For the use of a Registered Medical Practitioner only.

1.0 GENERIC NAME & BRAND NAME

Progesterone Soft Gelatin Capsules 200 mg
Preservgest™ 200

Progesterone Soft Gelatin Capsules 400 mg
Preservgest™ 400

2.0 QUALITATIVE & QUANTITATIVE COMPOSITION

Preservgest™ 200
Each soft gelatin capsule contains:
Progesterone I.P. 200 mg
(Natural Micronized)
Excipients q.s.
Colour: Titanium Dioxide I.P.
(Methylparaben I.P. & Propylparaben I.P. used as preservatives)

Preservgest™ 400
Each soft gelatin capsule contains:
Progesterone I.P. 400 mg
(Natural Micronized)
Excipients q.s.
Colour: Titanium Dioxide I.P.
(Methylparaben I.P. & Propylparaben I.P. used as preservatives)

3.0 DOSAGE FORM & STRENGTH

Refer section 1 & 2

4.0 CLINICAL PARTICULARS

4.1 Therapeutic indications

A. Infertility and Pregnancy

- Luteal support during assisted reproductive techniques (ART)
- To provide luteal support in luteal phase defects
- Threatened abortion/recurrent abortion with proven luteal phase insufficiency/ defects
- Oocyte donation programme
- To prevent preterm delivery

B. Menstrual Irregularities

- As progesterone challenge test in secondary amenorrhoea
- Dysfunctional uterine bleeding (DUB)

C. Postmenopausal women

- Pre-menopause

- Prevention of endometrial hyperplasia in non-hysterectomised postmenopausal women who are receiving estrogen as Hormone Replacement Therapy (HRT)

D. Premenstrual syndrome

E. Benign Mastopathies

4.2 Posology and Method of Administration

Flexible dosage regimen can be followed depending on the indication and requirements of patients. Lower dose is required when vaginal route is used.
Vaginal Administration
Each capsule should be inserted deeply into the vagina. Rectal administration should be considered whenever vaginal administration is not possible.

- Luteal support during assisted reproductive techniques (IVF-ET): Progesterone 200 mg thrice a day from the day of embryo transfer till pregnancy is confirmed. If pregnant, it is continued till 12th week of pregnancy.
- To provide luteal support in luteal phase defects: Progesterone 100 mg thrice a day from the 17th day of the cycle for 10 days. If pregnant, it is continued till12th week of pregnancy.
- Threatened abortion / recurrent abortion with proven luteal phase insufficiency/defects: Progesterone 100 mg thrice a day till 12th week of pregnancy.
- Oocyte donation programme: 100 mg thrice daily from the day of embryo transfer till pregnancy is confirmed. If pregnant it is continued till 12th week of pregnancy.
- Prevention of preterm delivery: Progesterone 100 mg administered once daily at bedtime from 24th to 34th week of pregnancy.
- Oral Administration
- The evening dose/once daily dose is preferably taken at bedtime.
- In secondary amenorrhoea: Progesterone 400 mg daily at bedtime for 10 days.
- Dysfunctional uterine bleeding (DUB): Progesterone 300 mg once daily from 12th day of the cycle for 10 days.
- Postmenopausal women with intact uterus (in addition to estrogen treatment): Progesterone 200 mg at bed time for 12 days sequentially per 28 day cycle.
- Premenstrual syndrome: Progesterone 100-200 mg once daily from 14th day of the cycle for 10 days.

4.3 Contraindications

Known allergy or hypersensitivity to progesterone or to any of the excipients. The capsules contain arachis oil (peanut oil) and should never be used by patients allergic to peanuts. Severe hepatic dysfunction. Undiagnosed vaginal bleeding. Mammary or genital tract carcinoma. Thrombophlebitis. Thromboembolic disorders. Cerebral haemorrhage. Porphyria.

4.4 Special Warnings & Precautions

The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis).

Should any of these occur or be suspected, the drug should be discontinued immediately.

Discontinue medication pending examination if there is sudden, partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilloedema or retinal vascular lesions, medication should be withdrawn.

Natural micronized progesterone contains the hormone progesterone, which is present in significant concentrations in women during second half of menstrual cycle and during pregnancy. This should be borne in mind when treating patients with conditions that may be hormone-sensitive.
The utilization of natural micronized progesterone in the course of pregnancy is reserved to the first trimester and to the vaginal tract. Natural micronized progesterone is not a treatment against the risk of premature labor pains; the administration of micronized progesterone during the second and third trimester of pregnancy may result in appearance of severe cholestasis or hepatitis.
The pretreatment physical examination should include special reference to breast and pelvic organs, as well as Papanicolaou smear.
Vaginal administration is not recommended if barrier methods of contraception are used, if patient suffers from vaginal infection (especially moniliasis) or recurrent cystitis, in patients who have recently given birth. Rectal administration is advisable in this group of patients.
Because progesterone may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, diabetes, mild to moderate hepatic dysfunction, photosensitivity and breastfeeding mothers require careful observation.
In cases of breakthrough bleeding, as in any cases of irregular vaginal bleeding, nonfunctional causes should be considered. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated.
Patients who have a history of clinical depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.
Although concomitant use of conjugated estrogens and micronized progesterone capsules did not result in a decrease in glucose tolerance, diabetic patients should be carefully observed while receiving estrogen-progestin therapy.
It should be noted that, particularly in case of people who drive vehicles or operate machines, there is risk of drowsiness or giddiness associated with the use of this medicine.
Rare instances of syncope and hypotension of possible orthostatic origin have been observed in patients taking micronized progesterone capsules.
More than half of the spontaneous premature abortions are due to genetic abnormalities. Further infectious phenomena and mechanical troubles can be responsible for abortions.

4.5 Drug Interactions

Progesterone Capsules may interfere with the effects of bromocriptine and may raise the plasma concentration of cyclosporine. Progesterone Capsules may affect the results of laboratory tests of hepatic and/or endocrine functions.
Metabolism of Progesterone Capsules is accelerated by rifamycin an antibacterial agent. The metabolism of progesterone by human liver microsomes was inhibited by ketoconazole (IC50 <0.1µM Ketoconazole is a known inhibitor of cytochrome P450 3A4. These data therefore suggest

that ketoconazole may increase the bioavailability of progesterone. The clinical relevance of the in vitro findings is unknown.

4.6 Use in Special populations

RENAL IMPAIRMENT
No formal studies have evaluated the effect of renal disease on the disposition of progesterone. Since progesterone metabolites are eliminated mainly by the kidneys, micronized progesterone capsules should be used with caution and only with careful monitoring in patients with renal dysfunction.

HEPATIC IMPAIRMENT
No formal studies have evaluated the effect of hepatic disease on the disposition of progesterone. However, since progesterone is metabolized by the liver, use in patients with severe liver dysfunction or disease is contraindicated. If treatment with progesterone is indicated in patients with mild to moderate hepatic dysfunction, these patients should be monitored carefully.

PREGNANCY & LACTATION
Pregnancy: The administration of this medicine in the course of the second and third trimester of pregnancy can favour the appearance of severe cholestesis or hepatitis. Reproductive studies performed in mice reveal little or no evidence of impaired fertility or harm to the fetus due to progesterone.

Lactation: Detectable amounts of progesterone enter the breast milk. There is no indication for prescribing HRT during lactation.

PEDIATRIC USE
Natural micronized progesterone should not be used in children.

GERIATRIC USE
Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

4.7 Effects on ability to drive and use machines

Progesterone Capsules may cause transient dizziness and drowsiness and should be used with caution when driving a motor vehicle or operating machinery. Progesterone Capsules should be taken as a single daily dose at bedtime.

4.8 Undesirable Effects

Micronized progesterone is devoid of oestrogenic, androgenic and mineralocorticoid effects.

Oral Route
Drowsiness or giddiness may arise 1 - 3 hours after ingestion of the product. At times, there can

be breast tenderness and abdominal bloating. In case of drowsiness after 1 - 3 hours of oral administration, the dosage may be reduced or the patient may be put on once daily evening dose. Alternatively, the vaginal route of administration of the drug could be used.

Vaginal / Rectal Route
Soreness, diarrhoea, flatulence, irritation or dryness may occur when administered by these routes. As with other vaginal and rectal preparations, some leakage of the capsule base may occur.

Menses
The menstrual cycle may be shortened or there may by intermenstrual bleeding.
Menstruation may occur earlier than expected, or more rarely menstruation may be delayed. In case of shortening of menstrual cycle or intermittent bleeding shift the initiation of treatment to a later date (e.g. 19th day of cycle instead of 17th day).

4.9 Overdosage

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

5.0 PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

Progesterone is a natural progestogen, the main hormone of the corpus luteum and the placenta. It acts on the endometrium by converting the proliferating phase to the secretory phase. Progesterone Capsules have all the properties of endogenous progesterone with induction of a full secretory endometrium and in particular gestagenic, antiestrogenic, slightly anti-androgenic and anti-aldosterone effects.

5.2 Pharmacodynamic Properties
Progesterone is a naturally occurring steroid that is secreted by the ovary, placenta and adrenal gland. Its synthesis is stimulated by LH, which primarily acts to regulate the conversion of cholesterol to pregnenolone, a progesterone precursor. It is present in highest concentrations in the ovarian corpus luteum. Progesterone is lipophilic in nature and diffuses freely into cells, where it binds to the progesterone receptors and oxen their progestational activity. Progesterone receptors are located in the uterus, central nervous system, mammary glands and pituitary gland. The steroid receptor complex binds to DNA in the nucleus, thereby inducing the synthesis of specific proteins. Progesterone receptor concentrations are low in absence of oestrogen and increase following oestrogen administration. In the presence of adequate oestrogen, progesterone transforms a proliferative endometrium into a secretory endometrium. Progesterone is essential for the development of decidual tissue and the effect of progesterone on the differentiation of glandular epithelia and stroma has been extensively studied. Progesterone is necessary to increase endometrial receptivity for implantation of an embryo. Once an embryo is implanted, progesterone acts to maintain the pregnancy. Normal or near normal endometrial responses to exogenous oestrogen and progesterone have been noted in functionally a gonadal women through the sixth

decade of life. Progesterone administration decreases the circulatory levels of gonadotropins.

5.3 Pharmacokinetic Properties

Oral
Absorption: Micronized progesterone is absorbed by the digestive tract. Pharmacokinetic studies conducted in healthy volunteers have shown that after oral administration of 2 capsules (200mg), plasma progesterone levels increased to reach the Cmax of 13.8ng/ml +/- 2.9ng/ml in 2.2 +/- 1.4 hours. The elimination half-life observed was 16.8+/- 2.3 hours. Although there were inter-individual variations, the individual pharmacokinetic characteristics were maintained over several months, indicating predictable responses to the drug.

Distribution: Progesterone is approximately 96%-99% bound to serum proteins, primarily to serum albumin (50%-54%) and transcortin (43%-48%).

Elimination: Urinary elimination is observed for 95% in the form of glycuro-conjugated metabolites, mainly 3 a, 5 b–pregnanediol (pregnandiol).

Metabolism: Progesterone is metabolized primarily by the liver. Some progesterone metabolites are excreted in the bile and these may be deconjugated and further metabolized in the gut via reduction, dehydroxylation and epimerization. The main plasma and urinary metabolites are similar to those found during the physiological secretion of the corpus luteum.

Vaginal
Vaginal application results in avoidance of first-pass metabolism in the gastrointestinal tract and liver, and in sustained plasma concentrations. After vaginal administration of progesterone, plasma progesterone levels reach maximal concentrations within 3-8 hours, depending on the formulation used and gradually fall during the next 8 hours. Vaginally administered progesterone disappears more rapidly from the circulation than the I.M. Furthermore, higher doses are necessary of vaginal progesterone (100 mg) than of I.M. progesterone (25 mg) in order to achieve serum progesterone concentrations of the luteal phase range. The comparison of the same doses (300 mg) of micronized progesterone in a non-liquefying cream vaginally and capsules of micronized progesterone orally favoured the use of the vaginal formulation, since all the patients achieved luteal phase progesterone concentrations in the vaginal group compared with only two out of five patients in the oral group.

6.0 NON-CLINICAL PROPERTIES

6.1 Animal Toxicology & Pharmacology-
Progesterone has not been tested for carcinogenicity in animals by the oral route of administration. When implanted into female mice, progesterone produced mammary carcinomas, ovarian granulosa cell tumors and endometrial stromal sarcomas. In dogs, long-term intramuscular injections produced nodular hyperplasia and benign and malignant mammary tumors. Subcutaneous or intramuscular injections of progesterone decreased the latency period and increased the incidence of mammary tumors in rats previously treated with a chemical carcinogen. Progesterone did not show evidence of genotoxicity in in vitro studies for point mutations or for

chromosomal damage. In vivo studies for chromosome damage have yielded positive results in mice at oral doses of 1000 mg/kg and 2000 mg/kg. Exogenously administered progesterone has been shown to inhibit ovulation in a number of species and it is expected that high doses given for an extended duration would impair fertility until the cessation of treatment.

7.0 DESCRIPTION:

Preservgest 200- PRESERVGEST is supplied for oral administration, as a soft gelatin capsule of Progesterone. Each soft gelatin capsule of PRESERVGEST contains Progesterone 200 mg.

Preservgest 400- PRESERVGEST is supplied for oral administration, as a soft gelatin capsule of Progesterone. Each soft gelatin capsule of PRESERVGEST contains Progesterone 400 mg.

8.0 PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

Not applicable

8.2 Packaging Information

Refer Pack

8.3 Shelf-Life

Refer Pack

8.4 Storage and Handling Instructions

Refer Pack

9.0 PATIENT COUNSELLING INFORMATION

Preservgest™
Capsules 200 mg
Capsules 400 mg

Read this PATIENT INFORMATION before you start taking Progesterone Capsules and read what you get each time you refill your Progesterone Capsules prescription. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

1. WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT PRESERVGEST CAPSULES (A Progesterone Hormone)?

- Progestins with estrogens should not be used to prevent heart disease, heart attacks, strokes, or dementia.
- Using progestins with estrogens may increase your chance of getting heart attacks, strokes, breast cancer, and blood clots.
- Using progestins with estrogens may increase your chance of getting dementia, based on a study of women age 65 and older.
- You and your healthcare provider should talk regularly about whether you still need treatment with Progesterone Capsules.

THIS PRODUCT CONTAINS PEANUT OIL AND SHOULD NOT BE USED IF YOU ARE ALLERGIC TO PEANUTS.

2. What is PRESERVGEST Capsules?

PRESERVGEST Capsules contain the female hormone called progesterone.

2. What is PRESERVGEST Capsules used for?

Treatment of Menstrual Irregularities

PRESERVGEST Capsules are used for the treatment of secondary amenorrhea (absence of menstrual periods in women who have previously had a menstrual period) due to a decrease in progesterone. When you do not produce enough progesterone, menstrual irregularities can occur. f your healthcare provider has determined your body does not produce enough progesterone on its own, PRESERVGEST Capsules may be prescribed to provide the progesterone you need.

Protection of the Endometrium (Lining of the Uterus)-

PRESERVGEST Capsules are used in combination with estrogen-containing medications in a postmenopausal woman with a uterus (womb). Taking estrogen-alone increases the chance of developing a condition called endometrial hyperplasia that may lead to cancer of the lining of the uterus (womb). The addition of a progestin is generally recommended for a woman with a uterus to reduce the chance of getting cancer of the uterus (womb).

3. Who should not take PRESERVGEST Capsules?

Do not start taking PRESERVGEST Capsules if you:

- Are allergic to peanuts
- Have unusual vaginal bleeding
- Currently have or have had certain cancers
  Estrogen plus progestin treatment may increase the chance of getting certain types of cancers, including cancer of the breast or uterus. If you have or have had cancer, talk with your healthcare provider about whether you should take PRESERVGEST Capsules.
- Had a stroke or heart attack
- Currently have or have had blood clots
- Currently have or have had liver problems

- Are allergic to PRESERVGEST Capsules or any of its ingredients. See the list of ingredients in PRESERVGEST Capsules at the end of this leaflet.
- Think you may be pregnant

Tell your healthcare provider:

- If you are breastfeeding. The hormone in PRESERVGEST Capsules can pass into your breast milk.
- About all of your medical problems. Your healthcare provider may need to check you more carefully if you have certain conditions, such as asthma (wheezing), epilepsy (seizures), diabetes, migraine, endometriosis, lupus, problems with your heart, liver, thyroid, or kidneys, or have high calcium levels in your blood.
- About all the medicines you take. This includes prescription and non-prescription medicines, vitamins, and herbal supplements. Some medicines may affect how PRESERVGEST Capsules work. PRESERVGEST Capsules may also affect how your other medicines work.

2. How should I take PRESERVGEST Capsules?

- Prevention of Endometrial Hyperplasia: A postmenopausal woman with a uterus who is taking estrogens should take a single daily dose of 200 mg PRESERVGEST Capsules at bedtime for 12 continuous days per 28-day cycle.
- Secondary Amenorrhea: PRESERVGEST Capsules may be given as a single daily dose of 400 mg at bedtime for 10 days.
- PRESERVGEST Capsules are to be taken at bedtime as some women become very drowsy and/or dizzy after taking PRESERVGEST Capsules. In a few cases, symptoms may include blurred vision, difficulty speaking, difficulty with walking, and feeling abnormal. If you experience these symptoms, discuss them with your healthcare provider right away.
- If you experience difficulty in swallowing PRESERVGEST Capsules, it is recommended that you take your daily dose at bedtime with a glass of water while in the standing position.

3. What are the possible side effects of PRESERVGEST Capsules?

Side effects are grouped by how serious they are and how often they happen when you are treated:

Serious, but less common side effects include:

- Risk to the Fetus: Cases of cleft palate, cleft lip, hypospadias, ventricular septal defect, patent ductus arteriosus, and other congenital heart defects.
- Abnormal Blood Clotting: Stroke, heart attack, pulmonary embolus, visual loss or blindness.

Some of the warning signs of serious side effects include:

- Changes in vision or speech
- Sudden new severe headaches
- Severe pains in your chest or legs with or without shortness of breath, weakness and fatigue
- Dizziness and faintness
- Vomiting

Call your healthcare provider right away if you get any of these warning signs, or any other unusual symptoms that concern you.

Less serious, but common side effects include:

- Headaches
- Breast pain
- Irregular vaginal bleeding or spotting
- Stomach or abdominal cramps, bloating, Nausea and vomiting
- Hair loss
- Fluid retention
- Vaginal yeast infection

These are not all the possible side effects of PRESERVGEST Capsules. For more information, ask your healthcare provider or pharmacist for advice about side effects. You may report side effects by writing to **webmasterindia@abbott.com**

4. What can I do to lower my chances of getting a serious side effect with PRESERVGEST Capsules?

- Talk with your healthcare provider regularly about whether you should continue taking
- PRESERVGEST Capsules.
- See your healthcare provider right away if you get unusual vaginal bleeding while taking
- PRESERVGEST Capsules.
- Have a pelvic exam, breast exam, and mammogram (breast X-ray) every year unless your healthcare provider tells you something else. If members of your family have had breast cancer or if you have ever had breast lumps or an abnormal mammogram, you may need to have breast exams more often.
- If you have high blood pressure, high cholesterol (fat in the blood), diabetes, are overweight, or if you use tobacco, you may have higher chances for getting heart disease. Ask your healthcare provider for ways to lower your chances for getting heart disease.

General information about safe and effective use of PRESERVGEST Capsules:

- Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not take PRESERVGEST Capsules for conditions for which it was not prescribed.
- Your healthcare provider has prescribed this drug for you and you alone. Do not give PRESERVGEST Capsules to other people, even if they have the same symptoms you have. It may harm them.
- PRESERVGEST Capsules should be taken as a single daily dose at bedtime. Some women may experience extreme dizziness and/or drowsiness during initial therapy. In a few cases, symptoms may include blurred vision, difficulty speaking, difficulty with walking, and feeling abnormal. If you experience these symptoms, discuss them with your healthcare provider right away.
- Use caution when driving a motor vehicle or operating machinery as dizziness or drowsiness may occur.

Keep PRESERVGEST Capsules out of the reach of children.

This leaflet provides a summary of the most important information about PRESERVGEST

Capsules. If you would like more information, talk with your healthcare provider or pharmacist. You can ask for information about PRESERVGEST Capsules that is written for health professionals. You can get more information by writing to **webmasterindia@abbott.com**

10. DETAILS OF MANUFACTURER-

Refer Pack for manufacturer details.

Marketed by-
Abbott India Limited
Angel Space, Lifestyle Bldg. No. D-4,
Gala No. 7 to 10 & 17 to 20 Ground Floor,
107 to 110 & 117 to 120 First Floor,
Pimplas Village, Dist. Thane,
Bhiwandi - 421 302, India

11. DETAILS OF LICENCE NUMBER
Refer Pack for Permission/License details

12. DATE OF REVISION-
Version 3, dated 13th Sept 2023

For product complaints and queries please write to **webmasterindia@abbott.com**