

ORALUTE

Tablets

Composition

Each tablet contains Medroxyprogesterone acetate 5 mg.

Action

Medroxyprogesterone acetate administered orally or parenterally in the recommended doses to women with adequate endogenous oestrogen, transforms proliferative into secretory endometrium. Androgenic and anabolic effects have been noted, but medroxyprogesterone acetate is apparently devoid of significant oestrogenic activity.

While parenterally administered medroxyprogesterone acetate inhibits gonadotropin production, which in turn prevents follicular maturation and ovulation, available data indicate that this does not occur when the usually recommended oral dosage is given as single daily doses.

Pharmacokinetics

Absorption: Medroxyprogesterone acetate is rapidly absorbed from the gastrointestinal tract after oral administration of the tablets. Mean time to peak serum levels is approximately 2 to 6 hours.

Distribution: Medroxyprogesterone acetate is 90 to 95% protein bound, with volume of distribution reported as 20+/- 3 liters. Medroxyprogesterone acetate crosses the blood - brain - barrier, and the placental barrier, and secreted in breast milk.

Metabolism: Numerous metabolites have been reported, however these have not been well quantified.

Excretion: The terminal half-life of orally administered medroxyprogesterone acetate is approximately 30 to 60 hours. Medroxyprogesterone acetate primarily excreted in the faeces, via biliary secretion, with approximately 44% of unchanged MPA excreted in the urine. Urinary metabolites classified in four groups; 1) non-conjugated neutrals, 2) glucuronide conjugated neutrals, 3) sulphate conjugated neutrals and 4) enzyme resistant acid fraction

Indications

- Secondary amenorrhea.
- Abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as fibroids or uterine cancer.
- Endometriosis.

Contraindications

- Thrombophlebitis, thromboembolic disorders, cerebral apoplexy or patients with a history of these conditions.
- Liver dysfunction or disease.
- Known or suspected malignancy of breast or genital organs.
- Undiagnosed vaginal bleeding.
- Missed abortion.
- As a diagnostic test for pregnancy.
- Known sensitivity to medroxyprogesterone acetate.

Warnings

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, this drug should be discontinued immediately.

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 withdrawn.

Pregnancy

Category X

Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Nursing Mothers

Progestin identified in detectable amounts in the milk of mothers receiving the drug. Although the effect on the nursing infants has not been determined, due caution should be exercised.

Adverse Reactions

Breasts

Breast tenderness or galactorrhoea reported rarely.

Skin

Sensitivity reactions consisting of urticaria, pruritus, edema and generalized rash have occurred occasionally. Acne, alopecia and hirsutism reported in a few cases.

Thromboembolic Phenomena

Thromboembolic phenomena, including thrombophlebitis and pulmonary embolism, have been reported.

The following adverse reactions observed in women taking progestins: breakthroughs bleeding, spotting, change in menstrual flow, amenorrhea, edema, change in weight (increase or decrease), change in cervical erosion and secretions, cholestatic jaundice, rash (allergic) with and without pruritus, and mental depression.

A statistically significant association demonstrated between the use of estrogen/progestin combination drugs and the following serious adverse reactions observed: thrombophlebitis, pulmonary embolism and cerebral thrombosis and embolism. For this reason, patients on progestin therapy carefully observed.

Precautions

The pre-treatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear.

Because progestins may cause some degree of fluid retention, conditions that might be influenced by this factor, such as epilepsy, migraine, asthma and cardiac or renal dysfunction, require careful observation.

In cases of breakthrough bleeding, as in all cases of irregular bleeding per vaginum, non-functional causes should be borne in mind.

In cases of undiagnosed vaginal bleeding, adequate diagnostic measures indicated.

Patients with a history of psychic depression should be carefully observed. If the depression recurs to a serious degree, the drug should be discontinued.

A decrease in glucose tolerance observed in a small percentage of patients on estrogen/progestin combination drugs. The mechanism of this decrease is obscure. For this reason, diabetic patients carefully observed while receiving progestin therapy.

The age of the patient constitutes no absolute limiting factor, although treatment with progestins may mask the onset of the climacteric.

The pathologist advised of progestin therapy when relevant specimens submitted. Because of the occasional occurrence of thrombotic disorders (thrombophlebitis, pulmonary embolism, retinal thrombosis, and cerebrovascular disorders) in patients taking estrogen/ progestin combinations and since the mechanism is obscure, physicians should be alert to the earliest manifestation of these disorders in patients receiving progestin therapy.

Dosage and Administration

Secondary Amenorrhea

Oralute may be given in dosages of 5-10 mg daily for 5-10 days. Therapy started at any time during the menstrual cycle.

A dose for inducing an optimum secretory transformation of an endometrium that has been adequately primed with either endogenous or exogenous estrogen is 10 mg of Oralute daily for 10 days.

Progestin withdrawal bleeding usually occurs within 3-7 days after discontinuing therapy with Oralute.

Abnormal Uterine Bleeding

Beginning on the calculated 16th or 21st day of the menstrual cycle, 5-10 mg of Oralute may be given daily for 5-10 days.

To produce an optimum secretory transformation of an endometrium that has been adequately primed with either endogenous or exogenous estrogen, a dosage of 10 mg of Oralute daily for 10 days, beginning on the 16th day of the cycle, is suggested.

Progestin withdrawal bleeding usually occurs within 3-7 days following discontinuing therapy with Oralute. Patients with a history of recurrent episodes of abnormal uterine bleeding may benefit from planned menstrual cycles using Oralute.

Mild to Moderate Endometriosis

Beginning on the 1st day of menstrual cycle, 10 mg of Oralute may be given 3 times a day, for 90 consecutive days.

Presentation

Box of 20 tablets.