Composition

Luterone 250 Depot

Each ampoule of 1 ml contains Hydroxyprogesterone caproate 250 mg in a sterile oily solution.

Luterone 500 Depot

Each ampoule of 2 ml contains Hydroxyprogesterone caproate 500 mg in a sterile oily solution.

Action

A long-acting progestin, Luterone Depot has duration of action lasting 9-17 days. Luterone Depot prevents follicular maturation and ovulation by inhibiting the secretion of pituitary gonadotropins. Luterone Depot transforms proliferative endometrium into secretory endometrium. Luterone Depot inhibits spontaneous uterine contraction.

Pharmacokinetics

Absorption

Peak serum levels of hydroxyprogesterone caproate appeared after 3-7 days in non-pregnant female subjects following a single intramuscular injection of 1000 mg hydroxyprogesterone caproate. The elimination half-life of hydroxyprogesterone caproate was 7.8 (\pm 3.0) days. Once-weekly intramuscular administration of 1000 mg hydroxyprogesterone caproate to non-pregnant women resulted in trough concentration of 60.0 (\pm 14) ng/mL after 13 weeks.

Distribution

Hydroxyprogesterone caproate binds extensively to plasma proteins including albumin and corticosteroid binding globulins.

Metabolism

In vitro studies have shown that hydroxyprogesterone caproate can be metabolized by human hepatocytes, both by phase I and phase II reactions. Hydroxyprogesterone caproate undergoes extensive reduction, hydroxylation and conjugation. The conjugated metabolites include sulfated, glucuronidated and acetylated products. In vitro data indicate that the metabolism of hydroxyprogesterone caproate is predominantly mediated by CYP3A4 and CYP3A5. The in vitro data indicate that the caproate group is retained during metabolism of hydroxyprogesterone caproate.

Excretion

Both conjugated metabolites and free steroids are excreted in the urine and feces, with the conjugated metabolites being prominent. Following intramuscular administration to pregnant women at 10-12 weeks gestation, approximately 50% of a dose was recovered in the feces and approximately 30% recovered in the urine.

Indications

- Amenorrhea (primary and secondary).
- Functional uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer.
- Production of secretory endometrium and desquamation. Adenocarcinoma of uterine corpus in advanced stage (stage III or IV).
- Test for endogenous estrogen production.

Contraindications

- Known hypersensitivity to Hydroxyprogesterone caproate or other progestins.
- Use during the first 4 months of pregnancy is contraindicated.
- Hydroxyprogesterone caproate is contraindicated in patients who suffer from thrombophlebitis, cerebral hemorrhage, impaired liver function, thromboembolic disorders, miscarriage, suspected or incomplete abortion, carcinoma of the breast or reproductive organs, undiagnosed vaginal bleeding.

• Hydroxyprogesterone caproate should not be used as a diagnostic test for suspected pregnancy and a history of herpes gestationis.

Warnings & Precautions

Thromboembolic Disorders

Discontinue if an arterial or deep venous thrombotic or thromboembolic event occurs.

Allergic Reactions

Allergic reactions, including urticaria, pruritus and angioedema, have been reported with use of Hydroxyprogesterone. Consider discontinuing the drug if such reactions occur.

Decrease in Glucose Tolerance

A decrease in glucose tolerance has been observed in some patients on progestin treatment. The mechanism of this decrease is not known. Carefully monitor prediabetic and diabetic women while they are receiving Hydroxyprogesterone.

Fluid Retention

Because progestational drugs may cause some degree of fluid retention, carefully monitor women with conditions that might be influenced by this effect (e.g., preeclampsia, epilepsy, migraine, asthma, cardiac or renal dysfunction).

Depression

Monitor women who have a history of clinical depression and discontinue Hydroxyprogesterone if clinical depression recurs.

Jaundice

Carefully monitor women who develop jaundice while receiving Hydroxyprogesterone and consider whether the benefit of use warrants continuation.

Hypertension

Carefully monitor women who develop hypertension while receiving Hydroxyprogesterone and consider whether the benefit of use warrants continuation.

Pregnancy

Category D

There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Nursing Mothers

Hydroxyprogesterone is detected in breast milk. The effect on the infant has not been determined.

Adverse Reactions

Following the administration of Hydroxyprogesterone caproate, changes in the pattern of vaginal bleeding occur, including irregular cycle time, spotting, breakthrough bleeding, or complete lack of bleeding.

The following side effects occur less frequently: severe or sudden headaches, sudden loss of coordination, pains in the chest, pains in the groin or leg, sudden unexplained shortness of breath, sudden slurred speech, sudden changes in vision, weakness, numbness or pain in the arm or leg, galactorrhoea, hepatitis, gallbladder obstruction, skin rash or itching, mental depression, neuro-ocular lesions, bulging eyes, double vision, loss of vision (gradual, partial or complete), changes in appetite, changes in weight, edema, acne, fever, increased body and facial hair, increased breast tenderness, melasma or chloasma (brown blotchy spots on exposed skin), nausea, some loss of scalp hair, trouble in sleeping.

The patient should undergo physical examination prior to initiation of treatment. This examination should include the breasts and pelvic organs, and a Papanicolaou smear.

Fluid retention during therapy may occur. Therefore, conditions like epilepsy, migraine, asthma, cardiac or renal dysfunction require careful observation.

Patients who have a history of psychic depression must be monitored. Discontinue use of drug if depression recurs to a serious degree.

Diagnostic Interference

Laboratory test results of hepatic coagulation and endocrine functions may be affected in patients receiving this drug. Pregnanediol determination may be altered.

Dosage and Administration

Amenorrhea (primary and secondary) or Functional Uterine Bleeding

375 mg administered intramuscularly at any time during the menstrual cycle. After 4 days of desquamation, or 21 days after injection if there is no bleeding, start cyclic therapy (see cyclic therapy schedule below). Repeat cyclic therapy schedule every 4 weeks. Stop after 4 cycles. To determine onset of normal cyclic function, observe patient 2 or 3 cycles after cessation of therapy.

Production of Secretory Endometrium and Desquamation

For patients not on estrogen therapy, start cyclic therapy (see cyclic therapy schedule below). Repeat every 4 weeks until no longer required. Note that menstruation may not occur until estrogen has been given for several months, if estrogen deficiency has been prolonged.

Cyclic Therapy Schedule

20 mg estradiol valerate injection I.M. on day 1 of the cycle, followed by 250 mg injection of Luterone Depot and 5 mg estradiol valerate injection on day 15 of the cycle.

Adenocarcinoma of Uterine Corpus

In the treatment of advanced (stage III or IV) adenocarcinoma of the uterine corpus, administer 1 gram injections, repeating up to 7 times a week. Stop when relapse occurs, or after 12 weeks of therapy if there is no satisfactory result.

Test for Endogenous Estrogen Production

Administer a single injection of 250 mg. Repeat, if necessary, 4 weeks later. Stop after the second injection. In the non-pregnant patient with responsive endometrium, bleeding 7-14 days after injection indicates endogenous estrogen.

Pharmaceutical Precautions

Store below 30 °C, preferably between 15 °C and 30 °C.

Protect from freezing, in case freezing occurs, warm the ampoule with hot water until contents redissolve.

Presentation

Luterone Depot 250 Injection

Box of 5 ampoules.

Luterone Depot 500 Injection

Box of 1 ampoule.