For the use of a Registered Medical Practitioner only.

1.0 GENERIC NAME & BRAND NAME

Progesterone Sustained Release Tablets 200 mg
Preservgest™ SR 200

Progesterone Sustained Release Tablets 300 mg
Preservgest™ SR 300

Progesterone Sustained Release Tablets 400 mg
Preservgest™ SR 400

2.0 QUALITATIVE & QUANTITATIVE COMPOSITION

Preservgest™ SR 200
Each film coated sustained release tablet contains:

Progesterone I.P. (Natural Micronized)	200 mg
Excipients	q.s.

Colour: Titanium Dioxide I.P.

Preservgest™ SR 300
Each film coated sustained release tablet contains:

Progesterone I.P. (Natural Micronized)	300 mg
Excipients	q.s.

Colour: Titanium Dioxide I.P.

Preservgest™ SR 400
Each film coated sustained release tablet contains:

Progesterone I.P. (Natural Micronized)	400 mg
Excipients	q.s.

Colour: Titanium Dioxide I.P.

3.0 DOSAGE FORM & STRENGTH

Refer section 1 & 2

4.0 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of Secondary amenorrhea associated with normal Progesterone level in women

4.2 Posology and Method of Administration

Secondary amenorrhea: May be given as a single daily dose of 400 mg at bedtime for 10 days.

4.3 Contraindications

Progesterone sustained release tablets should not be used in women with any of the following conditions:

- In patients with a known hypersensitivity to its ingredients.
- Undiagnosed abnormal genital bleeding.
- Known, suspected, or a history of breast cancer
- Active deep vein thrombosis, pulmonary embolism or a history of these conditions.
- Active arterial thromboembolic disease (e.g. stroke and myocardial infarction), or a history of these conditions.
- Known liver dysfunction or disease.

4.4 Special Warnings & Precautions for use

Cardiovascular Disorders

An increased risk of pulmonary embolism, deep vein thrombosis (DVT), stroke and myocardial infarction has been reported with estrogen plus progestin therapy. Should any of these occur or be suspected, estrogen with progestin therapy should be discontinued immediately. Risk factors for arterial vascular disease (e.g., hypertension, diabetes mellitus, tobacco use, hypercholesterolemia, and obesity) and/or
thromboembolism

Endometrial Cancer

Clinical surveillance of all women using estrogen plus progestin therapy is important. Adding a progestin to estrogen therapy in postmenopausal women has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer.

Ovarian Cancer

Estrogen plus progestin sub study reported a statistically nonsignificant increased risk of ovarian cancer.

Vision Abnormalities

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 papilledema or retinal vascular lesions, medication should be permanently discontinued.

Fluid Retention
Progesterone may cause some degree of fluid retention. Women with conditions that might be influenced by this factor, such as cardiac or renal dysfunction warrant careful observation.

Dizziness and Drowsiness
Progesterone in sustained release formulation may cause transient dizziness and drowsiness and should be used with caution when driving a motor vehicle or operating machinery.
Should be taken as a single daily dose at bedtime. 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.

4.5 Drug Interactions
Drug Interactions - Ketoconazole or other known inhibitors of the cytochrome P4503A4 enzyme may increase the bioavailability of progesterone.

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 tablets 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.

4.6 Use in Special populations
Pregnancy /Lactation
Detectable amounts of progestin have been identified in the milk of nursing mothers receiving progestins. The effect of this on the nursing infant has not been determined. Hence, caution should be exercised when progesterone tablets are administered to a nursing mother.

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

4.8 Undesirable Effects

The menstrual cycle may be shortened or there may be intermenstrual bleeding. Menstruation may occur earlier than expected or, more rarely, menstruation may be delayed. In case of shortening of the menstrual cycle or intermittent bleeding, shift the initiation of treatment to a later date (e.g. the 19th day of the cycle instead of the 17th day). Adverse experiences reported were headache, breast pain, breast tenderness, joint pain, depression, dizziness, drowsiness or giddiness, abdominal pain, fatigue, abdominal distension,
abnormal bloating, hot flashes, nausea, vomiting, emotional liability and irritability. In clinical trials in patients with secondary amenorrhoea, overall, the most frequently reported treatemergent adverse reactions, reported in greater than or equal to 5% of subjects, were nausea, fatigue, vaginal mycosis, nasopharyngitis, upper respiratory tract infection, headache, dizziness, breast tenderness, abdominal distension, acne, dysmenorrhoea, mood swing and urinary tract infection.

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure:

Genitourinary System

Endometrial carcinoma, hypospadias, intrauterine death, menorrhagia, menstrual disorder, metrorrhagia, ovarian cyst, spontaneous abortion. Cardiovascular: circulatory collapse, congenital heart disease (including ventricular septal defect and patent ductus arteriosus), hypertension, hypotension, tachycardia.

Gastrointestinal

Acute pancreatitis, cholestasis, cholestatic hepatitis, dysphagia, hepatic necrosis, hepatitis, increased liver function tests (including alanine aminotransferase increased, aspartate aminotransferase increase, gamma glutamyl transferase increased), jaundice, swollen tongue. Skin: alopecia, pruritus, urticaria. Eyes: blurred vision, diplopia, visual disturbance.

Central Nervous System
Aggression, convulsion, depersonalization, depressed, consciousness, disorientation, dysarthria, loss of consciousness, paraesthesia, sedation, stupor, syncope (with and without hypotension), transient ischemic attack, suicidal ideation. During initial therapy, a few women have experienced a constellation of many or all of the following symptoms: extreme dizziness and/or drowsiness, blurred vision, slurred speech, difficulty walking, loss of consciousness, vertigo, confusion, disorientation, feeling drunk and shortness of breath.

Miscellaneous
Abnormal gait, anaphylactic reaction, arthralgia, blood glucose increased, choking, cleft lip, cleft palate, difficulty walking, dyspnoea, face oedema, feeling abnormal, feeling drunk, hypersensitivity, asthma, muscle cramp, throat tightness, tinnitus, vertigo, weight decreased, weight increased.

4.9 Overdosage

Although no studies on overdosage have been conducted in humans and there is a wide margin of safety with progesterone, overdosage may produce euphoria or dysmenorrhoea. In the case of overdosage, Progesterone sustained release tablets should be discontinued, and the patient should be treated symptomatically.

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 Tablets 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.

5.3 Pharmacodynamic Properties

Progesterone is lipophilic in nature and diffuses freely into cells, where it binds to the progesterone receptorsand exerts its progestational activity. The steroid receptor complex binds to DNA in the nucleus, thereby inducing the synthesis of specific proteins. Progesterone receptor concentrations are low in the absence of oestrogens and increase following oestrogen administration. Progesterone is a naturally occurring steroid that is secreted by the ovaries, placenta and adrenal glands. In the absence 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 oral oestradiol and intramuscular progesterone have been noted in functionally agonadal women through the sixth decade of life. Progesterone administration decreases the circulatory levels of gonadotropins.

5.3 Pharmacokinetic Properties

Oral route
The progesterone is absorbed through the digestive tract. The rise in progesterone starts from the first hour.
Progesterone is taken up by fat, from which it is slowly released. Circulating progesterone is extensively bound to plasma proteins, especially albumin and corticosteroid binding globulin. Only small amounts are associated with erythrocytes or platelets.
Progesterone is metabolized, mainly in the liver, by reduction of the A-ring, hydroxylation and conjugation. The principal metabolite is pregnanediol, other metabolites, notably 20α - dihydroprogesterone,which is present in small concentrations in plasma, and 5α-pregnane-3, 20 - dione, have weak progestational activity.
Progesterone undergoes extensive bio-transformation, mainly in the liver and in tissue such-as kidneys, brain, uterus and skin. The metabolites of progesterone are conjugated in the liver with glucuronic acid and excerted primarily in the urine;
A smaller quantity is excreted in the feces and there is extensive enterohepatic circulation of metabolites. Metabolites of progesterone are mainly excreted in the urine as glucuronide conjugates.

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 SR 200: PRESERVGEST is supplied for oral administration, as a sustained release tablets of Progesterone. Each film coated sustained release tablet of PRESERVGEST contains Progesterone 200 mg.

Preservgest SR 300: PRESERVGEST is supplied for oral administration, as a sustained release tablets of Progesterone. Each film coated sustained release tablet of PRESERVGEST contains Progesterone 300 mg.

Preservgest SR 400: PRESERVGEST is supplied for oral administration, as a sustained release tablets of Progesterone. Each film coated sustained release tablet of PRESERVGEST contains Progesterone 400 mg.

8. Pharmaceutical particulars

8.1 Incompatibilities

NA

8.2 Shelf-Life

Refer Pack

8.3 Packaging Information

Refer Pack

8.4 Storage and Handling Instructions

Refer Pack

9.0 PATIENT COUNSELLING INFORMATION

PRESERVGEST SR ™ Tablets 200 mg, 300 mg, 400 mg

Read this PATIENT INFORMATION before you start taking Progesterone Tablets and read what you get each time you refill your Progesterone Tablets 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.

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. What is PRESERVGEST SR Tablets?

PRESERVGEST SR Tablets contain the female hormone called progesterone.

What is PRESERVGEST SR Tablets used for?

Treatment of Secondary Amenorrhoea

4. Who should not take PRESERVGEST SR Tablets?

Do not start taking PRESERVGEST SR Tablets 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 SR Tablets.

Had a stroke or heart attack

Currently have or have had blood clots

Currently have or have had liver problems

Are allergic to PRESERVGEST SR Tablets or any of its ingredients. See the list of ingredients in PRESERVGEST SR Tablets at the end of this leaflet.

Think you may be pregnant

Tell your healthcare provider:

If you are breastfeeding. The hormone in PRESERVGEST SR Tablets 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 SR Tablets work. PRESERVGEST SR Tablets may also affect how your other medicines work.

5. How should I take PRESERVGEST SR Tablets?

Secondary Amenorrhea: PRESERVGEST SR Tablets may be given as a single daily dose of 400 mg at bedtime for 10 days.

PRESERVGEST SR Tablets are to be taken at bedtime as some women become very drowsy and/or dizzy after taking PRESERVGEST SR Tablets. 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 SR Tablets, it is recommended that you take your daily dose at bedtime with a glass of water while in the standing position.

6. What are the possible side effects of PRESERVGEST SR Tablets?

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 SR Tablets. For more information, ask your healthcare provider or pharmacist for advice about side effects. You may report side effects to webmasterindia@abbott.com

7. What can I do to lower my chances of getting a serious side effect with PRESERVGEST SR Tablets?

Talk with your healthcare provider regularly about whether you should continue taking PRESERVGEST SR Tablets.

See your healthcare provider right away if you get unusual vaginal bleeding while taking PRESERVGEST SR Tablets.

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 SR Tablets

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not take PRESERVGEST SR Tablets for conditions for which it was not prescribed.

Your healthcare provider has prescribed this drug for you and you alone. Do not give PRESERVGEST SR Tablets to other people, even if they have the same symptoms you have. It may harm them.

PRESERVGEST SR Tablets 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 SR Tablets out of the reach of children.

This leaflet provides a summary of the most important information about PRESERVGEST SR Tablets. If you would like more information, talk with your healthcare provider or pharmacist. You can ask for information about PRESERVGEST SR Tablets 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 PERMISSION OR LICENCE NUMBER

Refer Pack for Permission/License details

12. DATE OF REVISION-

Version 3.0, dated 31/05/2024

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