Rehanzil™

Relugolix, Estradiol &
Norethindrone Acetate Tablet

2149

Presentation
Rehanzil™ : Each Tablet contains Relugolix INN 40 mg, Estradiol BP 1 mg & Norethindrone Acetate USP 0.5 mg.

Pharmacology
Rehanzil is a combination of Relugolix, Estradiol (E2), and Norethindrone Acetate (NETA). Relugolix is a non-peptide GnRH receptor antagonist that competitively binds to pituitary GnRH receptors, thereby reducing the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to decreased serum concentrations of the ovarian sex hormones estradiol and progesterone and reduced bleeding associated with uterine fibroids.

Estradiol acts by binding to nuclear receptors that are expressed in estrogen-responsive tissues. As a component of Rehanzil, the addition of exogenous estradiol may reduce the increase in bone resorption and resultant bone loss that can occur due to a decrease in circulating estrogen concentrations from Relugolix alone.

Progestins such as Norethindrone act by binding to nuclear receptors that are expressed in progesterone-responsive tissues. As a component of Rehanzil, norethindrone may protect the uterus from the potential adverse endometrial effects of unopposed estrogen.

Indications
Rehanzil is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women.

Dosage & Administration

Prior to Initiation of Rehanzil
- Exclude pregnancy
- Discontinue hormonal contraceptives

Recommended Dosage
- Take 1 tablet orally once daily at approximately the same time, with or without food
- Start Rehanzil as early as possible after the onset of menses but no later than seven days after menses has started
- The recommended total duration of treatment with Rehanzil is 24 months

Missed Dose
Take the missed dose of Rehanzil as soon as possible the same day and then resume regular dosing the next day at the usual time.

Side Effects
Most common adverse reactions (incidence ≥ 3%) are hot flush, hyperhidrosis or night sweats, uterine bleeding, alopecia, and decreased libido.

Precautions & Warnings
Cautions should be taken if patients have any one of the following:
Thromboembolic Disorders and Vascular Events, Bone Loss, Depression, Mood Disorders, and Suicidal Ideation, Hepatic Impairment and Transaminase Elevations, Elevated Blood Pressure, Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy, Risk of Early Pregnancy Loss, Uterine Fibroid Prolapse and Expulsion and Hypersensitivity Reactions.

Avoid or discontinue Rehanzil if patient have above complication or symptoms.

Contraindications
Rehanzil is contraindicated if patients have any one of the following:
High risk of arterial, venous thrombotic, or thromboembolic disorder, Pregnancy, Known osteoporosis, Current or history of breast cancer or other hormone-sensitive malignancies, Known hepatic impairment or disease, Undiagnosed abnormal uterine bleeding, Known hypersensitivity to components of Rehanzil.

Pregnancy & Lactation
Pregnancy: Rehanzil is contraindicated in pregnancy. Rehanzil may cause early pregnancy loss. Discontinue Rehanzil if pregnancy occurs during treatment.

Lactation: There are no data on the presence of Relugolix or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production Detectable amounts of estrogen and progestin have been identified in the breast milk of women receiving estrogen plus progestin therapy and can reduce mild production in breast-feeding women. This reduction can occur at any time but is less likely to occur once breast-feeding is well established.

Pediatric Use
Safety and effectiveness of Rehanzil in pediatric patients have not been established.

Hepatic Impairment
Rehanzil is contraindicated in women with hepatic impairment or disease. The use of E2 (a component of Rehanzil) in patients with hepatic impairment is expected to increase the exposure to E2 and increase the risk of E2-associated adverse reactions.

Drug Interactions
• *Combined P-gp and Moderate CYP3A Inhibitor:* Co-administration with Erythromycin (P-gp and moderate CYP3A inhibitor) increased the AUC and Cmax of Relugolix by 6.2-fold.
• *Combined P-gp and Strong CYP3A Inducer:* Co-administration with Rifampin (P-gp and strong CYP3A inducer) decreased the AUC and Cmax of Relugolix by 55% and 23%, respectively.
• *Other Drugs:* No clinically significant differences in the pharmacokinetics of Relugolix were observed when co-administered with Voriconazole (strong CYP3A inhibitor), Fluconazole (moderate CYP3A inhibitor), or Atorvastatin (weak CYP3A inhibitor). No clinically significant differences in the pharmacokinetics of Midazolam (sensitive CYP3A substrate) or Rosuvastatin (BCRP substrate) were observed upon co-administration with Relugolix.

Overdose
Overdosage of estrogen plus progestin may cause nausea, vomiting, breast tenderness, abdominal pain, drowsiness, fatigue, and withdrawal bleeding.
Supportive care is recommended if an overdose occurs. The amount of Relugolix, Estradiol, or Norethindrone removed by hemodialysis is unknown.

Storage Conditions
Do not store above 30 ºC. Keep away from light and out of the reach of children.

Commercial Pack
Rehanzil™: Each box contains 1 blister strip containing 10 tablets.

Manufactured by
Incepta Pharmaceuticals Ltd
Dhamrai Unit, Dhaka, Bangladesh
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