Epazole Tablet

(R a b e p r a z o l e)

ایپازول ٹیبلیٹ

(ریبی پرازول)

COMPOSITION:

EPAZOLE Tablet 10mg

Each enteric coated tablet contains:

Rabeprazole Sodium (USP) eq. to Rabeprazole….10mg

EPAZOLE Tablet 20mg

Each enteric coated tablet contains:

Rabeprazole Sodium (USP) eq. to Rabeprazole….20mg

DESCRIPTION:

EPAZOLE (Rabeprazole) is a proton pump inhibitor that suppresses gastric acid production in the stomach. It has several medical uses: the management of conditions that involve excess gastric acid production (e.g. Zollinger Ellison syndrome), conditions that are worsened by gastric acid (e.g. ulcerations of the gastrointestinal tract), and conditions involving prolonged exposure to gastric acid (e.g. symptomatic gastroesophageal reflux disease).

MODE OF ACTION:

Rabeprazole belongs to a class of anti secretory compounds (substituted benzimidazole proton-pump inhibitors) that do not exhibit anticholinergic or histamine H2-receptor antagonist properties, but suppress gastric acid secretion by inhibiting the gastric H+/K+ATPase (hydrogen-potassium adenosine triphosphatase) 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 sulfenamide.

INDICATIONS:

Rabeprazole tablets are indicated for the treatment of:

- Active duodenal ulcer.
- Active benign gastric ulcer.
- Symptomatic erosive or ulcerative gastro-oesophageal reflux disease (GORD).
- Gastro-Oesophageal Reflux Disease Long-term Management (GORD Maintenance).
- Symptomatic treatment of moderate to very severe gastro-oesophageal reflux disease (symptomatic GORD)
- Zollinger-Ellison Syndrome.
- Prevention of gastrointestinal bleeds with NSAID use.

DOSAGE & ADMINISTRATION:

Adults/elderly:

Active Duodenal Ulcer and Active Benign Gastric Ulcer: The recommended oral dose for both active duodenal ulcer and active benign gastric ulcer is 20mg to be taken once daily in the morning.

Most patients with active duodenal ulcer heal within four weeks. However, a few patients may require an additional four weeks of therapy to achieve healing. Most patients with active benign gastric ulcer heal within six weeks. However again a few patients may require an additional six weeks of therapy to achieve healing.

Erosive or Ulcerative Gastro-Oesophageal Reflux Disease (GORD): The recommended oral dose for this condition is 20mg to be taken once daily for four to eight weeks.

Gastro-Oesophageal Reflux Disease Long-term Management (GORD Maintenance): For long-term management, a maintenance dose of Rabeprazole Sodium20mg or 10mg once daily can be used depending upon patient response.

Symptomatic treatment of moderate to very severe gastro-oesophageal reflux disease (symptomatic GORD): 10mg once daily in patients without oesophagitis. If symptom control has not been achieved during four weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using an on-demand regimen taking 10mg once daily when needed.

Zollinger-Ellison Syndrome: The recommended adult starting dose is 60 mg once a day. The dose may be titrated upwards to 120mg/day based on individual patient needs. Single daily doses up to 100mg/day may be given. 120mg dose may require divided doses, 60mg twice daily. Treatment should continue for as long as clinically indicated.

For indications requiring once daily treatment Rabeprazole Sodium tablets should be taken in the morning, before eating; and although neither the time of day nor food intake was shown to have any effect on rabeprazole sodium activity, this regimen will facilitate treatment compliance.

Patients should be cautioned that the Rabeprazole Sodium tablets should not be chewed or crushed, but should be swallowed whole.

Renal and hepatic impairment: No dosage adjustment is necessary for patients with renal or hepatic impairment.

Children:

Rabeprazole Sodium is not recommended for use in children, as there is no experience of its use in this group.

PHARMACODYNAMICS:

Rabeprazole prevents the production of acid in the stomach. It reduces symptoms and prevents injury to the esophagus or stomach in patients with gastroesophageal reflux disease (GERD) or ulcers. Rabeprazole is also useful in conditions that produce too much stomach acid such as Zollinger-Ellison syndrome. Rabeprazole may also be used with antibiotics to get rid of bacteria that are associated with some ulcers. Rabeprazole is a selective and irreversible proton pump inhibitor, suppresses gastric acid secretion by specific inhibition of the H+, K+ -ATPase, which is found at the secretory surface of parietal cells. In doing so, it inhibits the final transport of hydrogen ions (via exchange with potassium ions) into the gastric lumen.

PHARMACOKINETICS:

Rabeprazole's bioavailability is approximately 52%, meaning that 52% of orally administered dose is expected to enter systemic circulation (the bloodstream).Once in the blood, rabeprazole is approximately 96.3%-97% bound to plasma proteins. The biological half-life of rabeprazole in humans is approximately 1 hour. It takes about 3.5 hours for rabeprazole to reach the maximum concentration in human plasma after a single orally administered dose. Oral absorption is independent of the dose administered

Rabeprazole is extensively metabolized by the liver 90% of the drug is rendered into metabolites by the liver, which are then excreted by the kidneys. 10% of the dose is excreted in the feces. The drug metabolizing enzymes primarily responsible for rabeprazole's metabolism are CYP2C19 and CYP3A4. However, rabeprazole is mainly metabolized through non-enzymatic reduction to a

thioether metabolite. Some of rabeprazole's metabolites include the following: a thioether carboxylic acid metabolite, a thioether glucuronide metabolite, and a sulfone metabolite. The most common metabolites excreted in the urine are the mercaptouric acid conjugate and carboxylic acid.

PRECAUTIONS:

Liver disease: People with reduced liver function or liver disease should discuss with their doctor how this medication may affect their medical condition, how their medical condition may affect the dosing and effectiveness of this medication, and whether any special monitoring is needed.

Magnesium levels: Rabeprazole may rarely cause low magnesium levels in people who take this medication a for prolonged period of time. Low magnesium may occur after at least 3 months, but usually after a year of treatment. If you have low magnesium levels in your blood, you should discuss with your doctor about how this medication may affect your medical condition, how your medical condition may affect the dosing and effectiveness of this medication, and whether any special monitoring is needed.

Osteoporosis fractures: Long term use of rabeprazole may be related to an increased risk of bone fractures in the hip, wrist or spine, as a result of weakened bones. This risk is further increased if you are at risk of developing osteoporosis. If you have osteoporosis or have risk factors for developing osteoporosis, discuss with your doctor how this medication may affect your medical condition, how your medical condition may affect the dosing and effectiveness of this medication, and whether any special monitoring is needed.

Pregnancy: This medication should not be used during pregnancy unless the benefits outweigh the risks. If you become pregnant while taking this medication, contact your doctor immediately.

Breast-feeding: It is not known if rabeprazole passes into breast milk. If you are a breast-feeding mother and are taking this medication, it may affect your baby. Talk to your doctor about whether you should continue breast-feeding.

Children and adolescents: The safety and effectiveness of using this medication have not been established for children and adolescents under 18 years of age.

SIDE EFFECTS:

In general, rabeprazole is fairly well tolerated, even up to 5 years after clinical trial follow-up. The side effect profile is similar to that of omeprazole. The most common side effects include headache, nausea, and diarrhea. Rare side effects include rashes, flu-like symptoms, and infections (including by the gastrointestinal pathogen Clostridium difficile. Rare instances of rabeprazole-induced liver injury (also known as hepatotoxicity) have been reported. Characteristic proton-pump inhibitor hepatoxicity usually occurs within the first 4 weeks of starting the medication.

Rabeprazole is associated with elevated serum gastrin levels, which are thought to be dependent upon the degree of CYP2C19 metabolism the drug undergoes. In comparison, rabeprazole is not as significantly metabolized by this enzyme compared to other medications in the same class, like omeprazole. Elevated serum gastrin may be associated with gastric cancer.

Acid suppression via rabeprazole can decrease the absorption of vitamin B12 and magnesium, leading to deficiency.

Very serious side effects have been reported in people taking rabeprazole, but these effects have not been "correlated directly" with the use of rabeprazole. These include Stevens-Johnson syndrom, serious hematological abnormalities, coma, and death. Other possible side effects, common to other PPIs medications in the same class, include bone fractures due to osteoporosis and serious infections with Clostridium difficile.

DRUG INTERACTIONS:

Rabeprazole does not interfere with the plasma concentration of drugs that are also metabolized by the same enzymes (i.e. CYP2C19) that it is metabolized by. Therefore, it is not expected to react with CYP2C19 substrates like theophylline, warfarin, diazepam, and phenytoin. However, the acid-suppression effects of rabeprazole, like other PPIs, may interfere with the absorption of drugs that require acid, such as ketoconazole and digoxin.

There is some evidence that omeprazole and esomeprazole, two medications in the same class as rabeprazole, can disturb the conversion of an anticoagulant medication called clopidogrel to its active metabolite. However, because this is thought to be mediated by the effect of omeprazole and esomeprazole on CYP2C19, the enzyme that activates clopidogrel, this drug interaction is not expected to occur as strongly with rabeprazole. However, whether the effect of omeprazole and esomeprazole on clopidogrel's metabolism actually leads to poor clinical outcomes is still a matter of intense debate among healthcare professionals.

Clinically serious drug-drug interactions may involve the acid-suppression effects of rabeprazole. For example, rabeprazole should not be used concomitantly with rilphivirine, an anti-HIV therapy, which requires acid for absorption. Lowered plasma concentrations of rilpivirine could lead to progression of HIV infection. Other drugs that require acid for absorption include antifungal drugs like ketoconazole and itraconazole, digoxin, iron, mycophenolate, and tyrosine kinase inhibitors like erlotinib, dasatinib, and nilotinib. There is no clinically relevant drug interaction between rabeprazole and antacids.

CONTRAINDICATIONS:

Rabeprazole is contraindicated in the following populations and situations:

- People with a known hypersensitivity to rabeprazole, substituted benzimidazoles (which are chemically similar to rabeprazole, like omeprazole), or any other component of the capsule formulation (e.g. certain dyes).
- Concurrent use of rilpivirine, a medication used to treat HIV infection.

STORAGE & INSTRUCTIONS:

Store between 15-25°C.

Protect from heat, sunlight and moisture. Do not freeze.

Keep away from the reach of children.

To be sold on the prescription of a registered medical practitioner only.

HOW SUPPLIED:

EPAZOLE Tablet 10mg

10's tablets.

EPAZOLE Tablet 20mg

10's tablets.

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۱۵-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔

دھوپ، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:

PHARMASOL

PRIVATE LIMITED

549,Sundar Industrial Estate,

Lahore, Pakistan.