

Pregolix®

120mg TABLETS

(Relugolix)

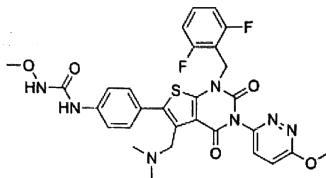
پریگولیکس
120 ملی گرام گولیاں
(ریلوگولیکس)

Each film coated tablet contains:

Relugolix ... 120 mg (Innovator's Specs).

Description

Pregolix® contains Relugolix, a gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the treatment of advanced prostate cancer. The chemical name of Relugolix is N-[4-[1-[(2,6-difluorophenyl)methyl]-5-[(dimethylamino)methyl]-3-(6-methoxypyridazin-3-yl)-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidin-6-yl]phenyl]-N'-methoxyurea. Its molecular formula is C₂₉H₂₇F₂N₇O₅S and the structural formula is:



Relugolix

Clinical Pharmacology

Mechanism of Action

Relugolix is a nonpeptide gonadotropin-releasing hormone (GnRH) receptor antagonist that competitively binds to pituitary GnRH receptors, thereby reducing the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and consequently testosterone. In men, this results in rapid and sustained suppression of testosterone to castrate levels without an initial testosterone surge.

Pharmacokinetics

Absorption

After oral administration, Relugolix is rapidly absorbed. The absolute bioavailability is approximately 12%. Peak plasma concentrations are reached at a median T_{max} of approximately 2.25 hours (range 0.5–5 hours). Food has no clinically meaningful effect on the pharmacokinetics of Relugolix.

After administration of a single 360 mg loading dose, the mean (± SD) AUC and C_{max} of Relugolix are 985 (± 742) ng·hr/mL and 215 (± 184) ng/mL, respectively. After administration of 120 mg once daily, the mean (± SD) steady-state AUC and C_{max} are 407 (± 168) ng·hr/mL and 70 (± 65) ng/mL, respectively.

Distribution

The plasma protein binding of Relugolix is 68%–71%, mainly to albumin and to a lesser extent to α₁-acid glycoprotein. Relugolix is widely distributed to tissues.

Metabolism

Relugolix is primarily metabolized by CYP3A and to a lesser extent by CYP2C8 in vitro. No major metabolites account for more than 10% of total drug-related material in plasma.

Excretion

Following oral administration of radiolabeled Relugolix, approximately 81% of the dose was recovered in feces (4.2% as unchanged drug) and 4.1% in urine (2.2% as unchanged drug). The mean effective half-life is approximately 25 hours, and the mean terminal elimination half-life is approximately 61 hours. Steady state is achieved within approximately 2 weeks of once-daily dosing.

Therapeutic Indications

Pregolix® (Relugolix) is indicated for the treatment of adult patients with advanced prostate cancer.

For the treatment of advanced hormone-sensitive prostate cancer, as specified in the approved prescribing information.

Key Clinical Effects

- Rapid suppression of testosterone to castrate levels
- No initial testosterone surge or clinical flare
- Sustained testosterone suppression with once-daily oral dosing
- Oral administration without the need for injections

Dosage and Administration

The recommended adult dose is a loading dose of 360 mg (three 120 mg tablets of Pregelox®) on the first day of treatment, followed by 120 mg (one tablet) taken orally once daily at approximately the same time each day.

Pregelox® can be taken with or without food. Tablets should be swallowed whole and not crushed or chewed.

If treatment is interrupted for more than 7 days, restart with a loading dose of 360 mg on the first day, followed by 120 mg once daily thereafter.

Adverse Reactions

The most common adverse reactions ($\geq 10\%$) and laboratory abnormalities ($\geq 15\%$) include: hot flush, glucose increased, triglycerides increased, musculoskeletal pain, hemoglobin decreased, alanine aminotransferase (ALT) increased, fatigue, aspartate aminotransferase (AST) increased, constipation, and diarrhea.

Other reported adverse reactions may include: weight increase, hypertension, hyperhidrosis, rash, nausea, decreased libido, erectile dysfunction, gynecomastia, insomnia, and depression.

Contraindications

Relugolix is contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients of the product.

Precautions

- Androgen deprivation therapy may prolong the QT/QTc interval. Correct electrolyte abnormalities (potassium, calcium, magnesium) prior to initiation and consider periodic monitoring of ECGs and electrolytes.
- Relugolix can cause fetal harm. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 2 weeks after the last dose.
- Monitor serum prostate-specific antigen (PSA) periodically. If PSA increases, measure serum testosterone concentrations.
- Use with caution in patients with a history of QT prolongation or concurrent use of medications known to prolong the QT interval.
- Relugolix should be used with caution in elderly patients and those with severe renal or hepatic impairment as appropriate.

Pregnancy & Nursing Mothers

Based on findings in animals and mechanism of action, Relugolix can cause fetal harm and loss of pregnancy when administered to a pregnant woman. There are no data on the presence of Relugolix or its metabolites in human milk, the effects on the breastfed child, or milk production. Advise women not to breastfeed during treatment with Pregelox® and for 2 weeks after the final dose.

Drug Interactions

P-gp Inhibitors

Concomitant use of Pregelox® with oral P-glycoprotein (P-gp) inhibitors may increase Relugolix exposure. Avoid co-administration with oral P-gp inhibitors. If unavoidable, take Pregelox® first and separate dosing by at least 6 hours.

Combined P-gp and Strong CYP3A Inducers

Concomitant use of Pregelox® with combined P-gp and strong CYP3A inducers may decrease Relugolix exposure. Avoid co-administration. If unavoidable, increase the Pregelox® dose to 240 mg once daily.

Other considerations

Androgen deprivation therapy may prolong the QT interval; use caution with drugs known to prolong the QT/QTc interval.

Overdosage

In the event of overdose, appropriate supportive treatment should be instituted according to the patient's clinical signs and symptoms. There is no specific antidote for Relugolix.

Storage

Do not store above 30°C in a dry place. Protect from sunlight, heat and moisture. The expiration date refers to the product correctly stored at the required conditions.

How Supplied

Pregolix® (Relugolix) 120 mg tablets are supplied in a blister pack of 20's.

Dosage: As directed by the physician.

Instructions: Store below 30°C at dry place. Protect from heat, light and moisture. Keep all medicines out of the reach of children. For oral use only. To be sold on the prescription of registered medical practitioner only.

Manufactured by:



Skywin Pharmaceuticals (Pvt.) Ltd.
Plot No. 01, Al Badar Industrial Estate, Phase II, 18
Km, Sheikhpura Road.

Manufactured for:

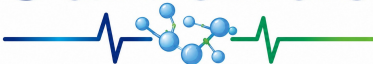


Wimits Pharmaceuticals (Pvt.) Ltd.
129, Sundar Industrial Estate, Lahore, Pakistan.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت اور خشک جگہ پر رکھیں۔ گرمی، نمی اور روشنی سے بچائیں۔ تمام
دوائیں بچوں کی پہنچ سے دور رکھیں۔ صرف منہ کے ذریعے استعمال کے لیے۔ صرف مستند ڈاکٹر کے نسخے کے
مطابق فروخت کریں۔

Marketed by:

Salventis



Salventis Pharma SMC (Pvt.) Ltd.

Bahria Town, Phase 4
Islamabad-Pakistan.