Rabecid®

(Rabeprazole Sodium)

Highnoon

COMPOSITION

Rabecid 10mg Enteric-coated Tablet:
Each enteric-coated tablet contains:
Rabeprazole sodium 10mg
Rabecid 20mg Enteric-coated Tablet:
Each enteric-coated tablet contains:
Rabeprazole sodium 20mg

DESCRIPTION

The active ingredient contained in Rabecid tablets is rabeprazole sodium, which is a substituted benzimidazole that inhibits gastric secretion.

MECHANISM OF ACTION

Rabeprazole belongs to a class of antisecretory compounds (substituted benzimidazole proton-pump inhibitors) that do not exhibit anticholinergic or histamine H2-receptor antagonist properties, but suppress gastric acid secretion by irreversible inactivation of 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. 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

Rabeprazole is rapidly absorbed and peak plasma concentration occur about 3.5 hours after an oral dose. The oral bioavailability is about 52% with enteric coated tablet formulation because of first pass metabolism and does not appear to vary after single or repeated doses. Rabeprazole is about 97% bound to plasma proteins. It is mainly metabolized via nonenzymatic reduction and to a lesser extent via the cytochrome P450 isoenzymes CYP2C19 and CYP3A4. Metabolite are excreted principally in the urine (about 90%) with the remainder in the faeces. The plasma half-life is about 1 to 2 hours, increased at least two to threefold in hepatic impairment, 1.6 times in CYP2C19 slow metabolizers and by 30% in elderly.

INDICATIONS AND USAGE

It is indicated in adults for:

- Treatment of symptomatic GERD.
- Healing of erosive or ulcerative GERD
- Maintenance of healing of erosive or ulcerative GERD.
- Healing of duodenal ulcers
- Helicobacter pylori eradication to reduce the risk of duodenal ulcer recurrence
- Treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome
- Treatment of symptomatic GERD in adolescent patients 12 years of age and older
- Benign gastric ulcers
- Severe esophagitis

DOSAGE AND ADMINISTRATION

It should be swallowed whole. It should not be chewed, crushed, or split.

Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease: The recommended dose is 20 mg once daily for 4 to 8 weeks.

Maintenance of Healing of Erosive or Ulcerative GERD: 20 mg once daily.

Treatment of Symptomatic GERD: 20 mg once daily for up to 4 weeks

Healing of Duodenal Ulcers: 20 mg once daily after the morning meal.

Helicobacter Pylori Eradication to Reduce the Risk at Duodenal Ulcer Recurrence: (Three Drug Regimen): All three medications Rabeprazole 20 mg, Amoxicillin 1000 mg, Clarithromycin 500 mg should be taken twice daily with morning and evening meals for 7 days.

Treatment of Pathological Hypersecretory Conditions, Including Zollinaer-Ellison Syndrome: Starting dose 60 mg once daily then adjust to patient needs.

Symptomatic GERD in Adolescent 12 years of age and older: 20 mg once daily for up to 8 weeks.

Benign Gastric Ulcers: Dose is 20 mg tablet once daily for 8 weeks. Dose to be taken in the morning.

Severe esophagitis: The dose is 20 mg tablet once daily for 8 weeks, continues as maintenance treatment if appropriate.

CONTRAINDICATIONS

History of hypersensitivity to rabeprazole.

- It 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 tubulointerstitial nephritis, and urticaria.
- Proton pump inhibitors including rabeprazole are contraindicated with rilpivirine-containing products.

ADVERSE REACTIONS

The reported adverse events of rabeprazole are: acute interstitial nephritis, clostridium difficile-associated diarrhea, bone fracture, cutaneous and systemic lupus erythematosus, cyanocobalamin (Vitamin B-12) deficiency, hypomagnesemia, fundic gland polyps, asthenia, cough, influenza like illness, pain, pharyngitis, flatulence, infection, constipation, headache, abdominal pain, diarrhea, dry mouth, dizziness, peripheral edema, hepatic enzyme increase, hepatitis, hepatic encephalopathy, myalgia, arthralgia, taste perversion, nausea, vomiting, burping, dyspepsia, leg cramps, nervousness, decreased appetite, gastritis, weight increased, leukocytosis, chest pain, chills and fever.
The additional reported adverse events of rabeprazole are: agranulocytosis, hemolytic anemia, leukopenia, pancytopenia, thrombocytopenia, vertigo, blurred vision, sudden death, jaundice, anaphylaxis, angioedema, systemic lupus erythematosus, Stevens-Johnson syndrome, toxic epidermal necrolysis, increase in prothrombin time/INR, TSH elevations, hyperammonemia, hypomagnesemia, rhabdomyolysis, coma, delirium, disorientation, interstitial pneumonia, tetany, arrhythmias, seizures, severe dermatologic reactions including bullous and other drug eruptions of the skin, erythema multiforme.

WARNINGS AND PRECAUTIONS

- In adults, symptomatic response to therapy with rabeprazole does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adult patients who have a suboptimal response or an early symptomatic relapse after completing treatment with a PPI.
- Rabeprazole has drug interaction with warfarin and cyclosporine. Monitoring is required when Rabeprazole is used with warfarin (increase in INR and prothrombin time monitoring).
- PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.
- Acute tubulointerstitial nephritis (TIN) has been observed in patients taking proton pump inhibitors and may occur at any point during such PPI therapy. Patients may present with varying signs and symptoms from symptomatic hypersensitivity reactions to non-specific symptoms of decreased renal function (e.g., malaise, nausea, anorexia). Discontinue rabeprazole and evaluate patients with suspected acute TIN.
- PPI therapy like rabeprazole may be associated with an increased risk of Clostridium difficile-associated diarrhea, especially in hospitalized patients. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents.
- Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with the use of proton pump inhibitors. These events have occurred as both new onset and an exacerbation of existing autoimmune disease. The majority of PPI-induced lupus erythematosus cases were CLE. The most common form of CLE reported in patients treated with proton pump inhibitors was subacute CLE (SCLE) and occurred within weeks to years after continuous drug therapy in patients ranging from infants to the elderly. Systemic lupus erythematosus (SLE) is less commonly reported than CLE in patients receiving proton pump inhibitors. PPI associated SLE is usually milder than non-drug induced SLE. Onset of SLE typically occurred within days to years after initiating treatment primarily in patients ranging from young adults to the elderly. The majority of patients presented with rash, however, arthralgia and cytopenia were also reported. Avoid administration of proton pump inhibitors for longer than medically indicated. If signs or symptoms consistent with CLE or SLE are noted in patients receiving rabeprazole, discontinue the drug and refer the patient to the appropriate specialist for evaluation. Most patients improve with discontinuation of the PPI alone in 4 to 12 weeks. Serological testing (e.g. ANA) may be positive and elevated serological test results may take longer to resolve than clinical manifestations.
- 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-orachlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature.
- Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. Hypomagnesemia may lead to hypocalcemia and/or hypokalemia and may exacerbate underlying hypocalcemia in at-risk patients. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI. For patients expected to be on prolonged treatment or who take proton pump inhibitors with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics.) healthcare professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.
- Consider monitoring magnesium and calcium levels prior to initiation of Rabeprazole and periodically while on treatment in patients with a preexisting risk of hypocalcemia (e.g., hypoparathyroidism).
- PPI use is associated with an increased risk of fundic gland polyps that increases with long-term use, especially beyond one year. Most PPI users who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy. Use the shortest duration of PPI therapy appropriate to the condition being treated.

DRUG INTERACTION

- The effect of PPI on antiretroviral drugs is variable. Decreased exposure of some antiretroviral drugs (e.g., rilpivirine, atazanavir and nelfinavir) when used concomitantly with rabeprazole may reduce antiviral effect and promote the development of drug resistance. Increased exposure of other antiretroviral drugs (e.g., saquinavir) when used concomitantly with rabeprazole may increase toxicity.
- Concomitant use of rabeprazole with rilpivirine-containing products is contraindicated (atazanavir, nelfinavir, saquinavir).
- Increased INR and prothrombin time in patients receiving PPIs, including rabeprazole, and warfarin concomitantly. Increase in INR and prothrombin time may lead to abnormal bleeding and even death. Monitor INR and prothrombin time. Dose adjustment of warfarin may be needed to maintain target INR range.
- Concomitant use of rabeprazole with methotrexate (primarily at high dose) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities. A temporary withdrawal of rabeprazole may be considered in some patients receiving high dose methotrexate administration.
- Potential for increased exposure of digoxin, monitor digoxin concentrations. Dose adjustment of digoxin may be needed to maintain therapeutic drug concentrations.
- Due to its effects on gastric acid secretion, rabeprazole can reduce the absorption of drugs where gastric pH is an important determinant of their bioavailability. Like with other drugs that decrease the intragastric acidity, the absorption of drugs such as ketoconazole, atazanavir, iron salts, erlotinib, and mycophenolate mofetil (MMF) can decrease, while the absorption of drugs such as digoxin can increase during treatment with rabeprazole. Co-administration of digoxin with rabeprazole is expected to increase the systemic exposure of digoxin. Therefore, patients may need to be monitored when digoxin is taken concomitantly with rabeprazole. Co-administration of omeprazole in transplant patients receiving MMF has been reported to reduce the exposure to the active metabolite, mycophenolic acid (MPA), possibly due to a decrease in MMF solubility at an increased gastric pH. Use rabeprazole with caution in transplant patients receiving MMF.
- Concomitant administration of clarithromycin with other drugs can lead to serious adverse reactions, including potentially fatal arrhythmias, and are contraindicated.
- Potentially increased exposure of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19. Monitor tacrolimus whole blood trough concentrations. Dose adjustment of tacrolimus may be needed to maintain therapeutic drug concentrations.
- Serum chromogranin A (CgA) levels increase secondary to PPI-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Temporarily stop rabeprazole treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high.
- Hyper-response in gastrin secretion in response to secretin stimulation test, falsely suggesting gastrinoma. Temporarily stop treatment with rabeprazole at least 14 days before assessing to allow gastrin levels to return to baseline.
- There have been reports of false positive urine screening tests for tetrahydrocannabinol (THC) in patients receiving proton pump inhibitors. An alternative confirmatory method should be considered to verify positive results.

USE IN SPECIFIC POPULATIONS

Pregnancy
There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Nursing Mothers
Since many drugs are excreted in milk, and because of the potential for adverse reactions to nursing infants from rabeprazole, a decision should be made to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Paediatric Use
The safety and effectiveness are established in patients for 12 years of age and older for the treatment of symptomatic GERD with Rabeprazole. The use of Rabeprazole for treatment of GERD in paediatric patients 1 to 11 years of age is supported. The safety and effectiveness of Rabeprazole have not been established in paediatric patients for:

- Healing of Erosive or Ulcerative GERD
- Maintenance of Healing of Erosive or Ulcerative GERD
- Treatment of Symptomatic GERD
- Healing of Duodenal Ulcers
- Helicobacter pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence
- Treatment of Pathological Hypersecretory Conditions, Including Zollinger-Ellison Syndrome

Symptomatic GERD in Infants 1 to 11 Months of Age: The use of Rabeprazole is not recommended because there has not been demonstration of efficacy for the treatment of GERD in paediatric patients younger than 1 year of age.
Neonates <1 Month and Preterm Infants <44 weeks corrected gestational age: The use of Rabeprazole is not recommended for the treatment of GERD, based on the risk of prolonged acid suppression and lack of demonstrated safety and effectiveness in neonates.

Geriatric Use
No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

Hepatic Impairment
Administration of rabeprazole to patients with mild to moderate hepatic impairment (Child-Pugh Class A and B, respectively) resulted in increased exposure and decreased elimination. No dosage adjustment is necessary in patients with mild to moderate hepatic impairment. There is no information in patients with severe hepatic impairment (Child-Pugh Class C). Avoid use of rabeprazole in patients with severe hepatic impairment; however, if treatment is necessary, monitor patients for adverse reactions.

OVERDOSAGE

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 INSTRUCTIONS

To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in dry place. Protect from light.

PRESENTATION

Rabecid 10mg Enteric-coated Tablets:
Alu. Alu Blister Pack of 1 x 14's.
Rabecid 20mg Enteric-coated Tablets:
Alu. Alu Blister Pack of 1 x 14's.

ربی سِڈ®

(ریبیپرازول سوڈیم)

خوراک و ہدایات:

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by
HIGHNOON LABORATORIES LTD
17.5 KM, Multan Road, Lahore, Pakistan.
www.highnoon-labs.com

Item Code No. 14002656