Revolt®

(Rabeprazole Sodium 10mg & 20mg Tablets)

ریوالٹ

(ریبی پرازول سوڈیم ۱۰ ملی گرام اور ۲۰ ملی گرام ٹیبلٹس)

COMPOSITION

Revolt 10mg Tablet

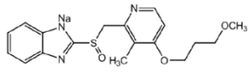
Each enteric coated tablet contains:
Rabeprazole Sodium (MS) equivalent to
Rabeprazole 10mg

Revolt 20mg Tablet

Each enteric coated tablet contains:
Rabeprazole Sodium (MS) equivalent to
Rabeprazole 20mg

DESCRIPTION

The active ingredient in delayed-release tablets is rabeprazole sodium, which is a proton pump inhibitor. It is a substituted benzimidazole known chemically as 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridinyl]-methyl]sulfinyl]- 1H–benzimidazole sodium salt. It has an empirical formula of $C_{18}H_{20}N_3NaO_3S$ and a molecular weight of 381.42.



CLINICAL PHARMACOLOGY

Mechanism Of Action

Rabeprazole belongs to a class of antisecretory compounds (substituted benzimidazole protonpump 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 protonpump inhibitor. Rabeprazole blocks the final step of gastric acid secretion. In gastric parietal cells, rabeprazole is protonated, accumulates, and is transformed to an active sulfenamide. When studied in vitro, rabeprazole is chemically activated at pH 1.2 with a half-life of 78 seconds. It inhibits acid transport in porcine gastric vesicles with a half-life of 90 seconds.

Pharmacokinetics

Absorption

Absorption After oral administration to healthy adults of 10 mg Rabeprazole (delayed-release capsules opened and granules sprinkled on one tablespoon (15mL) of applesauce) under fasting condition, median time (T_{max}) to peak plasma concentrations (C_{max}) of rabeprazole was 2.5 hours and ranged 1.0 to 6.5 hours. The plasma half-life of rabeprazole ranges from 1 to 2 hours. In healthy adults, a concomitant high fat meal delayed the absorption of rabeprazole from Rabeprazole (granules sprinkled on one tablespoon (15mL) of applesauce) resulting in the median T_{max} of 4.5 hours and decreased the C_{max} and AUC_{last} on average by 55% and 33%, respectively.

Distribution

Rabeprazole is 96.3% bound to human plasma proteins.

Metabolism

Rabeprazole is extensively metabolized. A significant portion of rabeprazole is metabolized via systemic nonenzymatic reduction to a thioether compound. Rabeprazole is also metabolized to sulphone and desmethyl compounds via cytochrome P450 in the liver. The thioether and sulphone are the primary metabolites measured in human plasma. These metabolites were not observed to have significant antisecretory activity.

Excretion

Following a single 20mg oral dose of 14^C-labeled rabeprazole, approximately 90% of the drug was eliminated in the urine, primarily as thioether carboxylic acid; its glucuronide, and mercapturic acid metabolites. The remainder of the dose was recovered in the feces. Total recovery of radioactivity was 99.8%. No unchanged rabeprazole was recovered in the urine or feces.

INDICATIONS

- Healing of Erosive or Ulcerative GERD in Adults
- Maintenance of Healing of Erosive or Ulcerative GERD in Adults
- Treatment of Symptomatic GERD in Adults
- Healing of Duodenal Ulcers in Adults
- Helicobacter Pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence in Adults
- Treatment of Pathological Hypersecretory Conditions, Including Zollinger-Ellison Syndrome in Adults
- Treatment of Symptomatic GERD in Adolescent Patients 12 Years of Age and Older

DOSAGE

Indication	Dosage of Rabeprazole delayed-release tablets	Treatment Duration
Adults		
Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD)	20mg once daily	4 to 8 weeks*
Maintenance of Healing of Erosive or Ulcerative GERD	20mg once daily	Controlled studies do not extend beyond 12 months
Symptomatic GERD in Adults	20mg once daily	Up to 4 weeks**
Healing of Duodenal Ulcers	20mg once daily after the morning meal	Up to 4 weeks***
Helicobacter pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence	Rabeprazole 20mg Amoxicillin 1000mg Clarithromycin 500mg Take all three medications twice daily with morning and evening meals; it is important that patients comply with the full 7-day regimen	7 days
Pathological Hypersecretory Conditions, Including Zollinger-Ellison Syndrome	Starting dose 60mg once daily then adjust to patient needs; some patients require divided doses Dosages of 100mg once daily and 60mg twice daily have been administered	As long as clinically indicated Some patients with Zollinger-Ellison syndrome have been treated continuously for up to one year
Adolescents 12 Years of Age and Older		
Symptomatic GERD	20mg once daily	Up to 8 weeks

* For those patients who have not healed after 8 weeks of treatment, an additional 8-week course of Rabeprazole may be considered.

** If symptoms do not resolve completely after 4 weeks, an additional course of treatment may be considered.

*** Most patients heal within 4 weeks; some patients may require additional therapy to achieve healing.

SIDE EFFECTS

The following serious adverse reactions are described below and elsewhere in labeling:

- Acute Interstitial Nephritis
- Cyanocobalamin (vitamin B-12) Deficiency
- Clostridium difficile Associated Diarrhea
- Bone Fracture
- Hypomagnesemia

DRUG INTERACTIONS

Effects of Other Drugs on Rabeprazole

Antacids: Co-administration of rabeprazole sodium delayed-release tablets and antacids produced no clinically relevant changes in plasma rabeprazole concentrations.

Effects of Rabeprazole on Other Drugs

Studies in healthy adult subjects have shown that rabeprazole does not have clinically significant interactions with other drugs metabolized by the CYP450 system, such as theophylline (CYP1A2) given as single oral doses, diazepam (CYP2C9 and CYP3A4) as a single intravenous dose, and phenytoin (CYP2C9 and CYP2C19) given as a single intravenous dose (with supplemental oral dosing). Steady state interactions of rabeprazole and other drugs metabolized by this enzyme system have not been studied in patients.

Clopidogrel: The mean AUC of the active metabolite of clopidogrel was reduced by approximately 12% (mean AUC ratio was 88%, with 90% CI of 81.7 to 95.5%) when rabeprazole sodium delayed- release tablets was co-administered compared to administration of clopidogrel with placebo.

Digoxin: In healthy adult subjects (n=16), co-administration of 20mg rabeprazole sodium delayed-release tablets with 2.5mg once daily doses of digoxin at steady state resulted in approximately 29% and 19% increase in mean C_{max} and $AUC_{(0-24)}$ of digoxin.

Ketoconazole: In healthy adult subjects (n=19), co-administration of 20mg rabeprazole sodium delayed- release tablets at steady state with a single 400 mg oral dose ketoconazole resulted in approximately an average of 31% reduction in both Cmax and $AUC_{(0-inf)}$ of ketoconazole.

Cyclosporine: In vitro incubations employing human liver microsomes indicated that rabeprazole inhibited cyclosporine metabolism, concentration that is over 50 times higher than the Cmax in healthy volunteers following 14 days of dosing with 20mg of Rabeprazole delayed-release tablets. This degree of inhibition is similar to that by omeprazole at equivalent concentrations.

CONTRAINDICATIONS

- Rabeprazole is contraindicated in patients with known hypersensitivity to rabeprazole, substituted benzimidazoles, or to any component of the formulation. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, acute interstitial nephritis, and urticaria.
- PPIs, including Rabeprazole, are contraindicated with rilpivirine-containing products

SPECIAL WARNINGS AND PRECAUTIONS

Presence of Gastric Malignancy: Symptomatic response to therapy with rabeprazole sodium does not preclude the presence of gastric malignancy. Adult patients with healed GERD were treated for up to 40 months with rabeprazole sodium delayed-release tablets and monitored with serial gastric biopsies. Adult patients without H. pylori infection (221 of 326 patients) had no clinically important pathologic changes in the gastric mucosa.

Interaction with Warfarin: Steady state interactions of rabeprazole and warfarin have not been adequately evaluated in patients. There have been reports of increased INR and prothrombin time in patients receiving a proton pump inhibitor and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death.

Acute Interstitial Nephritis: Acute interstitial nephritis has been observed in patients taking PPIs including rabeprazole sodium. Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue Rabeprazole if acute interstitial nephritis develops.

Cyanocobalamin (vitamin B-12) Deficiency: Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B-12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature.

Clostridium difficile Associated Diarrhea: Published observational studies suggest that PPI therapy like Rabeprazole may be associated with an increased risk of Clostridium difficile associated diarrhea, especially in hospitalized patients.

Bone Fracture: Several published observational studies in adults suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine.

Hypomagnesemia: Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in adult patients treated with PPIs for at least three months, in most cases after a year of therapy.

Interaction with Methotrexate: Concomitant use of PPIs with methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate and/or its metabolite.

OVERDOSE

There were no clinical signs or symptoms associated with any reported overdose. Patients with Zollinger-Ellison syndrome have been treated with up to 120mg rabeprazole once daily. No specific antidote for rabeprazole is known. Rabeprazole is extensively protein bound and is not readily dialyzable. In the event of over dosage, treatment should be symptomatic and supportive.

STORAGE

Store below 30°C.
Protect from light, heat and moisture.
Tablet should be swallowed whole, not chewed.
Keep out of the reach of Children.

PRESENTATION

Revolt (Rabeprazole) 10mg Tablet:
Pack of 10's in Alu-Alu blister

Revolt (Rabeprazole) 20mg Tablet:
Pack of 10's in Alu-Alu blister

خوراک اور ہدایات:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دوا کو **30** درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گولی کو چبائے بغیر پانی سے نگل لیں۔
روشنی، گرمی اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔

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ISO-9001:2008 certified company