Brand Name – Sugest Capsules [Natural Micronized Progesterone]

Therapeutic Category – Progesterones

FOR ORAL /VAGINAL USE

Drug Description:

Sugest (Progesterone) is synthesized from material initially taken from a plant and is chemically identical to human ovarian originated progesterone. Chemically, progesterone is Pregn-4-ene-3, 20 dione. Its molecular formula is C21H30O2 and its molecular weight is 314.47

Sugest Capsules are available in multiple strengths for dosage flexibility for optimum management. Sugest Capsules contain 100 mg, 200 mg or 400 mg micronized progesterone.

Indications & Dosage

Infertility and Pregnancy

- Luteal Support During Assisted Reproductive Techniques (ART)
- To Provide Luteal Support in Luteal Phase Defects [LPD]
- Threatened Abortion / Recurrent Pregnancy Loss [Luteal Phase Insufficiency/ Defects]
- Oocyte Donation Programme
- Prevention of Preterm Delivery

Menstrual Disorders

- Premenstrual Syndrome
- Menstrual Irregularities
- Benign Mastopathy

Post-Menopausal Women

- Prevention of Endometrial Hyperplasia in non - hysterectomized postmenopausal women receiving conjugated estrogens tablets

Dosage

Vaginal Route - Each Capsule must be Deeply Inserted into the Vagina
- 400 – 600 mg/day, starting on the day of HCG injection or ovulation day, up to the 12th week of pregnancy for ART Procedures[IVF, IUI] and Oocyte Donation Programme 11 / -
- 200 – 400 mg / day either in single or divided doses for Luteal Phase Defects and Luteal Phase Support in ART procedures
- 100 – 200 mg/day either in single or divided doses, starting from the 14th day of the menstrual cycle and continue the treatment till menstruation starts

Oral Route- Capsules must not be consumed along with food. The capsules must be taken either 1 hour before a meal or 1 hour after a meal. The capsule must not be crushed or opened, but consumed as whole along with water.

• 200 – 300 mg/day, 10 days per cycle, usually starting on the 14th day of the cycle up to commencement of menstruation for Premenstrual Syndrome, Benign Mastopathy, Menstrual irregularities, Pre-Menopause
• One 200 mg capsule/day taken nightly during the last 14 days of estrogen treatment per cycle. Estrogen should be given at the lowest effective dose. Patients being treated with high doses of estrogen should be given 300 mg Sugest capsules for Menopause. In case side effects occur with oral administration (such as drowsiness), or in case of severe hepatic disease, vaginal administration is a preferred alternative route.

Missed Dose

If a patient is treated with 200 mg daily (total dose at bedtime) and she forgets to take this dose, she should take an extra dose of one capsule (100 mg) the following morning and continue taking the rest of the capsules as prescribed. If a patient is treated with 300 mg daily, and she forgets to take a morning or evening dose, she should not take the missed dose. The Physician should be informed about the missed dose.

How Supplied

• **SUGEST 100**

Each soft gel capsule contains:
Progesterone B.P. ..... 100 mg
(Natural, Micronized)
Excipients ..... q. s.
Approved colors are used in the capsule shell.

• **SUGEST 200**

Each soft gel capsule contains:
Progesterone B.P. ..... 200 mg
(Natural, Micronized)
Excipients ..... q. s.
Approved colors are used in the capsule shell.

• **SUGEST 400**

Each soft gel capsule contains:
Progesterone B.P. ..... 400 mg
(Natural, Micronized)
Excipients ..... q. s.
Approved colors are used in the capsule shell.

Storage:

Store below 25o C (77o F). Protect from humidity and light

Shelf Life:

36 months as of manufacturing date.

Presentation

1. Each carton contains 2 blister packs of 10 Sugest 100 mg soft gel capsules / Strip
2. Each carton contains 2 blister packs of 10 Sugest 200 mg soft gel capsules / Strip
3. Each carton contains 1 blister pack of 10 Sugest 400 mg soft gel capsules / Strip

Adverse Drug Reactions

Nausea; vomiting; abdominal discomfort (cramps, pressure, pain, bloating , fatigue are some of the symptoms in susceptible individuals and usually resolve during the course of the time

Drug-Laboratory Interactions

Laboratory Tests

The following laboratory results may be altered by the use of progesterone: levels of gonadotropin, plasma progesterone, and urinary pregnanediol. The results of certain endocrine and liver function tests may be affected by progestin-containing products.The pathologist should be informed, about the medication.

Warnings

• Vision disturbances have been reported in some individuals, and must be reported to the Physician if any signs or symptoms are observed.
• The administration of any drug to nursing mothers should be undertaken only if clearly necessary, since many drugs are excreted in human milk. Detectable quantities of progestin have been identified in the milk of mothers receiving progestin. The effect on the nursing infant has not been determined

Precautions

General:
• Pre-treatment physical exam should include special reference to breasts and pelvic organs, as well as a Papanicolaou smear
• Administer with care in conditions such as epilepsy, migraine, asthma, cardiac or renal dysfunction
• Patients with a history of psychic depression should be carefully observed, and the drug should be discontinued if depression recurs to a serious extent.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Progesterone did not show evidence of genotoxicity in in-vitro studies for point mutations or for chromosomal damage. Exogenous administration of 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.

Pregnancy And Lactation

Although many studies have been unable to demonstrate an increment in teratogenicity when progesterone is given during the first trimester, the possibility of genital abnormalities in male and female fetuses exposed to progesterone during this period has been suggested in some studies.

Nursing Mothers

Detectable quantities of progesterone have been identified in the milk of nursing mothers. The effect of this on the nursing infant has not been determined.

Pediatric Use

This drug is not intended for pediatric use, and no clinical data have been collected on children. Therefore, the safety and effectiveness of Sugest capsules in pediatric patients have not been established.

Geriatric Use

There have not been sufficient numbers of geriatric women involved in clinical studies utilizing Sugest Capsules to determine whether those over 65 years of age differ from younger subjects in their response to Sugest Capsules.

Over-Dosage

Symptoms

The toxicity of progesterone is very low. Symptoms that may occur are: nausea, vomiting, somnolence and dizziness. No studies on over-dosage have been conducted in humans. In the case of over-dosage, Sugest Capsules should be discontinued and the patient should be treated symptomatically. There are no specific treatment modalities for over-dosage; however, standard procedures of gastric lavage etc. must be instituted under the supervision of an experienced Physician

Contraindications

Sugest Capsules (micronized progesterone) is contraindicated in patients with any of the following disorders:

• Hypersensitivity to this drug, soya, peanut or to any ingredient in the formulation of the capsule.
• Active hepatic dysfunction or disease, especially of the obstructive type
• Personal history of known or suspected estrogen-dependent or progestin-dependent malignant Neoplasia (e.g. breast cancer or endometrial cancer)
• Endometrial hyperplasia
• Undiagnosed abnormal genital bleeding
• Known or suspected pregnancy
• Active or past history of arterial thromboembolic disease (e.g. stroke, myocardial infarction, coronary heart disease)
• Classical migraine
• Active or past history of confirmed venous thromboembolism (such as deep venous thrombosis or pulmonary embolism) or active thrombophlebitis
• Partial or complete loss of vision due to ophthalmic vascular disease.

Clinical Pharmacology

Progesterone is a naturally produced steroid, which is secreted by the ovary, the placenta and the adrenal gland. In the presence of adequate estrogen, progesterone transforms the proliferating endometrium into a secretory endometrium. Progesterone is necessary to increase receptivity. Progesterone is necessary to increase receptivity of the endometrium for the embryo to implant. Once the embryo has implanted,

progesterone acts to preserve the pregnancy.

Pharmacokinetics:

Absorption:

Distribution:

Approximately 90% or more of the Progesterone binds to serum protein, mainly to serum albumin
Vaginal

Sugest capsules is well absorbed when administered by vaginal route. Vaginal administration of 100 – 400 mg produces a concentration in the luteal range which peaks within 1 – 8 hours and then declines over a 24-hour period.

Oral Route

Following oral administration of progesterone in the form of a micronized capsule, peak serum concentrations were achieved within 3 hours. Absolute bio-availability of micronized progesterone is not known. Serum concentrations of progesterone appeared in linear form.

Pharmaco-kinetic Parameters	**Progesterone Soft Gel Capsules [As per Published Literature]**	
	100 mg	200 mg
Cmax [ng/mL]	17.3 ± 21.9	38.1 ± 37.8
Tmax[hr]	1.5 ± 0.8	2.3 ± 1.4
AUC [ngxhr/mL]	43.3 ± 30.8	101.2 ± 66.0

The absolute bio-availability of micronized progesterone is not known

Values - Mean ± SD

Distribution

Approximately 90% or more of the Progesterone binds to serum protein, mainly to serum albumin.

Metabolism

Progesterone is metabolized mainly in the liver into pregnanediol and pregnanolone. Pregnanediol and pregnanolone are conjugated in the liver into glucuronides and sulphate metabolites. Progesterone metabolites which are excreted in the bile can be de-conjugated and can be metabolized again in the intestine by reduction, dehydroxilation and epimerization.

Excretion

The glucuronides and sulphate conjugates of pregnanediol and prenanolone are excreted in the bile and the urine. Progesterone metabolites excreted in the bile can undergo enterohepatic recycling, or can be excreted in the feces.

Special Populations

The Pharmaco-kinetics of Sugest Capsules have not been assessed in low body weight or obese patients.
Hepatic Insufficiency: The effect of hepatic impairment on the pharmacokinetics of Sugest Capsules has not been studied.
Renal Insufficiency: The effect of renal impairment on the pharmacokinetics of Sugest Capsules has not been studied.

Drug-Food Interactions

Concomitant food ingestion increased the AUC and Cmax values of Sugest Capsules, with no effect on Tmax relative to a fasting state when administered to post-menopausal women at a dose of 200 mg

Drug Interactions and Incompatibilities

1. Progesterone metabolism by human liver microsomes was inhibited by Ketoconazole. Ketoconazole is a known cytochrome P450 3A4 inhibitor and, therefore, this data suggest that Ketoconazole and other known inhibitors of this enzyme increment bio-availability. The clinical relevance of this findings in vitro is unknown.

2. Sugest capsules can interfere with the effect of Bromocriptine. Sugest capsules can increase plasma concentration of Cyclosporine.

3. The use of Sugest capsules with other vaginal products (such as anti-fungal products) is not recommended, since this can alter progesterone release and its vaginal absorption

Drug-Herb Interactions

It was found that some herbal products (e.g. St-John's wort), which are available as OTC products, might affect metabolism, and therefore, efficacy and safety of estrogen/progestin products.
Physicians and other health care providers should be aware of other non-prescription products concomitantly used by the patient, including herbal and natural products, obtained from the widely spread Health Stores.