYP450-3A4 such as barbiturates, anti-epileptic agents (phenytoin, carbamazepine), rifampicin, phenylbutazone, bromcriptine, spironolactone, griseofulvin, some antibiotics (ampicillins, tetracyclines) and also herbal products containing St. John's wort, [Hypericum perforatum] may increase metabolism and the elimination of progesterone.

Enzyme inhibitors
Ketoconazole and other inhibitors of CYP450-3A4 such as ritonavir and nelfinavir may increase bioavailability of progesterone.
The metabolism of progesterone by human liver microsonmes was inhibited by ketoconazole (IC50< 0.1µ M).

Immunosuppressants
Progesterone may raise the plasma concentration of ciclosporin.

Antisteroidal drugs
Aminoglutethimide markedly reduces the plasma concentrations of medroxyprogesterone acetate and megestrol, possibly through a hepatic enzyme inducing effect.

Anticoagulants
Progesterone may enhance or reduce the anticoagulant effect of coumarins.
Progesterone antagonises the anticoagulant effect of phenindione.

Diabetic medications
An adjustment in anti-diabetic dosage may be required for women being treated concomitantly with progesterone.

Emergency contraceptives
The concomitant use of ulipristal acetate with progesterone is expected to result in reduced efficacy of progesterone.

Diazepam
Progesterone may increase the plasma concentration of diazepam.

Tizanidine
Progesterone may increase the plasma concentration of tizanidine.

Terbinafine
There have been occasional reports of breakthrough bleeding when terbinafine is used concomitantly with progesterone.

Laboratory tests
Progesterone may affect the results of laboratory tests of hepatic and/or endocrine functions.

4.6 Pregnancy and Lactation

Pregnancy
No association has been found between the maternal use of natural progesterone in early pregnancy and foetal malformation.
Lactation
Progesterone 400 mg soft gelatin Capsules 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 subfertile or infertile women and to prevent miscarriage in women, there is no deleterious known effect on fertility.

4.7 Effects on ability to drive and use machines

This medicine can have a moderate influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
The reporting rate of adverse drug reactions with Progesterone Oral and Vaginal formulations was calculated as 1.43/1,000 patient year's corresponding to approximately 1.5 spontaneously reported cases in every 1000 patients exposed to Progesterone.

Following vaginal administration, 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.
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).

Table 2: Tabulated adverse effects following vaginal administration

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	Burning sensation

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms

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

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

Vaginally accumulated progesterone 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%).

Elimination

Urinary elimination is observed for 95% in the form of glycuroconjugated metabolites, mainly 3α, 5β–pregnanediol (pregnandiol).

5.3 Preclinical safety data

Progesterone is metabolised primarily by the liver.
Following vaginal administration, only low plasma levels of pregnanolone and 5α-dihydroprogesterone are detected, due to the lack of first-pass metabolism.

6 Pharmaceutical Particulars

6.1 List of Excipients

Table 3: List of excipients

Name of ingredients	Grade	Used as
EXCIPIENTS FOR MEDICINE PREPARATION		
All-rac-Alpha-tocopherol	BP/Ph. Eur.	Antioxidant
Arachis oil	BP	Vehicle
Lecithin liquid	Pharma Grade	Emulsifying Agent
EXCIPIENTS FOR SOFT GELATIN CAPSULE SHELL		
Gelatin Bloom 200	USP-NF	Capsule shell former
Glycerin	USP	Plasticizer
Methyl Paraben	USP-NF	Preservative
Propyl Paraben	USP-NF	Preservative
Titanium Dioxide	USP	Opacifier
Purified Water	Ph. Eur. /BP	Vehicle
Mineral Oil	USP	Vehicle
Arachis oil	BP	Vehicle

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

Two (2) years from the date of manufacturing

6.4 Special Precautions for storage

Do not store above 30 °C. Store in the original package in order to protect from the moisture.

6.5 Nature and Content of container

Alu-PVC blister pack contains 5 capsule and IFC contains 2 blister packs.

6.6 Special precautions for disposal and other handling

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

7 Marketing Authorization Holder

Renata Limited,
Plot # 1, Milk Vita Road,
Section - 7, Mirpur,
Dhaka -1216, Bangladesh.

Site of Manufacturing:
Renata Limited,

Rajendrapur Potent Product Facility
Noyapara, Bhawal Mirzapur, Rajendrapur,
Gazipur-1700, Bangladesh

8 Marketing Authorization Number
CTD10646

9 Date of first authorization/renewal of the authorization
30/05/2024

10 Date of revision of the text
09/05/2025