RABEPRAZOLE SODIUM

BAROLE 10 / BAROLE 20

Proton Pump Inhibitor

FORMULATION

BAROLE 10

Each capsule contains:
Rabeprazole Sodium 10mg
(As enteric coated pellets)

BAROLE 20

Each capsule contains:
Rabeprazole Sodium 20mg
(As enteric coated pellets)

INACTIVE INGREDIENTS:

Non pareil seeds, Hypromellose, Methacrylic acid copolymer dispersion, Macrogol, Purified Talc, Light Magnesium Carbonate, Sodium Hydroxide, Titanium dioxide, Ferric oxide (Red), Ferric oxide (black).

INDICATIONS:

Treatment of severe (erosive and ulcerative) gastro-esophageal reflux disease, treatment of active peptic ulcer disease and for Zollinger - Ellison syndrome.

CLINICAL PHARMACOLOGY:

Rabeprazole belongs to a class of antisecretory compounds (substituted benzimidazole proton-pump inhibitors) that do not exhibit anticholinergic or histamine H_2 – receptor antagonist properties, but suppress gastric acid secretion by inhibiting the gastric H^+,K^+ ATPase at the secretory surface of the gastric parietal cell. Because this enzyme is regarded as the acid(proton) pump within the parietal cell, Rabeprazole has been characterized as a gastric proton-pump inhibitor. Rabeprazole blocks the final step of gastric acid secretion. In gastric parietal cells, Rabeprazole is protonated, accumulates, and is transformed to an active sulfonamide.

PHARMACOKINETICS:

After oral administration of 20 mg Rabeprazole, peak plasma concentrations (C_{max}) of Rabeprazole occur over a range of 2.0 to 5.0 hours (T_{max}). There is no appreciable accumulation when doses of 10mg to 40mg are administered every 24 hours; the pharmacokinetics of Rabeprazole is not altered by multiple dosing. The plasma half-life ranges from 1 to 2 hours.

Following oral administration of 20mg Rabeprazole, it is absorbed and can be detected in plasma by 1 hour. Absolute bioavailability for a 20mg oral capsule of Rabeprazole is approximately 52%. Rabeprazole is 96.3% bound to human plasma proteins.

Rabeprazole is extensively metabolized. The thioether and sulphone are the primary metabolites measured in human plasma. These metabolites were not observed to have significant antisecretory activity. In vitro studies have demonstrated that Rabeprazole is primarily metabolized in the liver by cytochromes P450 3A (sulphone metabolite) and 2C19 (desmethyl Rabeprazole). 90% of the drug is eliminated in the urine, primarily as thioether carboxylic acid; its glucuronide, and mercapturic acid metabolites.

The anti-secretory effect begins within one hour after oral administration of 20mg Rabeprazole. The median inhibitory effect of Rabeprazole on 24 hour gastric acidity is 88% of maximal after the first dose. Rabeprazole 20mg inhibits basal and peptone meal-stimulated acid secretion versus placebo by 86% and 95%, respectively and increases the percent of a 24-hour period that the gastric pH>3 from 10% to 65%. This relatively prolonged pharmacodynamic action compared to the short pharmacokinetic half-life (1-2 hours) reflects the sustained inactivation of the H^+, K^+ ATPase.

SPECIAL POPULATIONS:

Geriatric: Reported data from clinical studies in healthy elderly subjects indicates that AUC values are approximately doubled and Cmax increased by 60% compared to values in a parallel younger control group. There was no evidence of drug accumulation after once daily dosing.

Pediatric: The pharmacokinetics of Rabeprazole in pediatrics has not been studied.

Gender and race: In analysis of body mass and weight, Rabeprazole pharmacokinetics showed no clinically significant differences between male and female volunteers.

Renal disease: No clinically significant difference was observed in the pharmacokinetics of Rabeprazole between healthy volunteers and patients requiring maintenance haemodialysis.

Hepatic disease: Reported data from single dose clinical study indicates that AUC & elimination half lives are doubled in patients with mild to moderate liver cirrhosis as compared to healthy volunteers. No information exists on Rabeprazole disposition in patients with severe hepatic impairment.

CONTRAINDICATIONS:

Rabeprazole is contraindicated in patients with known hypersensitivity to Rabeprazole, substituted benzimidazole or to any component of the formulation.

PRECAUTIONS:

General

Symptomatic response to therapy with Rabeprazole does not preclude the presence of gastric malignancy.

Pregnancy and Lactation

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Since many drugs are excreted in milk, caution should be exercised when Rabeprazole is administered to a nursing mother.

Pediatric Use

The safety and effectiveness of Rabeprazole in pediatric patients have not been established.

Geriatric Use

No overall differences in safety or effectiveness were observed between geriatric subjects and younger subjects.

ADVERSE REACTIONS:

Adverse effects with Rabeprazole are mild to moderate in intensity and include malaise, diarrhea, nausea, skin eruptions, headache and dizziness.

Abnormal laboratory findings (increased hepatic enzymes, LDH, blood urea nitrogen) observed with Rabeprazole were similar in incidence and severity with comparator agents and reversible with cessation of therapy. Inform your doctor in case of any adverse reactions related to drug use.

DRUG INTERACTIONS:

Rabeprazole is metabolized by the cytochrome P450 (CYP450) drug metabolizing enzyme system. Rabeprazole does not have clinically significant interactions with other drugs metabolized by the CYP450 system, such as warfarin, theophylline, diazepam and phenytoin.

Rabeprazole produces sustained inhibition of gastric acid secretion. An interaction with compounds which are dependent on gastric pH for absorption like ketoconazole may occur due to magnitude of acid suppression observed with Rabeprazole. Therefore, patients may need to be monitored when such drugs are taken concomitantly with Rabeprazole. Co-administration of Rabeprazole and antacids produced no clinically relevant changes in plasma Rabeprazole concentrations.

OVERDOSAGE AND TREATMENT:
There has been experience with large overdoses with Rabeprazole.

Patients with Zollinger-Ellison syndrome have been treated with up to 120 mg Rabeprazole QD. No specific antidote for Rabeprazole is known. Rabeprazole is extensively protein bound and is not readily dialyzable. In the event of overdosage, treatment should be symptomatic and supportive.

DOSAGE AND ADMINISTRATION:
Rabeprazole should be administered before meals.

Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease(GERD):
The recommended adult oral dose is 20mg Rabeprazole to be taken daily for four to eight weeks.

Maintenance of Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD Maintenance):
The recommended adult oral dose is 20mg Rabeprazole to be taken daily.

Healing of Duodenal Ulcers:
The recommended adult oral dose is 20mg Rabeprazole to be taken daily after the morning meal for a period up to four weeks. Most patients with duodenal ulcer heal within four weeks.

Treatment of Pathological hypersecretory conditions, including Zollinger-Ellison Syndrome:
The dosage of Rabeprazole in patients with pathologic hypersecretory conditions varies with the individual patient. The recommended adult oral starting dose is 60mg once a day. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Doses up to 100mg QD and 60mg BID have been administered.

No dosage adjustment is necessary in elderly patients, in patients with renal disease or in patients with mild to moderate hepatic impairment. Administration of Rabeprazole to patients with mild to moderate liver impairment resulted in increased exposure and decreased elimination. Due to the lack of clinical data on Rabeprazole in patients with severe hepatic impairment, caution should be exercised in those patients.

Rabeprazole (Barole) Capsules should be swallowed whole. The capsules should not be chewed, crushed or split.

STORAGE CONDITION :
Store at temperatures not exceeding 30°C, away from direct sunlight.
Keep out of reach of children.

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

AVAILABILITY :
Barole Capsules are available in strengths of 10mg and 20mg. 10 capsules in each strip.

- 30 capsules (3 x 10's) in a box.

Manufactured by: **INVENTIA HEALTHCARE PVT. LTD.**
F1-F1/1, Additional Ambernath, M.I.D.C.,
Ambernath (East) 421 506. Dist.Thane, India

For: **MEGA LIFESCIENCES (Australia) PTY. LTD.**
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