Golinum
(Elagolix)

Tablets 150mg & 200mg

گولِنیم
(اِلاگولیکس)

COMPOSITION

Golinum Tablets 150mg

Each film coated tablet contains:
Elagolix Sodium Eq. to
Elagolix.....150mg
Product Complies Innovator's Specs.

Golinum Tablets 200mg

Each film coated tablet contains:
Elagolix Sodium Eq. to
Elagolix.....200mg
Product Complies Innovator's Specs.

DESCRIPTION

Elagolix is an orally-administered, nonpeptide small molecule gonadotropin-releasing hormone (GnRH) receptor antagonist that inhibits endogenous GnRH signaling by binding competitively to GnRH receptors in the pituitary gland Label. Administration of elagolix results in dose-dependent suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to decreased blood concentrations of the ovarian sex hormones, estradiol and progesterone.

INDICATIONS AND USAGE

Elagolix is indicated for the management of moderate to severe pain associated with endometriosis.

Limitations of Use: Limit the duration of use based on the dose and coexisting condition.

DOSAGE AND ADMINISTRATION

As directed by the physician.

Important Dosing Information:

• Exclude pregnancy before starting Elagolix or start Elagolix within 7 days from the onset of menses.
• Take Elagolix at approximately the same time each day, with or without food.
• Use the lowest effective dose, considering the severity of symptoms and treatment objectives
• Limit the duration of use because of bone loss

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Exposure Registry There is a pregnancy registry that monitors outcomes in women who become pregnant while treated with Elagolix.

Risk Summary: Use of Elagolix is contraindicated in pregnant women. Exposure to Elagolix early in pregnancy may increase the risk of early pregnancy loss. Discontinue Elagolix if pregnancy occurs during treatment. The limited human data with the use of Elagolix in pregnant women are insufficient to determine whether there is a risk for major birth defects or miscarriage. Although two cases of congenital malformations were reported in clinical trials with Elagolix, no pattern was identified and miscarriages were reported at a similar incidence across treatment groups.

Lactation Risk Summary: There is no information on the presence of Elagolix or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. There are no adequate animal data on the excretion of Elagolix in milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Elagolix and any potential adverse effects on the breastfed child from Elagolix.

Females and Males of Reproductive Potential: Based on the mechanism of action, there is a risk of early pregnancy loss if Elagolix is administered to a pregnant woman

Pregnancy Testing: Elagolix may delay the ability to recognize the occurrence of a pregnancy because it may reduce the intensity, duration, and amount of menstrual bleeding. Exclude pregnancy before initiating treatment with Elagolix . Perform pregnancy testing if pregnancy is suspected during treatment with Elagolix and discontinue treatment if pregnancy is confirmed. Contraception Advise women to use effective non-hormonal contraception during treatment with Elagolix and for 28 days after discontinuing Elagolix.

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

Renal Impairment: No dose adjustment of Elagolix is required in women with any degree of renal impairment or end-stage renal disease (including women on dialysis)

Hepatic Impairment: No dosage adjustment of Elagolix is required for women with mild hepatic impairment (Child-Pugh A). Only the 150 mg once daily regimen is recommended for women with moderate hepatic impairment (Child-Pugh B) and the duration of treatment should be limited to 6 months. Elagolix is contraindicated in women with severe hepatic impairment (Child-Pugh C)

CLINICAL PHARMACOLOGY

Mechanism of Action:

Elagolix is a GnRH receptor antagonist that inhibits endogenous GnRH signalling by binding competitively to GnRH receptors in the pituitary gland. Administration of Elagolix results in dose-dependent suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to decreased blood concentrations of the ovarian sex hormones, estradiol and progesterone.

Pharmacodynamics:

Effect on Ovulation and Estradiol. In a 3-menstrual cycle study in healthy women, Elagolix 150 mg once daily and 200 mg twice daily resulted in an ovulation rate of approximately 50% and 32%, respectively. In the Phase 3 trials in women with endometriosis, Elagolix caused a dose-dependent reduction in median estradiol concentrations to approximately 42pg/mL for 150 mg once daily regimen and 12 pg/mL for the 200 mg twice daily regimen.

Cardiac Electrophysiology:

The effect of Elagolix on the QTc interval was evaluated in a randomized, placebo- and positive controlled, open-label, single-dose, crossover thorough QTc study in 48 healthy adult premenopausal women. Elagolix concentrations in subjects given a single dose of 1200 mg was 17-times higher than the concentration in subjects given Elagolix 200 mg twice daily. There was no clinically relevant prolongation of the QTc interval.

Patients with Renal Impairment:

Elagolix exposures (Cmax and AUC) are not altered by renal impairment. The mean exposures are similar for women with moderate to

severe or end stage renal disease (including women on dialysis) compared to women with normal renal function.

Patients with Hepatic Impairment:

Elagolix exposures (Cmax and AUC) are similar between women with normal hepatic function and women with mild hepatic impairment. Elagolix exposures in women with moderate and severe hepatic impairment are approximately 3-fold and 7-fold, respectively, higher than exposures from women with normal hepatic function.

Racial or Ethnic Groups:

No clinically meaningful difference in the pharmacokinetics of Elagolix between White and Black subjects or between Hispanics and others was observed. There is no clinically meaningful difference in the pharmacokinetics of Elagolix between Japanese and Han Chinese subjects. Body weight/Body mass index Body weight or body mass index does not affect the pharmacokinetics of Elagolix.

Drug Interaction Studies: Drug interaction studies were performed with Elagolix and other drugs that are likely to be co-administered and with drugs commonly used as probes for pharmacokinetic interactions. No clinically significant changes in Elagolix exposures were observed when co-administered with rosuvastatin (20 mg once daily), sertraline (25 mg once daily) or fluconazole (200 mg single dose).

Pharmacogenomics: Hepatic uptake of Elagolix involves the OATP 1B1 transporter protein. Higher plasma concentrations of Elagolix have been observed in patients who have two reduced function alleles of the gene that encodes OATP 1B1 (SLCO1B1 521T>C) (these patients are likely to have reduced hepatic uptake of Elagolix and thus, higher plasma Elagolix concentrations). The frequency of this SLCO1B1 521 C/C genotype is generally less than 5% in most racial/ethnic groups. Subjects with this genotype are expected to have a 78% mean increase in Elagolix concentrations compared to subjects with normal transporter function (i.e., SLCO1B1 521T/T genotype). Adverse effects of Elagolix have not been fully evaluated in subjects who have two reduced function alleles of the gene that encodes OATP1B1 (SLCO1B1 521T>C).

ADVERSE REACTIONS

- Bone loss
- Change in menstrual bleeding pattern and reduced ability to recognize pregnancy
- Suicidal ideation, suicidal behavior, and exacerbation of mood disorders.
- Hepatic transaminase elevations

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility Two-year carcinogenicity studies conducted in mice (50, 150, or 500 mg/kg/day) and rats (150, 300, or 800 mg/kg/day) that administered Elagolix by the dietary route revealed no increase in tumors in mice at up to 19-fold the MRHD based on AUC. In the rat, there was an increase in thyroid (male and female) and liver (males only) tumors at the high dose (12 to 13-fold the MRHD). The rat tumors were likely species-specific and of negligible relevance to humans. Elagolix was not genotoxic or mutagenic in a battery of tests, including the in vitro bacterial reverse mutation assay, the in vitro mammalian cell forward mutation assay at the thymidine kinase (TK+/-) locus in L5178Y mouse lymphoma cells, and the in vivo mouse micronucleus assay. In a fertility study conducted in the rat, there was no effect of Elagolix on fertility at any dose (50, 150, or 300 mg/kg/day). Based on AUC, the exposure multiple for the MRHD in women compared to the highest dose of 300 mg/kg/day in female rats is approximately 5-fold. However, because Elagolix has low affinity for the GnRH receptor in the rat, and because effects on fertility are most likely to be mediated via the GnRH receptor, these data have low relevance to humans.

Missed Dose: Instruct the patient to take a missed dose of Elagolix on the same day as soon as she remembers and then resume the regular dosing schedule.

- 150 mg once daily: take no more than 1 tablet each day.
- 200 mg twice daily: take no more than 2 tablets each day.

CONTRAINDICATIONS

Elagolix is contraindicated in women:

- Who are pregnant, as exposure to Elagolix early in pregnancy may increase the risk of early pregnancy loss.
- With known osteoporosis because of the risk of further bone loss
- With severe hepatic impairment.
- Taking inhibitors of organic anion transporting polypeptide (OATP)1B1 (a hepatic uptake transporter) that are known or expected to significantly increase Elagolix plasma concentrations.
- With known hypersensitivity reaction to Elagolix. Reactions have included anaphylaxis and angioedema.

PRESENTATION

Golinum(Elagolix) tablets 150mg are available in blister pack of 1x14's in a carton.

Golinum(Elagolix) tablets 200mg are available in blister pack of 1x14's in a carton.

INSTRUCTIONS

Store below 30°C in a dry place, protect from light. To be dispensed on the prescription of a registered medical practitioner only. Keep out of the reach of children.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر خشک جگہ پر رکھیں،
روشنی سے بچائیں۔ صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کریں۔
بچّوں کی پہنچ سے دُور رکھیں۔

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