MICRO LABS LIMITED, BANGALORE, INDIA			
1	Product Name	Cartinex / Cartinex-OD	Colours Used
2	Strength		■ BLACK
3	Component	Leaflet	
4	Category	Export - Philippines	
5	Dimension	120 x 170 mm	
6	Artwork Code	EXG-ML01I-1170	
7	Pharma Code	N/A	
8	Reason for Change	New	

	Prepared by (DTP)	Checked by (PD)	Approved by			
			Head CQA	Head Production (Site)	Head QC (Site)	Head QA (Site)
Sign	Kantharaju L.					
Date	30-01-2015					

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RANOLAZINE

CARTINEX / CARTINEX-OD

ANTI-ANGINA

FORMULATION:
Ranolazine 500 mg (Cartinex):
Each extended-release tablet contains: Ranolazine …….....…… 500 mg.

Ranolazine 1 g (Cartinex-OD):
Each extended-release tablet contains: Ranolazine…….....……. 1g.

PHARMACOKINETICS:
Absorption: After oral administration of ranolazine, peak plasma concentrations (Cmax) are typically observed between 2 and 6 hours. Steady state is generally achieved within 3 days of twice-daily dosing. The mean absolute bioavailability of ranolazine after oral administration of immediate-release ranolazine tablets ranged from 35−50%, with large inter-individual variability. There was a 2.5- to 3-fold increase in steady-state AUC as the dose was increased from 500 mg to 1 g twice daily. *Distribution & Plasma Protein Binding:* Approximately 62% of ranolazine is bound to plasma proteins. The mean steady-state volume of distribution (Vss) is about 180 L. *Metabolism:* Ranolazine is eliminated primarily by metabolism. *Elimination:* Less than 5% of the dose is excreted unchanged in the urine and faeces. The elimination half life is about 2−3 hours after intravenous administration. The terminal half-life at steady state after oral administration of ranolazine is about 7 hours, due to the absorption rate-limited elimination.

INDICATIONS:
Ranolazine is indicated for the treatment of angina pectoris in patients who have not responded satisfactorily to other antianginals and should be given as an adjunct to standard therapy.

CONTRAINDICATIONS:
Ranolazine is contraindicated in patients with
- Hypersensitivity to the active substance or to any of the excipients.
- Severe renal impairment (creatinine clearance < 30 mL/min).
- Moderate or severe hepatic impairment.
- Concomitant administration of potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, posaconazole, HIV protease inhibitors, clarithromycin, telithromycin, nefazodone).
- Concomitant administration of Class Ia (e.g. quinidine) or Class III (e.g. dofetilide, sotalol) antiarrhythmics other than amiodarone.

DRUG INTERACTIONS:
Ranolazine is a substrate of cytochrome CYP3A4. Inhibitors of CYP3A4 increase plasma concentrations of ranolazine. The potential for dose-related adverse events (e.g. nausea, dizziness) may also increase with increased plasma concentrations. Combining ranolazine with potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, posaconazole, HIV protease inhibitors, clarithromycin, telithromycin, nefazodone) is contraindicated. Ranolazine is a substrate for P-gp. Inhibitors of P-gp (e.g. ciclosporin, quinidine, verapamil) increase plasma levels of ranolazine. Careful dose titration of ranolazine is recommended in patients treated with P-gp inhibitors. Ranolazine is partially metabolised by CYP2D6; therefore, inhibitors of this enzyme may increase plasma concentrations of ranolazine. An increase in plasma digoxin concentrations by an average of 1.5-fold has been reported when ranolazine and digoxin are co-administered. Therefore, digoxin levels should be monitored following initiation and termination of ranolazine therapy. There is a theoretical risk that concomitant treatment of ranolazine with other drugs known to prolong the QTc interval may give rise to a pharmacodynamic interaction and increase the possible risk of ventricular arrhythmias. Examples of such drugs include certain antihistamines (e.g. terfenadine, astemizole, mizolastine), certain antiarrhythmics (e.g. quinidine, disopyramide, procainamide), erythromycin, and tricyclic antidepressants (e.g. imipramine, doxepin, amitriptyline).

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ADVERSE EFFECTS:
Adverse events like anorexia, decreased appetite, dehydration, anxiety, insomnia, dizziness, headache, blurred vision, visual disturbance, hot flush, hypotension, dyspnoea, cough, epistaxis, constipation, vomiting, nausea, abdominal pain, dry mouth, dyspepsia, flatulence, stomach discomfort, asthenia have been reported.

PRECAUTIONS AND WARNINGS:
Caution should be exercised when prescribing or up titrating ranolazine to patients in whom an increased exposure is expected:
- Concomitant administration of moderate CYP3A4 inhibitors.
- Concomitant administration of P-gp inhibitors.
- Mild hepatic impairment.
- Mild to moderate renal impairment (creatinine clearance 3080 mL/min).
- Patients with low weight (60 kg).
- Patients with moderate to severe Congestive Heart Failure (CHF) NYHA Class III/IV.

The risk for increased exposure leading to adverse events in these different subgroups is higher in patients lacking CYP2D6 activity (poor metabolisers, PM) than subjects with CYP2D6 metabolising capacity (extensive metabolisers, EM). Renal function decreases with age and it is therefore important to check renal function at regular intervals during treatment with ranolazine. Caution should be observed when treating patients with a history of congenital or a family history of long QT syndrome, in patients with known acquired QT interval prolongation, and in patients treated with drugs affecting the QTc interval.

DOSAGE & ADMINISTRATION:
Initiate Ranolazine dosing at 500 mg twice daily and increase to 1 g 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 1 g 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 diltiazem, verapamil, and other moderate CYP3A inhibitors. Down-titrate Ranolazine based on clinical response in patients concomitantly treated with P-gp inhibitors, such as ciclosporin.

AVAILABILITY:
Ranolazine 500 mg (Cartinex) Alu/amber-colored PVC/PVDC Blister pack by 10's (Box of 30's)
Ranolazine 1 g (Cartinex-OD) Packed in Alu/PVC Blister pack by 10's (Box of 30's)

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

Manufactured by:
MICRO LABS LIMITED
92, Sipcot, Hosur - 635 126,
Tamil Nadu, India

Imported and Distributed by:
BROWN & BURK PHILIPPINES, INC.
U-501, 5/F SEDCCO 1 Bldg., 120 Rada cor.
Legaspi Sts., Legaspi Village, Makati City

EXG-ML01I-1170

Size: 120 x 170 mm