

Norlutate® 

Erf Canada Inc.

Norethindrone Acetate

Progestational Agent

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Pharmacology: Norethindrone acetate differs from norethindrone only in potency; the acetate is approximately twice as potent.

Transforms proliferative endometrium into secretory endometrium. Inhibits (at the usual dose range) the secretion of pituitary gonadotropins, which in turn prevents follicular maturation and ovulation. May also demonstrate some estrogenic, anabolic or androgenic activity but should not be relied upon.

Indications: Amenorrhea; in abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer; and in endometriosis.

Contraindications: Thrombophlebitis, thromboembolic disorders, cerebral apoplexy or patients with a past history of these conditions; markedly impaired liver function or disease; known or suspected carcinoma of the breast; undiagnosed vaginal bleeding; missed abortion.

Warnings: **The use of progestational agents during the first 4 months of pregnancy is not recommended.** Progestational agents have been used beginning with the first trimester of pregnancy in an attempt to prevent habitual abortion or to treat threatened abortion. There is no adequate evidence that such use is effective and there is evidence of potential harm to the fetus when such drugs are given during the first 4 months of pregnancy. Furthermore, in the vast majority of women, the cause of abortion is a defective ovum, which progestational agents could not be expected to influence. In addition, the use of progestational agents, with their uterine-relaxant properties, in patients with fertilized defective ova may cause a delay in spontaneous abortion. Therefore, the use of such drugs during the first 4 months of pregnancy is not recommended. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One study estimated a 4.7 fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal test for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 in 1 000.

If the patient is exposed to Norlutate during the first 4 months of pregnancy or if she becomes

pregnant while taking this drug, she should be appraised of the potential risk to the fetus.

Precautions: Discontinue medication pending examination if there is a 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, withdraw the medication.

Lactation: Detectable amounts of progestogens have been identified in the milk of mothers receiving them. The effect of this on the nursing infant has not been determined.

Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking progestogens, the physician should be alert for the earliest manifestations of the disease.

Pregnancy: Masculinization of the female fetus has occurred when progestogens have been used in pregnant women. Birth defects have been reported in the newborns of women who had received progestogens during the first trimester of pregnancy.

Some beagle dogs treated with medroxyprogesterone acetate developed mammary nodules. Although nodules occasionally appeared in control animals they were intermittent in nature, whereas nodules in treated animals were larger and more numerous, and they persisted. There is no general agreement as to whether the nodules are benign or malignant. Their significance with respect to man has not been established.

The pretreatment physical examination should include special reference to breasts and pelvic organs, as well as a Papanicolaou smear.

Because this drug may cause some degree of fluid retention, particular caution is indicated in epilepsy, migraine, asthma, cardiac or renal dysfunction.

In cases of breakthrough bleeding, as in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated.

Patients who have a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.

Any possible influence of prolonged progestogen therapy on pituitary, ovarian, adrenal, hepatic or uterine functions awaits further study.

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

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

Advise the pathologist of progestagen therapy when relevant specimens are submitted.

Steroid hormones are metabolized by the liver; therefore, these drugs should be administered with caution in patients with impaired liver function.

Adverse Effects: The following adverse reactions have been observed in women taking progestogens: breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, changes in weight (increase or decrease), changes in cervical erosion and cervical secretions, cholestatic jaundice, rash (allergic) with and without pruritus, melasma or chloasma, mental

depression.

The pregnanediol determination may be altered by the use of progestogens. In addition, the following laboratory results may be altered by the concomitant use of estrogens with progestogens: hepatic function; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; increase in PBI, BEI and a decrease in T3 uptake; metyrapone test.

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

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions have been observed in patients receiving estrogen/progestogen combination drugs: rise in blood pressure in susceptible individuals, premenstrual like syndrome, changes in libido, changes in appetite, cystitis like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, itching. In view of these observations, patients on progestogen therapy should be carefully observed for their occurrence.

Dosage: Adapt dosage to the specific indications and therapeutic response of the individual patient. This dosage schedule assumes the interval between menses to be 28 days. Amenorrhea, abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology: 2.5 to 10 mg starting with the fifth day of the menstrual cycle and ending on the 25th day. Endometriosis: Initial daily dose of 5 mg for 2 weeks with increments of 2.5 mg/day every 2 weeks until 15 mg/day is reached. Therapy may be held at this level for from 6 to 9 months or until annoying breakthrough bleeding demands temporary termination.

Supplied: Each grooved, salmon-colored, slightly mottled tablet, debossed "PD" on one side, contains: norethindrone acetate 5 mg. Nonmedicinal ingredients: acacia, cornstarch, D&C Yellow No. 10, FD&C Red No. 3, lactose, magnesium stearate, sugar and talc. Energy: 1.4 kJ (0.34 kcal). Sodium: 0.30 mg. Gluten-, paraben-, sulfite- and tartrazine-free. Bottles of 30.

(Shown in Product Identification Section)