To be prescribed

ATC Code : A02BC04

Antiulcerant drugs

RABEPRAZOLE-ASTERIA Tab.10mg, 20mg

(Rabeprazole sodium)

[Composition]

* Rabeprazole-Asteria film coated tablet 10mg

Each tablet contains

Active ingredient:

Rabeprazole sodium ---------- 10mg

Inactive ingredient:

D-mannitol, Magnesium oxide, Magnesium stearate, Iron oxide,Hypromellose phtalate 200731, Polyethylene glycol 6000,Talc,Hypromellose 2910, Titanum dioxide, Sodium hydroxide, Carboxymethylcellulose calcium, Low substituted Hydroxypropyl cellulose, Hydroxypropylcellulose

* Rabeprazole-Asteria film coated tablet 20mg

Each tablet contains

Active ingredient:

Rabeprazole sodium ---------- 20mg

Inactive ingredient:

D-mannitol, Magnesium oxide, Hyproxypropylcellulose, Low-substituted hydroxypropylcellulose, Magnesium stearate, Sodium hydroxide, Hypromellose phthalate 200731, Polyethylene glycol 6000, Talc, Hydroxypropylmethylcellulose 2910, Titanium dioxide, Iron oxide

[Indication]

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 , In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori in patients with peptic ulcer disease

[Dosage and 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 tablet 20mg 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.

Eradication of H. pylori: Patients with H. pylori infection should be treated with eradication therapy. The following combination given for 7 days is recommended. Rabeprazole sodium tablet 20mg twice daily + clarithromycin 500mg twice daily and amoxicillin 1g twice daily.

For indications requiring once daily treatment this 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 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.

[Contraindication]

Hypersensitivity to rabeprazole : Rabeprazole is contraindicated in patients with known hypersensitivity to rabeprazole, substituted benzimidazoles or to any component of the formulation.***Use of Clarithromycin and hypersentivity to macrolide antibiotics :*** Clarithromycin is contraindicated in patients with known hypersensitivity to any macrolide antibiotic. ***Concomitant use of Clarithromycin with pimozide and cisapride :*** Concomitant administration of clarithromycin with pimozide and cisapride is contraindicated. There have been post-marketing reports of drug interactions when clarithromycin and/or erythromycin are co-administered with pimozide resulting in cardiac arrhythmias (QT prolongation, ventricular tachycardia, ventricular fibrillation, and torsade de pointes) most likely due to inhibition of hepatic metabolism of pimozide by erythromycin and clarithromycin. Fatalities have been reported. (Please refer to full prescribing information for clarithromycin.)

Amoxicillin and hypersensitivity to penicilllin : Amoxicillin is contraindicated in patients with a known hypersensitivity to any penicillin.

[Warnings]

Symptomatic response to therapy with rabeprazole sodium does not preclude the presence of gastric or oesophageal malignancy, therefore the possibility of malignancy should be excluded prior to commencing treatment with Rabeprazole tablet. Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance. A risk of cross-hypersensitivity reactions with other proton pump inhibitor or substituted benzimidazoles cannot be excluded. Patients should be cautioned that Rabeprazole tablets should not be chewed or crushed, but should be swallowed whole. This medicine is not recommended for use in children, as there is no experience of its use in this group. There have been post marketing reports of blood dyscrasias (thrombocytopenia and neutropenia). In the majority of cases where an alternative aetiology cannot be identified, the events were uncomplicated and resolved on discontinuation of rabeprazole. Hepatic enzyme abnormalities have been seen in clinical trials and have also been reported since market authorisation. In the majority of cases where an alternative aetiology cannot be identified, the events were uncomplicated and resolved on discontinuation of rabeprazole. No evidence of significant drug related safety problems was seen in a study of patients with mild to moderate hepatic impairment versus normal age and sex matched controls. However because there are no clinical data on the use of Rabeprazole in the treatment of patients with severe hepatic dysfunction the prescriber is advised to exercise caution when treatment with This rabeprazole is first initiated in such patients.

[Precaution]

Clarithromycin use in pregnant women : Claritjromycin should not be used in pregnant women except in clinical circumstances whrere no alternative therapy is appropriate. If pregnancy occurs while taking clarithromycin, the patient should be apprised of the potential hazard to the fetus.

Anaphylactic reactions associated with antibiotic use Amoxicillin: Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been well-documented reports of individuals with a history of penicillin hypersensitivity reactions that have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillin, cephalosporin, and other allergens. If an allergic reaction occurs, amoxicillin should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with epinephrine, Oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.

Pseudomembranous colitis associated with antibiotic use: Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clarithromycin and amoxicillin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents. Treat reatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by Clostridium difficile is a primary cause of antibiotic-associated colitis. After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluid and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against Clostridium difficile colitis.

Presence of gastric malignancy : Symptomatic response to therapy with rabeprazole does not preclude the presence of gastric malignancy. Patients with healed GERD were treated for up to 40 months with rabeprazole and monitored with serial gastric biopsies. Patients without H. pylori infection (221 of 326 patients) had no clinically important pathologic changes in the gastric mucosa. Patients with H. pylori infection at baseline (105 of 326 patients) had mild or moderate inflammation in the gastric body or mild inflammation in the gastric antrum. Patients with mild grades of infection or inflammation in the gastric body tended to change to moderate, whereas those graded moderate at baseline tended to remain stable. Patients with mild grades of infection or inflammation in the gastric antrum tended to remain stable. At baseline 8% of patients had atrophy of glands in the gastric body and 15% had atrophy in the gastric antrum. At endpoint, 15% of patients had atrophy of glands in the gastric body and 11% had atrophy in the gastric antrum. Approximately 4% of patients had intestinal metaplasia at some point during follow-up, but no consistent changes were seen.

Concomitant use 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. Patients treated with a proton pump inhibitor and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time

[Interactions]

Drugs metabolized by CPY450:

Rabeprazole is metabolized by the cytochrome P450 (CYP450) drug metabolizing enzyme system. Studies in healthy subjects have shown that rabeprazole does not have clinically significant interactions with other drugs metabolized by the CYP450 system, such as warfarin and theophylline given as single oral doses, diazepam as a single intravenous dose, and phenytoin 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.

Warfarin : There have been reports of increased INR and prothrombin time in patients receiving proton pump inhibitors, including rabeprazole, and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Cyclosporine: In vitro incubations employing human liver microsomes indicated that rabeprazole inhibited cyclosporine metabolism with an IC50 of 62 micromolar a concentration that is over 50 times higher than the Cmax in healthy volunteers following 14 days of dosing with 20 mg of rabeprazole. This degree of inhibition is similar to that by omeprazole at equivalent concentrations.

Compounds dependent on gastric pH for absorption : Rabeprazole produces sustained inhibition of gastric acid secretion. An interaction with compounds which are dependent on gastric pH for absorption may occur due to the magnitude of acid suppression observed with rabeprazole. For example, in normal subjects, co-administration of rabeprazole 20 mg QD resulted in an approximately 30% decrease in the bioavailability of ketoconazole and increases in the AUC and Cmax for digoxin of 19% and 29%, respectively .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. Concomitant use of atazanavir and proton pump inhibitors is not recommended. Co-administration of atazanavir with proton pump inhibitors is expected to substantially decrease atazanavir plasma concentrations and thereby reduce its therapeutic effect.

Drugs metabolized by CYP2C19 : In a clinical study in Japan evaluating rabeprazole in patients categorized by CYP2C19 genotype (n=6 per genotype category), gastric acid suppression was higher in poor metabolizers as compared to extensive metabolizers. This could be due to higher rabeprazole plasma levels in poor metabolizers. Whether or not interactions of rabeprazole sodium with other drugs metabolized by CYP2C19 would be dif ferent between extensive metabolizers and poor metabolizers has not been studied. Combined Administration with Clarithromycin: Combined administration consisting of rabeprazole, amoxicillin, and clarithromycin resulted in increases in plasma concentrations of rabeprazole and 14-hydroxyclarithromycin. Concomitant administration of clarithromycin with pimozide and cisapride is contraindicated.

[Side effects]

Body as a Whole: asthenia, fever, allergic reaction, chills, malaise, chest pain substernal, neck rigidity, photosensitivity reaction. Rare: abdomen enlarged, face edema, hangover effect.

Cardiovascular System: hypertension, myocardial infarct, electrocardiogram abnormal, migraine, syncope, angina pectoris, bundle branch block, palpitation, sinus bradycardia, tachycardia.

Rare: bradycardia, pulmonary embolus, supraventricular tachycardia, thrombophlebitis, vasodilation, QTC prolongation and ventricular tachycardia. Digestive System: diarrhea, nausea, abdominal pain, vomiting, dyspepsia, flatulence, constipation, dry mouth, eructation, gastroenteritis, rectal hemorrhage, melena, anorexia, cholelithiasis, mouth ulceration, stomatitis, dysphagia, gingivitis, cholecystitis, increased appetite, abnormal stools, colitis, esophagitis, glossitis, pancreatitis, proctitis. Rare: bloody diarrhea, cholangitis, duodenitis, gastrointestinal hemorrhage, hepatic encephalopathy, hepatitis, hepatoma, liver fatty deposit, salivary gland enlargement, thirst. ***Endocrine System:*** hyperthyroidism, hypothyroidism.

Hemic & Lymphatic System: anemia, ecchymosis, lymphadenopathy, hypochromic anemia.

Metabolic & Nutritional Disorders: peripheral edema, edema, weight gain, gout, dehydration, weight loss. ***Musculo-Skeletal System:*** myalgia, arthritis, leg cramps, bone pain, arthrosis, bursitis.

Rare: twitching. ***Nervous System:*** insomnia, anxiety, dizziness, depression, nervousness, somnolence, hypertonia, neuralgia, vertigo, convulsion, abnormal dreams, libido decreased, neuropathy, paresthesia, tremor. Rare: agitation, amnesia, confusion, extrapyramidal syndrome, hyperkinesia.

Respiratory System: dyspnea, asthma, epistaxis, laryngitis, hiccup, hyperventilation.

Rare: apnea, hypoventilation. Skin and Appendages: rash, pruritus, sweating, urticaria, alopecia. Rare: dry skin, herpes zoster, psoriasis, skin discoloration.

Special Senses: cataract, amblyopia, glaucoma, dry eyes, abnormal vision, tinnitus, otitis media. Rare: corneal opacity, blurry vision, diplopia, deafness, eye pain, retinal degeneration, strabismus. Urogenital System: cystitis, urinary frequency, dysmenorrhea, dysuria, kidney calculus, metrorrhagia, polyuria. Rare: breast enlargement, hematuria, impotence, leukorrhea, menorrhagia, orchitis, urinary incontinence.

[Pregnancy/Breast Feeding]

Pregnancy: There are no data on the safety of rabeprazole in human pregnancy. Reproduction studies performed in rats and rabbits have revealed no evidence of impaired fertility or harm to the foetus due to rabeprazole sodium, although low foeto-placental transfer occurs in rats. Rabeprazole tablet is contraindicated during pregnancy.

Lactation: It is not known whether rabeprazole sodium is excreted in human breast milk. No studies in lactating women have been performed. Rabeprazole sodium is however excreted in rat mammary secretions. Therefore Rabeprazole tablet should not be used during breast feeding.

[Overdose]

Experience to date with deliberate or accidental overdose is limited. The maximum established exposure has not exceeded 60mg twice daily, or 160mg once daily. Effects are generally minimal, representative of the known adverse event profile and reversible without further medical intervention. No specific antidote is known. Rabeprazole sodium is extensively protein bound and is, therefore, not dialyzable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilized.

[Storage]

Store in air-tight container at room temperature(1~30℃). Protect from light.

Keep out of reach of children.

[Shelf life]

4 years

[Presentation]

10, 20, 30,100, 500 Tablets

Manufactured by
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