Med Choice™
Women's Health

Progesterone

℞

Progestedin®

200 mg Soft Gelatin Oral Capsule
PROGESTOGEN

FORMULATION:
Each soft gelatin capsule contains:
Progesterone USP ..... 200 mg
(Natural Micronized)
Excipients.....q. s.
(Methylparaben USP and Propylparaben USP are used as preservatives)

PRODUCT DESCRIPTION:
Soft Gelatin Capsules
Light yellow colored oil suspensions filled in a light-yellow color, oval shape (15 minim) soft gelatin capsules.

INDICATIONS:
Indicated for use in the prevention of endometrial hyperplasia in non-hysterectomized postmenopausal women who are receiving conjugated estrogen tablets. They are also indicated for use in secondary amenorrhea.

DOSAGE AND MODE OF ADMINISTRATION:
Prevention of Endometrial Hyperplasia
Capsules should be given as a single daily dose at bedtime, 200 mg orally for 12 days sequentially per 28-day cycle, to a postmenopausal woman with a uterus who is receiving daily conjugated estrogens tablets.
Treatment of Secondary Amenorrhea
Capsules may be given as a single daily dose of 400 mg at bedtime for 10 days.
Some women may experience difficulty swallowing capsules. For these women, capsules should be taken with a glass of water while in the standing position.
Premenstrual Syndrome, Benign Mastopathies, Menstrual Irregularities, Pre-Menopause
The treatment will be started at a dose of 200 mg to 300 mg per day, 10 days per cycle, usually from 14th day to until onset of menstruation.

CONTRAINDICATIONS:
Oral and vaginal administration:
- Severe liver disease (if the results of liver function tests have failed to return to normal), hepatic cell tumors, rotor syndrome and Dubin-Johnson syndrome;
- Hypersensitivity to progesterone or to any of the excipients.
- Thrombophlebitis, thromboembolic disorders, cerebral hemorrhage, or history of these conditions
- Carcinoma of the breasts
- Suspected or confirmed breast or genital organ neuplasia
- Undiagnosed vaginal bleeding.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
Progesterone capsules are not a treatment for premature labor. Prescription of progesterone beyond the first trimester of pregnancy may reveal gravidic cholestasis. Progesterone capsules are not suitable for use as a contraceptive. If unexplained, sudden or gradual, partial or complete loss of vision, proptosis or diplopia, papilloedema, retinal vascular lesions or migraine occur during therapy, the drug should be discontinued and appropriate diagnostic and therapeutic measures instituted. Progesterone capsules are intended to be co-prescribed with an estrogen product as hormone replacement therapy (HRT). Epidemiological evidence suggests that the use of HRT is associated with an increased risk of developing deep vein thrombosis (DVT) or pulmonary embolism. The prescribing information for the co-prescribed estrogen product should be referred to for information about the risks of venous thromboembolism.
There is suggestive evidence of a small increased risk of breast cancer with estrogen replacement therapy. It is not known whether concurrent progesterone influences the risk of cancer in postmenopausal women taking hormone replacement therapy. The prescribing information for the co-prescribed estrogen product should be referred to for information about the risks of breast cancer.

Progesterone should only be used in pregnancy during the first trimester and only by the vaginal route. Progesterone is not a treatment of threatening premature labor. The use of micronized progesterone during the second and third trimesters of pregnancy can lead to the development of cholestatic jaundice of pregnancy or hepato-cellular liver disease.

PRECAUTIONS:
Prior to taking hormone replacement therapy (and at regular intervals thereafter) each woman should be assessed. A personal and family medical history should be taken and physical examination should be guided by this and by the contraindications and warnings for this product. progesterone capsules should not be taken with food and should be taken at bedtime. Concomitant food ingestion increases the bioavailability of progesterone capsules.
Progesterone capsules should be used cautiously in patients with conditions that might be aggravated by fluid retention (e.g. hypertension, cardiac disease, renal disease, epilepsy, migraine, asthma); in patients with a history of depression, diabetes, mild to moderate hepatic dysfunction, migraine or photosensitivity and in breastfeeding mothers.
Clinical examination of the breasts and pelvic examination should be performed where clinically indicated rather than as a routine procedure. Women should be encouraged to participate in the national breast cancer screening programme (mammography) and the national cervical cancer screening programme (cervical cytology) as appropriate for their age. Breast awareness should also be encouraged and women are advised to report any changes in their breasts to their doctor or nurse.

DRUG INTERACTION:
Progesterone capsules may interfere with the effects of bromocriptine and may raise the plasma concentration of ciclosporin. 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 ($IC < 0.1$ μM). 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.

PREGNANCY AND LACTATION:
Pregnancy
Use of this medicine is not contraindicated during pregnancy. However, there is evidence of potential harm to the fetus (especially male fetus) during the first 4 months of pregnancy. Use during pregnancy is not recommended during the first 4 months, moreover, the use of this medicine during the second and third trimesters can lead to the development of hepatic diseases.

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

Effects on ability to drive and use machines
Progesterone capsules may cause drowsiness and/or dizziness in a minority of patients; therefore caution is advised in drivers and users of machines. Taking the capsules at bedtime should reduce these effects during the day.

ADVERSE DRUG REACTIONS:
Breakthrough bleeding, change in menstrual flow, amenorrhea, changes in cervical erosion and secretions, breast changes, edema, weight gain, catabolism, cholestatic jaundice, allergic reactions and rashes, acne, chloasma, mental depression, pyrexia, insomnia, somnolence, nausea, alopecia, hirsutism.

OVERDOSE AND TREATMENT:
Symptoms of overdosage may include somnolence, dizziness, euphoria or dysmenorrhea. Treatment is observation and, if necessary, symptomatic and supportive measures should be provided.

PHARMACOLOGICAL PROPERTIES:
Pharmacodynamic properties
Progesterone is a naturally occuring progestin or a synthetic form of the naturally occurring female sex hormone, progesterone. Progesterone shares the pharmacological actions of the progestins. Progesterone binds to the progesterone and estrogen receptors.
Target cells include the female reproductive tract, the mammary gland, the hypothalamus, and the pituitary. Once bound to the receptor, progestins like progesterone will slow the frequency of release of gonadotropin releasing hormone (GnRH) from the hypothalamus and blunt the pre-ovulatory LH (luteinizing hormone) surge. In women who have adequate endogenous estrogen, progesterone transforms a proliferative endometrium into a secretory one. Progesterone is essential for the development of decidual tissue and is necessary to increase endometrial receptivity for implantation of an embryo. Once an embryo has been implanted, progesterone acts to maintain the pregnancy. Progesterone also stimulates the growth of mammary alveolar tissue and relaxes uterine smooth muscle. It has little estrogenic and androgenic activity.

Pharmacokinetic properties
Absorption
After oral administration of progesterone as a micronized soft-gelatin capsule formulation, maximum serum concentrations were attained within 3 hours. The absolute bioavailability of micronized progesterone is not known.
Distribution
Progesterone is approximately 96 percent to 99 percent bound to serum proteins, primarily to serum albumin (50 to 54 percent) and transcortin (43 to 48 percent).
Metabolism
Progesterone is metabolized primarily by the liver largely to pregnanediols and pregnanolones. Pregnanediols and pregnanolones are conjugated in the liver to glucuronide and sulfate metabolites. Progesterone metabolites which are excreted in the bile may be deconjugated and may be further metabolized in the intestine via reduction, dehydroxylation, and epimerization.
Excretion
The glucuronide and sulfate conjugates of pregnanediol and pregnanolone are excreted in the bile and urine. Progesterone metabolites are eliminated mainly by the kidneys. Progesterone metabolites which are excreted in the bile may undergo enterohepatic recycling or may be excreted in the feces.

Preclinical safety data
Nonclinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction."

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

AVAILABILITY:
Alu-PVDC Blister Pack x 10's (Box of 30's, 60's and 100's).

DRP-11027-02
Date of First Authorization: January 17, 2023
Date of Revision of Package Insert: May 15, 2023

Manufactured by:
AKUMS DRUGS & PHARMACEUTICALS LTD.
(Plant IV-Hormonals)
Plot No. 47 & 48, Sector 6A, IIE, Sidcul,
Ranipur, Haridwar, Uttarakhand, India

Manufactured for:
UNOSOURCE PHARMA LTD.
503/504, 5th Floor, Hubtown Solaris, Prof NS Phadke Marg,
Andheri East, Mumbai, Maharashtra 400069, India

Imported by:
AMBICA INTERNATIONAL CORPORATION
No. 9 Amsterdam Extension, Merville Park Subd.,
Parañaque City, Metro Manila
www.ambicaglobal.com

Distributed by:
MEDCHOICE WOMEN'S HEALTH (MCWH), INC.
Unit 1002, 88 Corporate Center, Sedeño cor. Valero Sts.,
Salcedo Village, Makati, Metro Manila

xxxxxxxxx