

secretin, glucagon, follicle stimulating hormone (FSH), luteinising hormone (LH), renin, aldosterone or somatotrophic hormone.

Studies in healthy subjects have shown that rabeprazole sodium does not have clinically significant interactions with amoxicillin. Rabeprazole does not adversely influence plasma concentrations of amoxicillin or clarithromycin when co-administered for the purpose of eradicating upper gastrointestinal H. pylori infection.

Pharmacokinetic properties

Absorption: Rabeprazole is an enteric-coated (gastro-resistant) capsule formulation of rabeprazole sodium. This presentation is necessary because rabeprazole is acid-labile. Absorption of rabeprazole therefore begins only after the Capsule leaves the stomach. Absorption is rapid, with peak plasma levels of rabeprazole. Peak plasma concentrations (C_{max}) of rabeprazole and AUC are linear over the dose range of 10mg to 40mg. The bioavailability does not appear to increase with repeat administration.

The effects of food on the absorption of rabeprazole have not been evaluated.

Distribution: Rabeprazole is bound to human plasma proteins.

Metabolism: Rabeprazole sodium, as is the case with other members of the proton pump inhibitor (PPI) class of compounds, is metabolised through the cytochrome P450 (CYP450), hepatic drug metabolising system.

Excretion: Rabeprazole is eliminated in urine mainly as two metabolites: a mercapturic acid conjugate and a carboxy acid, plus two unknown metabolites.

Gender: Adjusted for body mass and height, there are no significant gender differences in pharmacokinetic parameters.

Renal dysfunction: In patients with stable, end-stage, renal failure requiring maintenance haemodialysis, the disposition of rabeprazole was very similar to that in healthy volunteers. The clearance of the drug in patients with renal disease requiring maintenance haemodialysis was approximately twice that in healthy volunteers.

Hepatic dysfunction: The single dose of Rabeprazole to patients with chronic mild to moderate hepatic impairment, the AUC doubled and increase in half-life of rabeprazole compared to the healthy volunteers.

Elderly: Elimination of rabeprazole was somewhat decreased in the elderly.

Indication and Usage:

Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD):
Rabeprazole is indicated for short-term (4 to 8 weeks) treatment in the healing and symptomatic relief of erosive or ulcerative gastroesophageal reflux disease (GERD).

Maintenance of Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD):
Rabeprazole is indicated for maintaining healing and reduction in relapse rates of heartburn symptoms in patients with erosive or ulcerative gastroesophageal reflux disease (GERD Maintenance).

Healing of Duodenal Ulcers:
Rabeprazole is indicated for short-term (up to four weeks) treatment in the healing and symptomatic relief of duodenal ulcers. Most patients heal within four weeks.

Treatment of Pathological hypersecretory Conditions, Including Zollinger-Ellison Syndrome:
Rabeprazole is indicated for the long-term treatment of pathological hypersecretory conditions including Zollinger-Ellison Syndrome.

Dosage and Administration:

Usual Adult Dose: 10 mg administered orally once daily. However, the dosage may be increased up to 20 mg orally once a day depending on the severity of symptoms. May be taken with or without food (Swallow whole, do not chew/crush).

Route of Administration

Oral.

Contraindications:

Patients with a history of hypersensitivity to sodium rabeprazole.

Warnings and Precautions:

Patients with a history of drug hypersensitivity; patients with impaired hepatic function [psychoneurotic adverse reactions have been reported in patients with liver cirrhosis (see Adverse Reactions)]; elderly patients (see Use in the elderly).

The patient should be carefully observed during administration and the cumulative dose should be kept to a minimum in accordance with the disease condition.

Rabeprazole can be administered at a dose of 20 mg once daily in case of severe disease conditions and recurrent and intractable ulcers.

Increases in thyroid weight and blood thyroxine levels have been reported in animal experiments (≥ 25 mg/kg/day in rats by oral administration), therefore, thyroid function should be carefully monitored during administration of Rabeprazole.

Interference with laboratory tests:

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. If the patient(s) are due to have a test on Chromogranin A level, Rabeprazole treatment should be stopped for atleast 5 days before CgA measurements to avoid this interference (see section Pharmacodynamic). If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

Regular Surveillance
Patients on proton pump inhibitor treatment (particularly those treated for long term) should be kept under regular surveillance.

Subacute Cutaneous Lupus Erythematosus (SCLE)
Proton pump inhibitors are associated with very infrequent cases of subacute cutaneous lupus erythematosus (SCLE). If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical

help promptly and the health care professional should consider stopping Rabeprazole .SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Hypomagnesaemia

Severe hypomagnesaemia has been reported in patients treated with PPI like Rabeprazole for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPI with digoxin or drugs that may cause hypomagnesaemia (e.g., diuretics), healthcare professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Fracture

Proton pump inhibitors, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in the elderly or in presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10-40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Clostridium Difficile Diarrhoea

Published observational studies suggest that PPI therapy may be associated with an increased risk of Clostridium difficile associated diarrhoea, especially in hospitalized patients. This diagnosis should be considered for diarrhoea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Vitamin B12 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 B12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed.

Carcinogenicity: It has been reported that in a carcinogenicity study in which ≥ 5 mg/kg/day of sodium rabeprazole was given to rats by oral administration for 2 years, carcinoids in the stomach were observed in female rats.

Use in pregnancy & lactation: Rabeprazole should only be used in pregnant women or women suspected of being pregnant if the expected therapeutic benefit outweighs the possible risk of treatment. (Fetotoxicity [delayed ossification in rats, weight loss and delayed ossification in rabbits] has been reported with sodium rabeprazole in animal experiments (400 mg/kg orally in rats, 30 mg/kg IV in rabbits).)

Rabeprazole should not be administered to nursing mothers. However, if indispensable, nursing should be discontinued. (It has been reported in animal studies that sodium rabeprazole is excreted in breast milk.)

Use in children: The safety of Rabeprazole in children has not been established (no clinical experience).

Use in the elderly: Rabeprazole is metabolized mainly in the liver. Since the elderly often have a physiological hepatic hypofunction, they are liable to experience adverse drug reactions. Therefore, it is advisable to take such measures as having a drug-free interval under careful supervision, if adverse reactions eg, gastrointestinal symptoms (see Adverse Reactions) occur.

Interactions with other medication:

Rabeprazole sodium produces a profound and long lasting inhibition of gastric acid secretion. An interaction with compounds whose absorption is pH dependent may occur. Co-administration of rabeprazole sodium with ketoconazole or itraconazole may result in a significant decrease in antifungal plasma levels. Therefore individual patients may need to be monitored to determine if a dosage adjustment is necessary when ketoconazole or itraconazole are taken concomitantly with Rabeprazole. Antacids were used concomitantly with the administration of Rabeprazole and, in a specific drug-drug interaction study, no interaction with liquid antacids was observed.

Co-administration of atazanavir 300mg/ritonavir 10mg with omeprazole (40 mg once daily) or atazanavir 400mg with lansoprazole (60mg once daily) to healthy volunteers resulted in a substantial reduction in atazanavir exposure. The absorption of atazanavir is pH dependent. Although not studied, similar results are expected with other proton pump inhibitors. Therefore PPIs, including rabeprazole, should not be co-administered with atazanavir

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.

Adverse Effects:

Shock: Anaphylactic reactions or shock occurred rarely with analogous compounds (omeprazole and lansoprazole). Rabeprazole should be discontinued if any abnormality and appropriate treatment should be given.

Hematology: Pancytopenia, thrombocytopenia, agranulocytosis and hemolytic anemia occurred rarely, and granulocytopenia and anemia occurred infrequently with analogous compounds (omeprazole and lansoprazole). Rabeprazole should be discontinued if any abnormality and appropriate treatment should be given.

Others:
Blood and the lymphatic system disorders -Rarely: Neutropenia, Leucopenia, Thrombocytopenia, Leucocytosis
Immune system disorders -Rarely Hypersensitivity.
Metabolism and nutrition disorders -Rarely: Anorexia.
Psychiatric disorders - Commonly: Insomnia, Uncommon: Nervousness, Rarely: depression.
Nervous system disorders - Commonly: Headache, Dizziness, Uncommon: Somnolence.
Eye disorders - Rarely: Visual disturbance.
Respiratory, thoracic and mediastinal disorders - Commonly Cough, Pharyngitis, Rhinitis, Uncommon: Bronchitis Sinusitis.