

Dydrosky

(Dydrogesterone U.S.P.)

ڈائڈروسکی
(ڈائڈروسٹیرون یو. ایس. پی)

COMPOSITION

Each **Dydrosky** 10mg film-coated tablet contains 10 mg dydrogesterone.

"This product contains lactose"

MECHANISM OF ACTION

Dydrogesterone is an orally-active progestogen which produces a complete secretory endometrium in an estrogen-primed uterus thereby providing protection against the increased risk for endometrium hyperplasia and/or carcinogenesis induced by estrogens. It is indicated in all cases of endogenous progesterone deficiency. Dydrogesterone has no estrogenic, no androgenic, no thermogenic, no anabolic and no corticoid activity.

PHARMACOKINETIC PROPERTIES

Absorption: Following oral administration, dydrogesterone film-coated tablets, is rapidly absorbed. Maximum plasma concentrations are attained between 0.5 and 1.5 hours after dosing for the parent drug dydrogesterone and its active metabolite 20 α -dihydrodydrogesterone (DHD) respectively.

After a single dose, food delays the peak plasma concentration of dydrogesterone with approximately 1 hour, resulting in approximately 20% lower dydrogesterone peak plasma concentrations without affecting the extent of exposure to dydrogesterone and DHD. The observed effect of concomitant food intake on the peak plasma concentration of dydrogesterone is considered not clinically relevant. Therefore, Dydrogesterone film-coated tablets can be taken without regards to food.

Distribution: Dydrogesterone and DHD are more than 90% bound to plasma proteins. **Metabolism:** Following oral administration, dydrogesterone is rapidly metabolized to DHD. The levels of the main active metabolite DHD peak at similar times as Dydrogesterone. The mean terminal elimination half-lives of both dydrogesterone and DHD is about 15 hours.

Elimination: After oral administration of labeled dydrogesterone on average 63% of the dose is excreted into the urine. Within 72 hours excretion is complete. Dydrogesterone is completely metabolized. The main metabolite of dydrogesterone is 20 α -dihydrodydrogesterone (DHD) and is present in the urine predominantly as the glucuronic acid conjugate.

Dose and time dependencies: Comparison of the single and multiple dose kinetics shows that the pharmacokinetics of dydrogesterone and DHD are not changed as a result of repeated dosing. Steady state conditions are generally reached after 3 days of treatment.

INDICATIONS

Progesterone deficiencies:

- Treatment of dysmenorrhea
- Treatment of endometriosis
- Treatment of secondary amenorrhea
- Treatment of irregular cycles
- Treatment of dysfunctional uterine bleeding
- Treatment of pre-menstrual syndrome
- Treatment of threatened miscarriage
- Treatment of habitual miscarriage
- Treatment of infertility due to luteal insufficiency
- Luteal support as part of an Assisted Reproductive Technology (ART) treatment

Hormone replacement therapy:

To counteract the effects of unopposed estrogen on the endometrium in hormone replacement therapy for women with disorders due to natural or surgical induced menopause with an intact uterus.

DOSAGE AND ADMINISTRATION

Dosages, treatment schedule and duration of treatment may be adapted to the severity of the dysfunction and the clinical response.

Dysmenorrhea: 10 or 20 mg dydrogesterone per day from day 5 to day 25 of the menstrual cycle.

Endometriosis: 10 to 30 mg dydrogesterone per day from day 5 to day 25 of the cycle or continuously.

Dysfunctional uterine bleeding: When treatment is started to arrest a bleeding episode, 20 or 30 mg dydrogesterone per day is to be given for up to 10 days.

For continuous treatment, 10 or 20 mg dydrogesterone per day should be given during the second half of the menstrual cycle. The starting day and the number of treatment days will depend on the individual cycle length. Withdrawal bleeding occurs if the endometrium has been adequately primed with either endogenous or exogenous estrogen.

Secondary amenorrhea: 10 or 20 mg dydrogesterone per day, to be given daily for 14 days during the second half of the theoretical menstrual cycle to produce an optimum secretory transformation of an endometrium that has been adequately primed with either endogenous or exogenous estrogen.

Pre-menstrual syndrome: 10 mg dydrogesterone twice daily starting with the second half of the menstrual cycle until the first day of the next cycle. The starting day and the number of treatment days will depend on the individual cycle length.

Irregular cycles: 10 or 20 mg dydrogesterone per day starting with the second half of the menstrual cycle until the first day of the next cycle. The starting day and the number of treatment days will depend on the individual cycle length.

Threatened miscarriage: An initial dose of up to 40 mg dydrogesterone may be given followed by 20 or 30mg per day until symptoms remit.

Habitual miscarriage: 10 mg dydrogesterone twice daily until the twelfth week of pregnancy. Infertility due to luteal insufficiency: 10 or 20 mg dydrogesterone daily starting with the second half of the menstrual cycle until the first day of the next cycle. Treatment should be maintained for at least three consecutive cycles.

Luteal support as part of an Assisted Reproductive Technology (ART) treatment: 1 tablet of Dydrogesterone three times a day (30 mg daily) starting at the day of oocyte retrieval and continuing for 10 weeks if pregnancy is confirmed.

Hormone replacement therapy:

- Continuous sequential therapy: An estrogen is dosed continuously and one tablet of 10 mg dydrogesterone is added for the last 14 days of every 28-day cycle, in a sequential manner.
- Cyclic therapy: When an estrogen is dosed cyclically with a treatment-free interval, usually 21 days on and 7 days off. One tablet of 10mg dydrogesterone is added for the last 12-14 days of estrogen therapy.
- Depending on the clinical response, the dosage can subsequently be adjusted to 20 mg dydrogesterone per day.

There is no relevant use of dydrogesterone before menarche. The safety and efficacy of dydrogesterone in adolescents aged 12-18 years has not been established.

Method of administration:

- For oral administration of higher dosages, the tablets should be taken evenly distributed over the day

UNDESIRABLE EFFECTS

The most commonly reported adverse drug reactions of patients treated with dydrogesterone in clinical trials of indications without estrogen treatment are vaginal hemorrhage, migraines/headache, nausea, vomiting, abdominal pain, menstrual disorders and breast pain/tenderness.

DRUG INTERACTIONS

- The main active metabolite DHD is substrate for metabolic transformation by CYP3A4. Therefore, the metabolism of dydrogesterone and DHD may be increased by concomitant use of substances known to induce CYP enzymes such as anticonvulsants (e.g., phenobarbital, phenytoin, carbamazepine), anti-infectives (e.g., rifampicin, rifabutin, nevirapine, efavirenz) and herbal preparations containing e.g. St John's Wort (*Hypericum perforatum*), sage, or ginkgo biloba.
- Although known as strong cytochrome enzyme inhibitors, by contrast exhibit enzyme-inducing properties when used concomitantly with steroid hormones.
- Clinically, an increased metabolism of dydrogesterone may lead to a decreased effect.
- In vitro studies have shown that dydrogesterone and DHD do not inhibit or induce CYP drug metabolizing enzymes at clinically relevant concentrations.

SPECIAL WARNINGS AND PRECAUTIONS

Before initiating dydrogesterone treatment for abnormal bleeding the etiology for the bleeding should be clarified.

Breakthrough bleeding and spotting may occur during the first months of treatment. If breakthrough bleeding or spotting appears after some time on therapy, or continues after treatment has been discontinued, the reason should be investigated, which may include endometrial biopsy to exclude endometrial malignancy. Conditions which need supervision: If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with dydrogesterone and ceasing the treatment should be considered:

- Porphyria
- Depression
- Abnormal liver function values caused by acute or chronic liver disease
- **Other conditions:** Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- The following warnings and precautions apply when using dydrogesterone in combination with estrogens for hormone replacement therapy (HRT):
- See also the warnings and precautions in the product information of the estrogen preparation.
- For the treatment of postmenopausal symptoms, HRT should only be initiated for symptoms that adversely affect quality of life.
- **Medical examination / follow-up:** Before initiating or reinstituting HRT, a complete personal and family medical history should be taken. Physical (including pelvic and breast) examination should be done. During treatment, periodic check-ups are recommended. Breasts changes should be reported to the doctor or nurse. Investigations, including e.g., mammography, should be carried out.
- **Endometrial hyperplasia and carcinoma:** The addition of a progestogen such as dydrogesterone cyclically for at least 12 days per month/28 day cycle or continuous combined estrogen-progesterone therapy in nonhysterectomized women can prevent the excess risk associated with estrogen-only HRT.
- **Breast cancer:** The overall evidence shows an increased risk of breast cancer in women taking combined estrogen-progesterone or estrogen only HRT, that is dependent on the duration of taking HRT.
- **Ovarian cancer:** Ovarian cancer is much rarer than breast cancer.
- **Venous thrombo-embolism:** HRT is associated with a 1.3-3-fold risk of developing venous thromboembolism (VTE), i.e., deep vein thrombosis or pulmonary embolism.
- **Coronary artery disease (CAD):** The relative risk of CAD during use of combined estrogen-progesterone HRT is slightly increased.
- **Ischemic stroke:** Combined estrogen-progesterone and estrogen-only therapy are associated with an up to 1.5-fold increase in risk of ischemic stroke.

Pregnancy: Dydrogesterone may be administered during pregnancy if there is a clear indication for this

Breastfeeding: Dydrogesterone is excreted in the milk of nursing mothers. A risk to the suckling child cannot be excluded. Dydrogesterone should not be used during breast-feeding.

Fertility: There is no evidence that dydrogesterone decreases fertility at therapeutic dose.

Effects on Ability to Drive and Use Machines: Infrequently, dydrogesterone may cause mild somnolence and/or dizziness, especially within the first few hours after intake. Therefore, care should be taken when driving or using machines.

CONTRAINDICATIONS

- Known hypersensitivity to the active substance or to any of the excipients.
- Known or suspected progesterone dependent neoplasms (e.g. meningioma)
- Undiagnosed vaginal bleeding
- Treatment for luteal support as part of an Assisted Reproductive Technology (ART) treatment should be discontinued upon diagnosis of abortion/miscarriage.
- Contraindications for use of estrogens in combination with progestogens such as dydrogesterone in combined therapy.

OVERDOSE

Specific treatment is clearly not necessary. In case of overdose symptomatic treatment may be considered

PRESENTATION

Dydrosky 10mg tablet : 20's/pack.

DOSAGE

As directed by the physician.

INSTRUCTIONS

Store below 30°C.

Protect from sunlight & moisture.

Keep out of reach of children.

To be sold on the prescription of registered medical practitioner only.

Detailed prescribing information is available on request.

Manufactured for:
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An ISO Certified Company

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خوراک:

ڈائڈروسکی 10mg ٹیبٹل : 20's/پیکج۔

ہدایات:

دوا کو دوسری دوا کی پہچان سے کم درجہ حرارت پر رکھیں۔

دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مستند ڈاکٹر کے نسخے پر فروخت کی جائے۔