Ranolin™ XR

Ranolazine

PRESENTATION

Ranolin™ XR 500 tablet: Each extended release tablet contains Ranolazine INN 500 mg.
Ranolin™ XR 1 gm tablet: Each extended release tablet contains Ranolazine INN 1 gm.

PHARMACOLOGY

Ranolazine has anti-ischemic and antianginal effects that do not depend upon reductions in heart rate or blood pressure. The exact mechanism of action of ranolazine is unknown. Ranolazine at therapeutic levels can inhibit the cardiac late sodium current (I_{Na}). However, the relationship of this inhibition to angina symptoms is uncertain.
The QT prolongation effect of ranolazine on the surface electrocardiogram is the result of inhibition of I_{Kr}, which prolongs the ventricular action potential.

INDICATIONS & USES

Ranolazine is indicated for the treatment of chronic angina. Ranolazine may be used with beta-blockers, nitrates, calcium channel blockers, anti-platelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers. It has been shown to decrease angina episodes in patients with coronary artery disease on maximal doses of amlodipine. Because Ranolazine prolongs the QT interval, it should be reserved for patients who have not achieved an adequate response with other antianginal drugs. The effect on angina rate or exercise tolerance appeared to be smaller in women than men.

DOSAGE & ADMINISTRATION

Initiate Ranolazine dosing at 500 mg twice daily and increase to 1 gm twice daily, as needed, based on clinical symptoms. Take Ranolazine with or without meals. Ranolazine tablets whole; do not crush, break, or chew.

The maximum recommended daily dose of Ranolazine is 1 gm twice daily. If a dose of Ranolazine is missed, take the prescribed dose at the next scheduled time; do not double the next dose.

ADVERSE EFFECTS

Cardiac Disorders – bradycardia, palpitations; Ear and Labyrinth Disorders – tinnitus, vertigo; Gastrointestinal Disorders – abdominal pain, dry mouth, vomiting; General Disorders and Administrative Site Adverse Events – peripheral edema; Respiratory, Thoracic, and Mediastinal Disorders – dyspnea; Vascular Disorders – hypotension, orthostatic hypotension

CONTRAINDICATION

Ranolazine is contraindicated in patients:

- With pre-existing QT prolongation
- With hepatic impairment
- Taking QT prolonging drugs
- Taking potent and moderately potent CYP3A inhibitors such as ketoconazole, itraconazole, clarithromycin, nefazodone, nelfinavir, ritonavir, indinavir, and saquinavir, including diltiazem.

PRECAUTION

Ranolazine blocks I_{Kr} and prolongs the QTc interval in a dose-related manner. Clinical experience in an acute coronary syndrome population did not show an increased risk of proarrhythmia or sudden death.

Co-administration of ranolazine with digoxin increases the plasma concentrations of digoxin by approximately 1.5-fold and the dose of digoxin may have to be reduced accordingly. The dose of other P-gp substrates may have to be reduced as well when ranolazine is co-administered. Caution should be exercised when co-administering ranolazine with P-gp inhibitors such as ritonavir or cyclosporine.

DRUG INTERACTION

- *CYP 3A Inhibitors*: Do not use Ranolazine with strong CYP 3A inhibitors. With moderate CYP 3A inhibitors (e.g., diltiazem, verapamil, erythromycin) limit maximum dose of ranolazine to 500 mg twice daily.
- *CYP 3A Inducers*: Do not use Ranolazine with inducers.
- *P-gp Inhibitors (e.g., Cyclosporin)*: May need to lower the Ranolazine dose based on clinical dose.
- *Drugs transported by P-gp or metabolized by CYP2D6 (e.g., digoxin, TCA)*: May need reduced doses of these drugs when used with ranolazine.

USE IN PREGNANCY AND LACTATION

Pregnancy Category C. There are no adequate studies assessing the effect of ranolazine on the developing fetus. There are no adequate well-controlled studies in pregnant women. Ranolazine should be used during pregnancy only when the potential benefit to the patient justifies the potential risk to the fetus. It is not known whether ranolazine is excreted in human milk. Because of the potentiality for serious adverse reactions from ranolazine in nursing infants, a decision should be made whether to discontinue nursing or to discontinue Ranolazine, taking into account the importance of the drug to the mother.

USE IN CHILDREN

Safety and effectiveness in pediatric patients have not been established.

STORAGE

Store Ranolazine tablets at 25°C (77°F) with excursion permitted to 15° to 30°C (59° to 86°F). Protect from light and moisture.

HOW SUPPLIED

Ranolin™ XR 500 tablet: Each box containing 20 extended release tablets in Alu-PVC blister pack.
Ranolin™ XR 1 gm tablet: Each box containing 10 extended release tablets in Alu-PVC blister pack.

Manufactured by :

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH

TM- Trade Mark.

Revision No.00