# U-Progest®

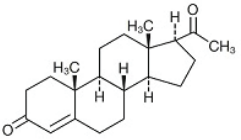
یو۔ پروجیسٹ

(Micronized Progesterone)

For oral / vaginal use

**QUALITATIVE AND QUANTITATIVE COMPOSITION**
**U-Progest 100mg Capsules:**
Each soft gel capsule contains:
Progesterone (Micronized).....100mg
**U-Progest 200mg Capsules:**
Each soft gel capsule contains:
Progesterone (Micronized).....200mg

**DESCRIPTION**
U-Progest Capsules contain micronized progesterone for oral/vaginal administration. Chemically, Progesterone is pregn-4-ene-3, 20-Dione. It has a molecular formula of $C_{21}H_{30}O_2$ and its molecular weight is 314.47. The structural formula is:



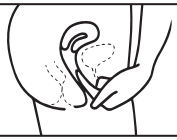
**INDICATIONS:**
1) Menace of habitual abortion or prevention of recurrent spontaneous abortions / threatened miscarriage due to diagnosed luteal phase defect.
2) Menace of preterm delivery / preterm birth.
3) Disorders associated with a progesterone deficit: pre-menstrual syndrome, menstrual irregularity, dysovulation, benign breast disease, pre-menopause.
4) Treatment of the menopause (as an adjuvant to oestrogen therapy).
5) Infertility caused by luteal phase defect.
6) Luteal support during In Vitro Fertilization cycles (IVF).

**Dosage**
The standard daily dosage regimen is 200 to 300 mg of progesterone taken in one or two doses, i.e. 200 mg in the evening at bedtime and another 100 mg in the morning, if needed.
**1)** ***In the case of threatened miscarriage / habitual abortion or in the prevention of LPD - related recurrent spontaneous abortions:*** the usual daily dosage is 200 mg to 400 mg progesterone, spread over two doses, to be taken up until gestation week 12.
**2)** ***In the case of threatened preterm delivery/preterm birth:*** 400 mg of progesterone every 6 to 8 hours, depending on the clinical results obtained during the acute phase, followed by a maintenance dose (e.g. 3 x 200 mg a day) to be taken up until gestational week 36.
**3)** ***In the case of luteal phase defect (pre-menstrual syndrome, menstrual irregularity, dysovulation, pre-menopause, benign breast disease):*** the daily dose is 200 mg progesterone, administered over 10 days per menstrual cycle, usually from cycle days 17 to 26 inclusive.
**4)** ***In the treatment of the menopause:*** given that stand-alone oestrogen therapy is not recommended, progesterone may be used as an adjuvant, to be given during the last two weeks of the treatment sequence, followed by a one-week suspension of all replacement therapy, during which withdrawal bleeding may be observed.
**5)** ***In the case of infertility associated with total luteal phase defect (oocyte donation):*** the initial progesterone dose is 100 mg, administered on days 13 and 14 of the transfer cycle, followed by 100 mg of progesterone given in the morning and evening of cycle days 15 to 25. From day 26 onwards, in the event of conception, dosage is increased in weekly increments of 100 mg progesterone per day, to reach a maximum daily dose of 600 mg progesterone, spread over three doses. This dosage is maintained up until day 60.
**6)** ***In the case of luteal phase supplementation during IVF:*** treatment is initiated in the evening of the transfer, at a rate of 600 mg progesterone spread over three doses (morning, noon and evening).

**Method of Administration:** Oral and Vaginal.

**Oral:** Best to take on an empty stomach because eating food can actually increase its absorption.

**Vaginal:** To be inserted deep into the vagina.



**Steps for vaginal administration**
- Wash your hands
- Remove the capsule from the blister
- Lie down on your back
- Bend your knees and part your thighs
- Push the capsule as deep into the vagina as is comfortable
- Straighten your legs and continue lying down for about 15 to 20 minutes to avoid leakage of the capsule base
- It is important to keep the capsule in the vagina to allow it to melt and the medicine to be absorbed
- Wash your hands

**Contraindications**
Known allergy or hypersensitivity to progesterone or to any of the excipients. Other contraindications include Severe hepatic dysfunction, Undiagnosed vaginal bleeding, Mammary or genital tract carcinoma, Thromboembolic or thrombophlebitis disorders, Cerebral haemorrhage and Porphyria.

**Warnings and Precautions**
This treatment, under the recommended conditions for use, is not a contraceptive. If the treatment schedule is initiated too early in the month, particularly before day 15 of the cycle, this may shorten the cycle or bleeding may occur.
- In the case of uterine bleeding, do not prescribe until a definite cause has been established, preferably via endometrial investigations.
- Due to the thromboembolic and metabolic risks which cannot totally be eliminated, treatment must be discontinued at the onset of:
- Eye disorders, such as loss of vision, diplopia, vascular lesions of the retina.
- Venous thromboembolisms or thrombotic events, regardless of the region.
- Severe headaches.
- Patients with a history of thrombophlebitis should be closely monitored.
- If amenorrhoea should occur during treatment, pregnancy must be excluded.
- More than half of spontaneous abortions are due to genetic complications. Furthermore, infectious manifestations and mechanical disorders may be responsible for miscarriages; in which case, the sole effect of administering progesterone would be a delay in the expulsion of a dead ovum. Progesterone administration must therefore only be reserved for cases where corpus luteum secretion is insufficient.

**Interactions**
Progesterone is metabolised primarily by the liver. Caution should be taken with drugs that are P450 enzyme inducers and inhibitors. Metabolism is inhibited by ketoconazole, which may increase the bioavailability of progesterone. Metabolism of progesterone is accelerated by P450 enzyme inducers such as barbiturates, antiepileptics (phenytoin), rifampicin, phenylbutazone, spironolactone and griseofulvin. Antibiotics (ampicillins, tetracyclines): changes intestinal flora leading to change in steroid enterohepatic cycle. May interfere with effects of bromocriptine and may raise the plasma concentration of cyclosporin. Progestogens, but not natural progesterone may impair glucose tolerance and, because of this, increase requirements for insulin or other antidiabetic agents in diabetic patients. Bioavailability of progesterone may be reduced by smoking and increased by alcohol abuse.

**Pregnancy and Breastfeeding**
Epidemiological studies have not revealed any association between progesterone and fetal malformations.

**Effects on ability to drive and use machines**
This medicine may cause drowsiness or dizziness; therefore, care should be taken when driving or using machines.

**Adverse Reactions**
The following effects have been observed:

| System organ class | Common undesirable effects ≥1/100; <1/10 | Uncommon adverse effects ≥1/1000; ≤1/100 | Rare undesirable effects ≥1/10 000; ≤1/1 000 | Very rare undesirable effects ≤1/10 000 |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| **Reproductive system and breast disorders** | Altered periods Amenorrhoea Intercurrent bleeding | Mastodynia | | |
| **Central nervous system disorders** | Headaches | Drowsiness Fleeting dizzy sensations | | Depression |
| **Gastrointestinal disorders** | | Vomiting Diarrhoea Constipation | Nausea | |
| **Hepatobiliary disorders** | | Cholestatic jaundice | | |
| **Immune system disorders** | | | | Urticaria |
| **Skin and subcutaneous tissue disorders** | | Pruritus Acne | | Chloasma |

Drowsiness and/or transient dizziness are observed particularly with concomitantly low levels of oestrogen. These effects are immediately reversible upon reduction of the dosage or escalation of the oestrogen dose, without compromising the therapeutic benefit.
If the treatment schedule is initiated too early in the month, particularly before day 15 of the cycle, this may shorten the cycle or intermenstrual bleeding may occur.
Altered menstrual cycles, amenorrhoea and intermenstrual bleeding have been observed and reported in association with general progestin use.
With oral administration, the undesirable effects described in Adverse Reactions are mostly symptomatic of overdosage. With vaginal administration, no case of overdose has so far been reported.

**Overdosage**
More often than not, the undesirable effects described above are signs of an overdose. They resolve spontaneously when the dosage is reduced. In some individuals, the usual dosage may prove to be too high, as evidenced by the persistence or recurrence of unstable endogenous progesterone secretion, marked sensitivity to the product or concomitantly low blood levels of oestradiol. In these cases, the following measures should be taken:
- In the event of drowsiness or transient dizziness, the dosage amount should be reduced or progesterone should be administered IN THE EVENING AT BEDTIME, over 10 days per cycle.
- In the event of spotting/shortening of the menstrual cycle, initiation of treatment should be deferred until later into the cycle (e.g. day 19 instead of day 17).
- Perimenopausal women/women receiving HRT should be tested to ensure that blood oestradiol levels are sufficient.

**PHARMACOLOGICAL PROPERTIES**
**Pharmacotherapeutic group:** Sex hormones and modulators of the genital system; Progestogens; Pregnen-(4) derivatives.
ATC code: G03DA04
**Pharmacodynamic properties**
Mechanism of Action
Progesterone (U-Progest), which contains progesterone in micronized form, significantly increases plasma progesterone levels following oral and vaginal administration, thus making it possible to correct any deficits in progesterone.
**Pharmacokinetics properties**
Absorption
Following oral administration, micronized progesterone is absorbed by the digestive tract. Pharmacokinetic studies conducted in healthy volunteers have shown that after oral administration of two 100 mg capsules (200mg), plasma progesterone levels increased to reach the $C_{max}$ 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.
Following vaginal administration, micronized progesterone is absorbed rapidly and achieves stable plasma levels in the range of 4-12 ng/ml, depending on the daily dose, with much less inter-subject variation than following oral administration.

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.
Elimination
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.

**PHARMACEUTICAL INFORMATION**
**Shelf life**
2 years

**Nature and Contents of Container**
U-Progest (Micronized Progesterone) 100 mg capsules are available in a blister pack of 30's (3 x 10's).
U-Progest (Micronized Progesterone) 200 mg capsules are available in a blister pack of 10's (1 x 10's).

**Instructions**
- Do not store above 30°C.
- Protect from light and moisture.
- Keep out of the reach of children.

**ہدایات:**
۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں۔
دوا کو روشنی اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔

**MANUFACTURED BY**

ASPIN
An OBS Group Company

**Aspin Pharma (Pvt.) Ltd.**
Plot No. 10 & 25, Sector No. 20,
Korangi Industrial Area, Karachi-74900, Pakistan.
www.aspin.com.pk

**REVISION DATE**
Oct 2024

UP-LF-C-01-01