AIMRAB (Rabeprazole Sodium)

Enteric Coated Tablets

COMPOSITION

Aimrab 10 mg tablets: Each enteric coated tablet contains Rabeprazole 10 mg
Aimrab 20 mg tablets: Each enteric coated tablet contains Rabeprazole 20 mg.

DESRIPTION

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

PHARMACODYNAMICS

Mechanism of Action

Rabeprazole belongs to a class of anti-secretory compounds (substituted benzimidazole proton-pump inhibitors) that suppress gastric acid secretion by inhibiting 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 rebeprazole has been characterized as a gastric proton-pump inhibitor Rabeprazole blocks the final step of gastric parietal cells, rebeprazole is protonated, accumulates, and is transformed to an active sulfonamide.

Anti-secretory Activity

The abti-secretory effect begins within one hour after oral administration of Aimrab. in patuents with gastroesophageal reflux disease (GERD) and moderate to severe esophageal acid exposure. Aimrab 20 mg and 40 mg per day descreases 24-hour esophageal acid exposure.

PHARMACOKINETICS

Aimrab tablets are coated to allow rabeprazole sodium, which is acid labile, to pass through the stomach relatively intact. After oral administration of 20 mg Aimrab, peak plasma concentrations (C) of rebeprazole occur over a rang of 2-0 to 5.0 hours (T) The rabeprazole C and AUC are linear over an oral dose range of 10mg to 40mg There is no appreciable accumulation when doses of 10mg to 40 mg are administered every 24 hours the pharmacokinetics of rabeprazole are not alterec by multiple dosing The plasma half-life ranges from 1 to 2 hours.

Absorption

Absolute bioavailability for a 20 mg oral tablet of Aimrab (compared to intravenous administration) is approximately 52% Rabeprazole may be taken without regards to meal times.

Distribution

Rabeprazole is 96.3% bound to human plasma proteins.

Metabolism

Rabeprazole is extensively metabolized Thioether and sulphone are the primary metabolites measured in human plasma These metabolites were not observed to have significant anti-secretory activity in vitro studies have demonstrated that rabeprazole is metabolized in the liver primarily by cytochrome P450 3A (CYP3A) to a sulphone metabolite and cytochrome P450 2C19 (CYP2C19) to desmethyl rabeprazo The thicether metabolite is formed nonenzymatically by reduction of rabeprazole.

Elimination

Following a single 20 mg oral dose of rabeprazole, approximately 90% of the drug was eliminated in the urine, primarily as thioether carboxylic acid, its glucoronide, and mercapturicaud metabolites the remainder of the dose was recovered in the feces. No unchanged rabeprazole was recovered in the urine or feces

INDICATIONS AND USAGE

Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD

Aimrab is indicated for short-term (4 to 8 weeks) treatment in the healing and symptomatic relief of erosive or ulcerative gastroesophageal refulx disease (GERD). For those patients who have not healed after 8 weeks of treatment an additional 8-week course of Aimrab may be considered.

Maintenance of Healing of Erosive or ulcerative Gastroesophageal Reflux Disease (GERD)

Aimrab is indicated for maintaining healing and reduction in relapse rates of heartburn symptoms in patients with erosive or ulcerative gastroesophageal reflux disease (GERD Maintenance)

Treatment of Symptomatic Gastroesphageal Reflux Disease (GERD)

Aimrab is indicated for the treatment of daytime and night time heartburn and other symptoms associated with GERD

Healing of Duodenal Ulcers

Aimrab is indicated for short-term (up to four weeks) treatment in the healing and symptomatic relief of duodenal ulcers. Most patients heal with in four weeks.

Helicobacter pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence

Rabeprazole in combination with amoxicillin and cianthromycin as a three drug regimen, is indicated for the treatment of patients with H pylori infection and duodenal ulcer disease (active or history within the past 5 years) to eradicate H pylori Eradication of H pylori has been shown to reduce the risk of duodenal ulcer recurrence. In patients who fail therapy susceptibility testing should be done. If resistance to clarithromycin is demonstrated or susceptibility testing is not possible alternative antimicrobial therapy should be instituted.

Treatment of Pathological Hypersecretory Conditions, including Zollinger-Ellison Syndrome

Aimrab is indicated for the long-term treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome.

DOSAE AND ADMINIS TRATION

Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD)

The recommend adult oral dose is one Aimrab 20 mg tablet to be taken once daily for four to eight weeks. For those patients who have not healed after 8 weeks of treatment, an additional 8-week course of Aimrab may be considered.

Maintenance of Healing of Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD Maintenance)

The recommended adult oral dose is one Aimrab 20 mg tablet to be taken once daily.

Treatment of Symptomatic gastroesophageal Reflux Disease (GERD)

The recommended adult oral dose is one Aimrab 20 mg tablet to be taken once daily for 4 wooks if symptoms do not resolve completely after 4 weeks, an additional course of treatment may be considered

Healing of duodenal Ulcers
The recommended a adult oral dose is one Aimrab 20 mg tablet to be taken once daily after the morning meal for a period up to four weeks. Most patients with duodenal ulcer heal within four weeks A few patients may require additional therapy to achieve healing.
Helicobacter pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence
Three Drug Regimen a
Aimrab 20 mg twice Daily for 7 days
Amoxicillin 1000mg Twice Daily for 7 Days
All three medications should be taken twice daily with the Morning and evening meals
It is important that patients comply with the full 7-day regimen.
Treatment of Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome
The dosage of Aimrab in patients with pathologic hypersecretory conditions varies with the individual patient.The recommended adult oral starting dose is 60 mg once a day Doses should be adjusted to individual patients needs and should continue for as long as clinically indicated Some patients may require divided doses Doses up to 100mg QD and 60 mg BID have been administered Some patients with Zollinger-Ellison syndrome have been treated continuously with rabeprazole for upto one year No dosage adjustment in necessary in elderly patients in patients with renal disease or in patients with mild to moderate hepatic impairment Administration of rabeprazole to patients with mild to moderate liver impairment resulted in increased exposure and decreased elimination Due to the lack of clinical data on rabeprazole in patients with severe hepatic impairment,caution should be exercised in those patients
Aimrab tablets should be swallowed whole The tablets should not be chewed, crushed or split Aimrab can be taken with or without food

CONTRAINDICATIONS
Rabeprazole is contraindicated in patients with knowm hypersensitivity to rebeprazole substituted benzimidazoles or to any component of the formulation

ADVERSE REACTIONS
In general rabeprazole treatment has been well tolerated in both short-term and long term trials in short and long term studies, the following advarse events have been reported in Aimrab treated patients headache diarrhoea, vomiting constipation dry month, muscle or bone pain drowsness, dizziness abdominal pain, pruritus, paresthesia and malsise

Pregnancy
Pregnancy Category B
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 breast 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.

Pediatric use
The safety and effectiveness of rabeprazole in pediatric patients have not been established.

WARNINGS AND PRECAUTIONS
Drug Interections
Rebeprazole is metabolized by the cytochrome P450 (CYP450) drug metabolizing enzyme system. Rabeprazole does not have clinically significant interactions with other drugs metabolized by the CYP450 system such as warfarin, theophylline, diazepam and phenytoin. Rabeprazole produces sustained inhibition of gastric acid secretion. An interactions with compounds which are dependent on gastric pH for absorption with compounds which are dependent on gastric PH for absorption like ketoconazole may occur due to the magnitude of acid suppression observed with rabeprazole. Therefore, patient may need to be monitored when such drugs are taken concomitantly with rabeprazole. Co-administration of mbeprazole and antacids produced no clinically relevant changes in plasma rebeprazole concentrations.

General
Syptomatic response to therapy with rabeprazole does not preclude the presence of gastric malignancy.

Renal Impairment
Aimrab should be used with caution in patients with renal impairment or in those at risk of fluid retention. in patients with severe renal insufficiency (serum creatinine more than 6 mg/100mL. i.e. more than 0.6 mmol/L) the dosing frequency should be altered depending on the severity of impairment, and the dose may need to be reduced. Patients on prolonged therapy should be reviewed regularly.

Hepatic Impairment
No dosage adjustment is necessary in patients with mild to moderate hepatic impairment. Administration of rabeprazole to patients with mild to moderate liver impairment resulted in increased exposure and decreased elimination Due to the lack of clinical data on rabeprazole in patients with severe hepatic impairment, caution should be exercised in those parents.

Lactation
Since many drugs are excreted in milk, caution should be exercised when this drugs is administered to a nursing mother.

Paediatric use
The safety and effectiveness of rabeprazole in paediatric patients under the age of 18 have not been established.

Overdosage
There has been no experience with large overdoses of rabeprazole. 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

STORAGE
Store at room temperature.
Protect from light.

Manufactured By:
Aims Pharmaceuticals
Plot # 291, Industrial Triangle, Kahuta Road,
Islamabad-Pakistan