Bosch

For Medical Professional Only

Rabosh® Tablets

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

رابوش ٹیبلیٹس

(رابپرازول)

DESCRIPTION:
The active ingredient in Rabosh 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.

COMPOSITION:
Rabosh 10mg Tablets:
Each enteric coated tablet contains:
Rabeprazole Sodium U.S.P.....10mg
(Product Specs.: Bosch)

Rabosh 20mg Tablets:
Each enteric coated tablet contains:
Rabeprazole Sodium U.S.P.....20mg
(Product Specs.: Bosch)

CLINICAL PHARMACOLOGY:
Pharmacodynamic properties
Pharmacotherapeutic group: Drugs for peptic ulcer and gastro-esophageal reflux disease (GORD), proton pump inhibitors. ATC code: A02B C04.

Mechanism of action
Rabeprazole sodium belongs to the class of anti-secretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H2 histamine antagonist properties, but suppress gastric acid secretion by the specific inhibition of the H+/K+-ATPase enzyme (the acid or proton pump). The effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.

Pharmacokinetic properties
Absorption
Rabeprazole 20mg Gastro-resistant Tablet is an enteric-coated (gastro-resistant) tablet formulation of rabeprazole sodium. Absorption of rabeprazole therefore begins only after the tablet leaves the stomach. Absorption is rapid, with peak plasma levels of rabeprazole occurring approximately 3.5 hours after a 20 mg dose. Peak plasma concentrations (Cmax) of rabeprazole and AUC are linear over the dose range of 10 mg to 40 mg. Absolute bioavailability of an oral 20 mg dose (compared to intravenous administration) is about 52 % due in large part to pre-systemic metabolism. Additionally the bioavailability does not appear to increase with repeat administration. In healthy subjects the plasma half-life is approximately one hour (range 0.7 to 1.5 hours), and the total body clearance is estimated to be 283 ± 98 ml/min. There was no clinically relevant interaction with food. Neither food nor the time of day of administration of the treatment affect the absorption of rabeprazole sodium.

Distribution
Rabeprazole is approximately 97 % 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. In vitro studies with human liver microsomes indicated that rabeprazole sodium is metabolised by isoenzymes of CYP450 (CYP2C19 and CYP3A4). In these studies, at expected human plasma concentrations rabeprazole neither induces nor inhibits CYP3A4.

Elimination
Approximately 90 % of the dose was eliminated in urine mainly as the two metabolites a mercapturic acid conjugate (M5) and a carboxylic acid (M6), plus two unknown metabolites. The remainder of the dose was recovered in faeces.

Renal dysfunction
In patients with stable, end-stage, renal failure requiring maintenance haemodialysis (creatinine clearance ≤5 ml/min/1.73 m2), the disposition of rabeprazole was very similar to that in healthy volunteers. The AUC and the Cmax in these patients was about 35 % lower than the corresponding parameters in healthy volunteers. The mean half-life of rabeprazole was 0.82 hours in healthy volunteers, 0.95 hours in patients during haemodialysis and 3.6 hours post dialysis. The clearance of the drug in patients with renal disease requiring maintenance haemodialysis was approximately twice that in healthy volunteers.

Hepatic dysfunction
Patients with chronic mild to moderate hepatic impairment the AUC doubled and there was a 2-3 fold increase in half-life of rabeprazole compared to the healthy volunteers.The half-life of rabeprazole in patients with hepatic impairment was 12.3 hours compared to 2.1 hours.

Therapeutic indications
Rabeprazole Gastro-resistant 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
- In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori in patients with peptic ulcer disease.

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

Erosive or Ulcerative Gastro-Oesophageal Reflux Disease (GORD): The recommended oral dose for this condition is 20 mg 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 20 mg or 10 mg once daily can be used depending upon patient response.

Symptomatic treatment of moderate to very severe gastro - oesophageal reflux disease (symptomatic GORD): 10 mg 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 as per need regimen taking 10 mg 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 120 mg/day based on individual patient needs. Single daily doses up to 100 mg/day may be given. 120 mg dose may require divided doses, 60 mg 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 20 mg twice daily + clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily.

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

Paediatric population
Rabeprazole tablets are not recommended for use in children due to a lack of data on safety and efficacy.

Method of administration
For indications requiring once daily treatment Rabeprazole 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.

Warnings and precautions for use
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.

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 Gastro-resistant Tablets should not be chewed or crushed, but should be swallowed whole.

Severe hypomagnesaemia has been reported in patients treated with PPIs 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. 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 PPIs with digoxin or drugs that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

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. 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.

Rabeprazole sodium, as all acid-blocking medicines, may reduce the

absorption of vitamin B12 (cyanocobalamin) due to hypo- or a-chlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy.

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.

Drug Interactions
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.

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
There are no data on the safety of rabeprazole in human pregnancy. Rabeprazole 20mg Gastro-resistant Tablets is contraindicated during pregnancy.

Lactation
It is not known whether rabeprazole sodium is excreted in human breast milk. Therefore Rabeprazole should not be used during breast feeding.

ADVERSE REACTIONS
The most commonly reported adverse drug reactions with rabeprazole were headache, diarrhoea, abdominal pain, asthenia, flatulence, rash and dry mouth. The majority of adverse events experienced were mild or moderate in severity, and transient in nature.

The following adverse events have been reported from clinical trial and post-marketed experience.

Common:
Infection, insomnia, headache, dizziness, cough, pharyngitis, rhinitis, diarrhoea, vomiting, nausea, abdominal pain, constipation, flatulence, non-specific pain, back pain, influenza like illness.

Uncommon:
Nervousness, somnolence, bronchitis, sinusitis, dyspepsia,dry mouth, eructation, rash, erythema, myalgia,leg cramps,arthralgia, urinary tract infection, chest pain, chills, pyrexia, increased hepatic enzymes.

Rare:
Neutropenia, leucopenia, thrombocytopenia, leucocytosis, anorexia, depression, visual disturbance, gastritis, stomatitis, taste disturbance, hepatitis, jaundice, pruritus, sweating, bullous reactions, interstitial nephritis. weight increased

Not known:
Hyponatremia, hypomagnesaemia, confusion, peripheral oedema, gynecomastia.

Overdose
Experience to date with deliberate or accidental overdose is limited. 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 dialysable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

PRESENTATIONS:
Rabosh 10mg Tablets: Pack of 14 tablets in cold form & cold seal (Alu Alu) Blister Packing.
Rabosh 20mg Tablets: Pack of 14 tablets in cold form & cold seal (Alu Alu) Blister Packing.

INSTRUCTIONS:
Protect from heat, sunlight and moisture, store below 25°C.
Keep out of the reach of children.
The expiration date refer to the product correctly stored at the required condition.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
To be sold on prescription of a registered medical practitioner only.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات: دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
Bosch Pharmaceuticals (Pvt) Ltd.
221-223, Sector 23, Korangi Industrial Area,
Karachi - Pakistan.

ISO 9001:2015 Certified Company

Bosch

For Medical Professional only

Rabosh® Tablets

(Rabeprazole)

رابوش ٹیبلیٹس

(رابپرازول)

FIRST & ONLY CERTIFIED HALAAL

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PHARMACEUTICAL COMPANY