EMERGENCY OVERVIEW

Ranolazine extended-release tablets are available as a film-coated, non-scored, extended-release tablet for oral administration. Ranolazine extended-release tablet may be used with beta-blockers, nitrates, calcium channel blockers, anti-platelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers. Ranolazine extended-release tablet dosing at 500 mg twice daily and increase to 1000 mg twice daily, as needed, based on clinical symptoms. Ranolazine extended-release tablet can be taken with or without meals or swallow Ranolazine extended-release tablet whole; do not crush, break, or chew it.

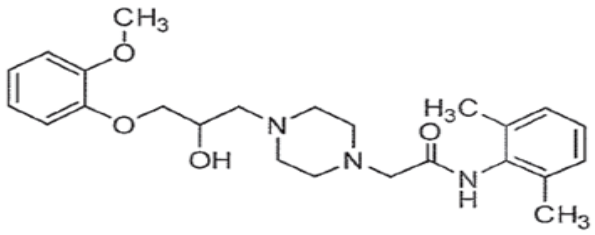
Section 1. IDENTIFICATION

Identification of the product

Product Name: Ranolazine Extended-Release Tablets 500mg/1000mg

Formula: $C_{24}H_{33}N_3O_4$

Chemical Name: 1-piperazineacetamide, N-(2,6-dimethylphenyl)-4-[2-hydroxy-3-(2-methoxyphenoxy)propyl]



Manufacturer / Supplier identification

Company:	**Cadila Healthcare Limited Baddi, India**
Address:	Cadila Healthcare Limited, Swaraj Majra, Judi Kalan, Post - Baddi, Tehsil - Nalagarh, District - Solan, Himachal Pradesh 173205.
Contact for information:	Tel: +91-1795-246841 Fax: +91-1795-246842
Emergency Telephone No.	Tel: +91-1795-246841
Recommended use /	
Therapeutic Category	Ranolazine is indicated for the treatment of chronic angina.
Restriction on Use / Contraindications:	Ranolazine is contraindicated in patients: Taking strong inhibitors of CYP3A Taking inducers of CYP3A With liver cirrhosis

Section 2. HAZARD(S) IDENTIFICATION

Dose and Administration

Initiate Ranolazine dosing at 500 mg twice daily and increase to 1000 mg twice daily, as needed, based on clinical symptoms. Take Ranolazine with or without meals. Swallow Ranolazine tablets whole; do not crush, break, or chew. The maximum recommended daily dose of Ranolazine is 1000 mg twice daily. If a dose of Ranolazine is missed, take the prescribed dose at the next scheduled time; do not double the next dose. Dose adjustments may be needed when Ranolazine is taken in combination with certain other drugs. Limit the maximum dose of Ranolazine to 500 mg twice daily in patients on moderate CYP3A inhibitors such as diltiazem, verapamil, and erythromycin. Use of Ranolazine with strong CYP3A inhibitors is contraindicated. Use of P-gp inhibitors, such as cyclosporine, may increase exposure to Ranolazine. Titrate Ranolazine based on clinical response.

Adverse Effects

The following additional adverse reactions occurred at an incidence of 0.5 to 4.0% in patients treated with Ranolazine and were more frequent than the incidence observed in placebo-treated patients:

Cardiac Disorders – bradycardia, palpitations

Ear and Labyrinth Disorders – tinnitus, vertigo

Eye Disorders – blurred vision

GI Disorders– abdominal pain, dry mouth, vomiting, dyspepsia

General Disorders & Administrative Site Adverse Events– asthenia, peripheral edema

Metabolism and Nutrition Disorders – anorexia

Nervous System Disorders – syncope (vasovagal)

Psychiatric Disorders – confusional state

Renal and Urinary Disorders – hematuria

Respiratory, Thoracic, and Mediastinal Disorders – dyspnea

Skin and Subcutaneous Tissue Disorders – hyperhidrosis

Vascular Disorders – hypotension, orthostatic hypotension

Over Dose Effect	High oral doses of Ranolazine produce dose-related increases in dizziness, nausea, and vomiting. High intravenous exposure also produces diplopia, paresthesia, confusion, and syncope. In addition to general supportive measures, continuous ECG monitoring may be warranted in the event of overdose. Severe tremor, unsteady gait/incoordination, dysphasia, and hallucinations have been reported in cases of overdose with Ranolazine. Since Ranolazine is about 62% bound to plasma proteins, hemodialysis is unlikely to be effective in clearing Ranolazine.
Contraindications	Ranolazine is contraindicated in patients: • Taking strong inhibitors of CYP3A • Taking inducers of CYP3A • With liver cirrhosis
Pregnancy Comments	Studies in rats and rabbits showed no evidence of fetal harm at exposures 4 times the maximum recommended human dose. In the U.S. general population, the estimated background risk of major birth defects and of miscarriage of clinically recognized pregnancies is 2-4% and 15-20%, respectively. Embryofetal toxicity studies were conducted in rats and rabbits orally administered Ranolazine during organogenesis. In rats, decreased fetal weight and reduced ossification were observed at doses (corresponding to 4-fold the AUC for the MRHD) that caused maternal weight loss. No adverse fetal effects were observed in either species exposed (AUC) to Ranolazine at exposures (AUC) equal to the MRHD.

Section 3. COMPOSITION/INFORMATION ON INGREDIENTS

Component	Exposure Limit	CAS No.
Principle Component:		
Ranolazine	Not Found	95635-55-5
Inactive Ingredients:		
Microcrystalline cellulose 101 (Comprecel M101D+)	Not Found	9004-34-6

Methacrylic acid copolymer [Type C] (Eudragit L 100-55)	Not Found	25212 – 88 – 8
Hypromellose 5 CPS, 2910 (Methocel E5 Premium LV)	Not Found	9004-65-3
Sodium hydroxide	Not Found	1310-73-2
Magnesium Stearate (Dr. Paul Lohmann)	Not Found	557-04-0
Opadry 02B565003 Brown (500mg)	Not Found	Not Available
Opadry 02B520004 Yellow (1000mg)	Not Found	Not Available

Section 4. FIRST-AID MEASURES

Eye Contact: In case of contact with eyes rinse thoroughly with plenty of water and get medical advice.

Skin Contact Immediately wash skin with soap and plenty of water for at least 15 minutes. Remove contaminated clothing. Get medical attention if symptoms occur. Wash clothing before reuse.

Inhalation Remove to fresh air. If not breathing, give artificial respiration or give oxygen by trained personnel. Get immediate medical attention.

Ingestion Wash out mouth with water provided person is conscious. Never give anything by mouth to an unconscious person. Get medical attention. Do NOT induce vomiting unless directed to do so by medical personnel.

Section 5. FIRE FIGHTING MEASURES

Flash Point Not data available

Extinguishing Media Use alcohol-resistant foam, carbon dioxide, water, or dry chemical spray. Use water spray to cool fire-exposed containers.

Unsuitable fire extinguishing media A Solid water- stream may be inefficient.

Unusual Fire and Explosion Hazards Not available

Explosive limits No data available

Auto ignition point Not available

Section 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	Avoid raising and breathing dust, and provide adequate ventilation. As conditions warrant, wear a NIOSH approved self-contained breathing apparatus, or respirator, and appropriate personal protection (rubber boots, safety goggles, and heavy rubber gloves).
Methods and materials for containment and cleaning up	Contain spill and collect, as appropriate. Transfer to a chemical waste container for disposal in accordance with local regulations.
Environmental precautions	Take steps to avoid release into the environment, if safe to do so.

Section 7. HANDLING AND STORAGE

Storage	Avoid breathing dust/ fume/ gas/ mist/ vapors/spray. Avoid prolonged or repeated exposure.
Precautions for safe handling	Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature.

Section 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Respiratory Protection	Use a NIOSH/MSHA approved respirator if there is a risk of exposure to dust/fume at levels exceeding the exposure limits. However, no personal respiratory protective equipment normally required.
Skin protection	For prolonged or repeated skin contact use suitable protective gloves.
Eye/face protection	If contact is likely, safety glasses with side shields are recommended.
Protective Clothing	Protective clothing is not normally necessary, however it is good practice to use apron.
Thermal hazards	Wear appropriate thermal protective clothing, when necessary.

General hygiene considerations	Handle in accordance with good industrial hygiene and safety practice.
Engineering controls	Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Section 9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Form	**Ranolazine extended-release tablets, 500 mg** are light orange colored, oval shaped, beveled edge, biconvex, film coated tablets debossed with "588" on one side and plain on other side **Ranolazine extended-release tablets, 1000 mg** are pale yellow colored, oval shaped, beveled edge, biconvex, film coated tablets debossed with "589" on one side and plain on other side

Section 10. STABILITY AND REACTIVITY

Stability	Stable under recommended storage conditions.

Section 11. TOXILOGICAL INFORMATION

Carcinogenesis, Mutagenesis, Impairment of Fertility

Ranolazine tested negative for genotoxic potential in the following assays: Ames bacterial mutation assay, Saccharomyces assay for mitotic gene conversion, chromosomal aberrations assay in Chinese hamster ovary (CHO) cells, mammalian CHO/HGPRT gene mutation assay, and mouse and rat bone marrow micronucleus assays.

There was no evidence of carcinogenic potential in mice or rats. The highest oral doses used in the carcinogenicity studies were 150 mg/kg/day for 21 months in rats (900 mg/m2/day) and 50 mg/kg/day for 24 months in mice (150 mg/m2/day). These maximally tolerated doses are 0.8 and 0.1 times, respectively, the daily maximum recommended human dose (MRHD) of 2000 mg on a surface area basis. A published study reported that ranolazine promoted tumor formation and progression to malignancy when given to transgenic APC (min/+) mice at a dose of 30 mg/kg twice daily [see References (15)]. The clinical significance of this finding is unclear.

In male and female rats, oral administration of ranolazine that produced exposures (AUC) approximatelty 3-fold or 5-fold higher, respectively, than the MRHD had no effect on fertility.

Section 12. ECOLOGICAL INFORMATION

Do not allow product to enter drinking water supplies, wastewater or soil.

Section 13. DISPOSAL CONSIDERATION

Disposal Recommendations Dispose the waste in accordance with all applicable Federal, State and local laws.

Section 14. TRANSPORT INFORMATION

The product is not hazardous when shipping via air (IATA), ground (DOT), or sea (IMDG).

Section 15. REGULATORY INFORMATION

Generic Medicine, ANDA Number 210188

Section 16. OTHER INFORMATION

The information presented in the safety data sheet is correct to the best our knowledge, accurate and reliable. It characterizes the product with regard to the appropriate safety precautions. It does not represent a guarantee of the properties of the product.